Received: 2 June 2021 | Revised: 6 January 2022 | Accepted: 22 April 2022

DOI: 10.1111/jocn.16352

Journal of Clinical Nursing WILEY

SPECIAL ISSUE ARTICLE

Longitudinal study of changes observed in quality of life, psychological state cognition and pulmonary and functional capacity after COVID-19 infection: A six- to seven-month prospective cohort

Tamara del Corral PhD[1] | Noemí Menor-Rodríguez PT[2] | Sara Fernández-Vega PT[2] | Celia Díaz-Ramos PT[2] | Sandra Aguilar-Zafra Msc[3,4] | Ibai López-de-Uralde-Villanueva PhD[1]

[1]Department of Radiology, Rehabilitation and Physiotherapy, Faculty of Nursing, Physiotherapy and Podiatry, Universidad Complutense de Madrid (UCM), IdISSC, Madrid, Spain

[2]Departamento de Fisioterapia, Facultad de Ciencias de la Salud, Centro Superior de Estudios Universitarios La Salle, Universidad Autónoma de Madrid, Madrid, Spain

[3]Departamento de Fisioterapia, Facultad de Ciencias de la Salud, Motion in Brains Research Group, Centro Superior de Estudios Universitarios La Salle, Universidad Autónoma de Madrid, Madrid, Spain

[4]Téxum S.L Physiotherapy Center, Coslada, Madrid, Spain

Correspondence
Tamara del Corral, Department of Radiology, Rehabilitation and Physiotherapy, Faculty of Nursing, Physiotherapy and Podiatry, Complutense University of Madrid, Plaza Ramón y Cajal no. 3, Ciudad Universitaria, 28040 Madrid, Spain.
Email: tamdelco@ucm.es

Funding information
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Abstract

Aims: To investigate the health-related quality of life (HRQoL), symptoms, psychological and cognitive state and pulmonary and physical function of nonhospitalised COVID-19 patients at long-term, and to identify factors to predict a poor HRQoL in this follow-up.

Background: Studies have focused on persistent symptoms of hospitalised COVID-19 patients in the medium term. Thus, long-term studies of nonhospitalised patients are urgently required.

Design: A longitudinal cohort study.

Methods: In 102 nonhospitalised COVID-19 patients, we collected symptoms at 3 months (baseline) and at 6–7 months (follow-up) from diagnosis (dyspnoea, fatigue/muscle weakness and chest/joint pain), HRQoL, psychological state, cognitive function, pulmonary and physical function. This study adhered to the STROBE statement.

Results: HRQoL was impaired in almost 60% of the sample and remained impaired 6–7 months. At 3 months, more than 60% had impaired physical function (fatigue/muscle weakness and reduced leg and inspiratory muscle strength). About 40%–56% of the sample showed an altered psychological state (post-traumatic stress disorder (PTSD), anxiety/depression), cognitive function impairment and dyspnoea. At 6–7-months, only a slight improvement in dyspnoea and physical and cognitive function was observed, with a very high proportion of the sample (29%–55%) remained impaired. Impaired HRQoL at 6–7 months was predicted with 82.4% accuracy (86.7% sensitivity and 83.3% specificity) by the presence at 3 months of muscle fatigue/muscle weakness (OR = 5.7 (1.8–18.1)), PTSD (OR = 6.0 (1.7–20.7)) and impaired HRQoL (OR = 11.7 (3.7–36.8)).

Conclusion: A high proportion of nonhospitalised patients with COVID-19 experience an impaired HRQoL, cognitive and psychological function at long-term. HRQoL, PTSD and dyspnoea at 3 months can identify the majority of patients with COVID-19 who will have impaired quality of life at long-term.

 © 2022 John Wiley & Sons Ltd.

Relevance to clinical practice: Treatments aimed at improving psychological state and reducing the fatigue/muscle weakness of post-COVID-19 patients could be necessary to prevent the patients' HRQoL from being impaired at 6–7 months after their reported recovery.

KEYWORDS
COVID-19, health-related quality of life, long-term, physical function, psychological status, pulmonary function

1 | INTRODUCTION

In December 2019, a novel member of the betacoronavirus genus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia infection spread in the Hubei province of China, causing coronavirus disease 2019 (COVID-19) (Esakandari et al., 2020). COVID-19 has caused a worldwide pandemic and has had a huge impact on human health, daily life and the worldwide economy.

Acute coronavirus infection is very similar to seasonal influenza, with the most common symptoms being fever, headache, shortness of breath, cough, myalgia and fatigue (Disser et al., 2020; Esakandari et al., 2020; Mao et al., 2020; Pascarella et al., 2020). The clinical presentation begins within 14 days of exposure, presenting symptoms after approximately 5 days (Lauer et al., 2020). The course of the infection is mild or asymptomatic in approximately 80%–90% of cases (Pascarella et al., 2020), although some patients develop severe symptoms such as difficulty breathing, chest pain and/or pressure and loss of speech and/or movement, which can be associated with pneumonia, sepsis, lung failure and cardiac injury, requiring urgent medical attention (Esakandari et al., 2020).

The epidemiological and clinical characteristics, pathogenesis and complications of patients with COVID-19 in the acute phase have been explicitly described; however, the long-term consequences of the illness remain largely unclear. To the best of our knowledge, only a few studies with 3-month follow-ups after discharge have been published (Bellan et al., 2021; González et al., 2021; Meys et al., 2020; Qu et al., 2021; Raman et al., 2021; Rass et al., 2021; Wong et al., 2020). These studies have reported certain persistent symptoms, such as extreme fatigue, breathlessness, coughing, limited exercise capacity, depression, cognitive deficits, neurological symptoms, sense of smell disorders and impaired lung function, as well as poor health-related quality of life (Anastasio et al., 2021; Bellan et al., 2021; González et al., 2021; Meys et al., 2020; Miskowiak et al., 2021; Qu et al., 2021; Raman et al., 2021; Rass et al., 2021). Given these symptoms, the medium-term changes in health-related quality of life, functional status and the cognitive and psychological consequences of COVID-19 infection are considerable. Only two studies have reported the health consequences 6 months after a COVID-19 infection: one in a Chinese cohort (C. Huang et al., 2021) that observed fatigue, muscle weakness, anxiety and depression; the other in a Norwegian population that reported a decline in health-related quality of life and function (Walle-Hansen et al., 2021). However, no study till date has followed the same patient cohort over time to monitor the progression of these symptoms.

What does this paper contribute to the wider global clinical community?

- A considerable number of nonhospitalised patients with COVID-19 experience an impaired health-related quality of life and symptoms such as dyspnoea, fatigue/muscle weakness, PTSD, anxiety, depression, cognitive deficits and reduced physical function at long-term.
- Our findings highlight the long-term impact of COVID-19 on patients, even after their reported recovery from the acute manifestations of this disease.
- It is important that health practitioners focus on improving the psychological state and reducing the fatigue of post-COVID-19 patients to improve the patients' health-related quality of life.

Since the beginning of the COVID-19 pandemic, most studies have focused on the health-related quality of life and persistent symptoms of hospitalised or post-discharge patients with COVID-19 in the medium term. Few have reported on the clinical characteristics of those patients post-COVID-19 who were able to manage their symptoms at home without needing hospitalisation due to their relatively mild symptoms; these patients account for 80%–90% of cases (Pascarella et al., 2020). For the diagnosis of post-COVID syndrome, a post-infection period of at least 6 months is required (Lamprecht, 2020). Thus, long-term follow-up studies on the persistent symptoms of nonhospitalised patients with COVID-19 are urgently required because they can provide more comprehensive information for observing changes in patient health and determining the long-term impact of COVID-19.

This longitudinal study was conducted to investigate the health-related quality of life, symptoms, psychological and cognitive state and pulmonary and physical function of a cohort of nonhospitalised patients with COVID-19. The study sought to identify factors

to predict a poor health-related quality of life over 6–7 months of follow-up.

2 | METHODS

2.1 | Study design

This cohort study was approved by the local ethics committee (registration number: CSEULS-PI-037/2020), was conducted in accordance with the Declaration of Helsinki, and reported its findings following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (Guidelines for reporting observational studies; Data S1) (von Elm et al., 2008). We obtained written informed consent from all the participants.

2.2 | Study population

The COVID-19 diagnosis was based on a typical clinical presentation coupled with a positive reverse-transcription–polymerase chain reaction (RT-PCR) SARS-CoV-2 test from a nasopharyngeal or oropharyngeal swab or serological tests positive for SARS-CoV-2 antibodies. The general inclusion criteria were as follows: (1) confirmed SARS-CoV-2 infection; (2) non-hospital management; (3) age ≥18 years and (4) no more than 3 months since the infection. Patients were excluded if they met any of the following criteria: (1) clinically evident cognitive impairment or active mental disorders; (2) difficulty understanding the language, or visual, abstraction or orientation impairment precluding the ability to complete the questionnaires; (3) presence of any concomitant condition that might affect the respiratory and/or functional state and (4) living outside the Community of Madrid.

2.3 | Study procedures

The patients were recruited via bulletin advertisements distributed by e-mail and flyers, using convenience sampling. Specifically, members of the research group combined several lines of contact, primarily based on the social network account at regular intervals, inviting personal friends who met the characteristics to participate in the study and in turn forwarding the invitation to their own friends via email, cell phone messages or their social network profile, as well as via the internet platforms of COVID-19 patient support groups. Between July 2020 and February 2021, all the participants underwent an evaluation of symptoms by trained clinical evaluators at 3 months after the confirmed diagnosis and at 6–7 months of follow-up in their homes. We collected data by interviewing the patients as to their demographic characteristics, current symptoms at 3 months and at 6–7 months of follow-up from the COVID-19 diagnosis, including dyspnoea, fatigue/muscle weakness and chest and joint pain, and we assessed the patients by performing a physical examination and employing questionnaires.

2.3.1 | Health-related quality of life

To assess the participant' quality of life, we employed the EuroQol-5D-3L life assessment tool, which consists of five dimensions (1, mobility; 2, self-care; 3, usual activities; 4, pain/discomfort and 5, anxiety/depression) with three response options based on severity level (1, no problems; 2, some problems and 3, extreme problems/disability) (Badia et al., 1999). Based on these five-dimension codes, a health state profile is provided (e.g. 11,123 would have no problems in mobility, self-care and usual activities, moderate pain/discomfort and extreme anxiety or depression). Each health state profile can potentially be assigned a summary index score based on societal preference weights for the health state. Index scores ranging from less than 0 (where 0 is a health state equivalent to death and negative values are valued as worse than death) to 1 (perfect health) (EuroQol Research Foundation, 2018). We used the reference values to calculate the proportion of patients with an EQ-5D index below the 25th percentile of the mean age-based and sex-based reference values (König et al., 2009). In addition, the participants had to rate their current overall health on a visual analog scale (EQ-VAS) ranging from 0 (worst imaginable health) to 100 (best imaginable health). In addition, we dichotomised the EQ-VAS on the basis of a receiver operating characteristics (ROC) curve analysis using the categorical variable of the EQ-5D index ("impaired" <25th percentile) as the status variable. Based on the results of the ROC curve analysis, scores ≤70 were considered as 'impaired'".

2.3.2 | Psychological status

Post-traumatic stress disorder (PTSD)

We used the 17-item self-rating PTSD Checklist-Civilian Version (PCL-C) questionnaire to assess this outcome (Miles et al., 2008). The participants rated the degree to which they were bothered by each symptom on a 5-point Likert scale ranging from 1 (not at all) to 5 (extremely). The cut-off score of 34 suggests a clinically relevant PTSD (Yeager et al., 2007).

Anxiety and depression levels

We used the Hospital Anxiety and Depression Scale (HADS) (Herrero et al., 2003), which consists of 14 items divided into two subscales for anxiety and depression. The subscales include seven items each, and the scores range from 0 to 42. Each item is scored on a 4-point Likert scale ranging from 0 to 3. The total scale score is obtained by summing the scores obtained for each item. The higher the total scores increase, the greater the risk of anxiety and depression. We used the HADS optimal cut-off score of ≥13 (Singer et al., 2009).

2.3.3 | Cognitive function

We used the Montreal Cognitive Assessment (MoCA) (www.mocatest.org) as a screening test to estimate the severity of global cognitive impairment (Delgado et al., 2019). The instrument consists of 14

subtests that assess the following cognitive domains: attention and concentration, executive functions, memory, language, visuoconstructional and visuospatial skills, conceptual thinking, calculation and orientation to time and space. The maximum score achievable is 30 points, and a correction was implemented based on years of education. We classified patients scoring below 26 points as having impairment.

2.3.4 | Pulmonary function

The forced spirometry measurements included forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), and their ratio (FEV1/FVC), assessed using a portable spirometer (Spirobank II USB, MIR) according to the American Thoracic Society/European Respiratory Society guidelines for standardising spirometry (Miller et al., 2005). The measurements are expressed as percentages of the predicted values.

2.3.5 | Physical function/strength

We evaluated inspiratory muscle strength by measuring maximum inspiratory pressure (MIP) using a Powerbreath Kinetic KH1 device (POWERbreathe International Ltd) according to American Thoracic Society/European Respiratory Society guidelines (Gibson et al., 2002). The estimated inspiratory muscle strength values were established following the reference equation for MIP for the adult population (Morales et al., 1997).

To test the participants' isometric hand and forearm strength, we employed a hand dynamometer (JAMAR®, Patterson Medical) (Peolsson et al., 2001). We used the predicted hand strength values in the adult population to predict impairment (Mateo Lázaro et al., 2008).

We used the 1-min sit-to-stand (1 min STS) test to assess lower muscle strength (Núñez-Cortés et al., 2021). We used the reference values to identify the participants with decreased lower body muscle strength (Strassmann et al., 2013).

2.4 | Data analysis

The data analysis was performed with SPSS version 21.0 (SPSS Inc.). In all statistical tests, a two-sided type I error below 0.05 was considered significant. The data are presented as mean ± SD, median ± inter quartile range for the continuous variables and as *n* (%) for the categorical variables. The continuous variables were converted into categorical variables according to the criteria proposed for the various study variables (<25th percentile, <80% of predicted or less than the cut-off from the questionnaires/scales) (Szende et al., 2014). The scores of all continuous variables were dichotomised to minimise the influence of factors such as age and sex on the results. This facilitates the comparison between individuals, as well as the extrapolation of the data, since dichotomisation allows us to know the degree to which the sample is affected with respect to what is expected. Differences between the assessment at 3 months and at 6–7 months after the COVID-19 diagnosis were examined using McNemar's test for the categorical variables and Student's *t* test for paired samples for the continuous variables. In the latter case, we calculated the effect sizes for the paired samples *t* test using Cohen's *d* as follows: small (0.20–0.49), medium (0.50–0.79), or large (≥0.8) (Cohen, 1988). Differences between participants with impaired health-related quality of life and those with preserved health-related quality of life were also shown by radar plots.

First, we performed a bivariate logistic regression analysis to determine the individual association of the various dichotomised potential predictor variables (examined at 3 months), with impaired quality of life at 6–7 months after the COVID-19 diagnosis. Next, variables that obtained a significance level of $p < .05$ in the bivariate logistic regression analysis were retained as potential predictors for a backward stepwise multivariate logistic regression. The removal of variables from the multivariate logistic regression model was determined at the .05 significance level. We examined the model's discriminant validity by means of an ROC analysis, determining (according to Youden's index) the optimal cut-off for the probability set by the model to identify the patients with impaired quality of life at 6–7 months after the COVID-19 diagnosis, with its corresponding sensitivity and specificity. We evaluated the diagnostic precision according to the area under the ROC curve (AUC), with values >0.7 being considered acceptable (Swets, 1988) and when at least 70% sensitivity and 50% specificity were obtained (Turner et al., 2009).

The sample size calculation was performed with the intention of examining which variables assessed at 3 months after COVID-19 diagnosis were associated with impaired quality of life at 6–7 months. In the absence of previous evidence, because it is a new pathology, the sample size was determined based on the results of a pilot study with a sample of 33 participants. The bivariate logistic regression analysis performed with the data obtained in the pilot study found that seven variables presented a statistically significant association with the presence of deterioration in quality of life at 6–7 months after COVID-19 diagnosis. Therefore, according to the rule of 10 cases per explanatory variable, it was considered necessary to include at least 70 participants to obtain a reasonably stable estimate of the regression coefficients of the multivariate logistic regression model (Peduzzi et al., 1996). However, following the recommendations proposed by Long (1997), a sample size of at least 100 participants was finally established.

3 | RESULTS

The final sample consisted of 102 participants (38 men and 64 women), with a mean age of 46.6 ± 14.1 years (height, 169 ± 10 cm; weight, 75.4 ± 15.9 kg; and body mass index, 26.4 ± 4.8 kg/m^2), who had a confirmed diagnosis of COVID-19 (Figure 1). None of

the participants required hospital admission, although 11 underwent a rehabilitation programme before entering the study. This rehabilitation programme consisted of bronchial hygiene manoeuvers, cough stimulation techniques, breathing exercises (e.g. diaphragmatic breathing and pursed-lip breathing) and/or light intensity physical exercises (e.g. walking and cycling). Almost half of the sample had never smoked (46.1%), while 23 participants were smokers at the time of the study and 32 were ex-smokers. During the 3–4 months of follow-up, weight increased statistically significantly [mean difference (95% CI), *p* value, Cohen's *d*; 0.8 (0.3–1.3), $p = .002$; $d = 0.05$] and, consequently, Body Mass Index also increased statistically significantly [0.3 (0.1–0.5), $p = .002$; $d = 0.07$]. However, these increases were minimal and probably not clinically important. Regarding their physical activity, the participants' physical activity level presented at baseline (2074 ± 1995 Mets, metabolic equivalent of the task) showed no difference with that obtained at 3–4 months of follow-up [217 (−257 to 691), $p = .367$; $d = 0.10$].

3.1 | Health-related quality of life

The health-related quality of life was impaired (<25th percentile) in almost 60% of the sample and remained impaired at 6–7 months after their COVID-19 diagnosis (Table 1). In fact, the participants who presented with impaired health-related quality of life remained practically the same in the various dimensions assessed in the EQ-5D-3L, except for mobility and pain/discomfort (Figure 2).

In terms of the differences between the participants with impaired health-related quality of life and those with preserved health-related quality of life, the dimensions that primarily determined the deterioration in health-related quality of life were pain/discomfort, anxiety/depression and the inability to perform usual activities, as shown in the radar plot in Figure 2. The differences remained virtually unchanged at 6–7 months in all dimensions, except for anxiety/depression, which increased.

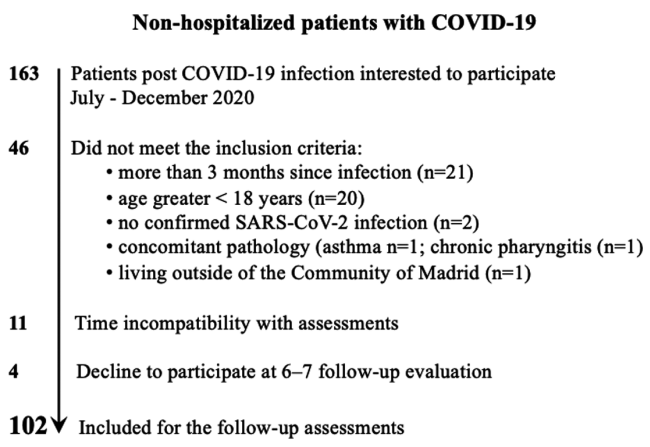


FIGURE 1 Flow-chart for recruitment of patients in post COVID-19 long-term follow-up assessments

3.2 | Symptoms, psychological state and cognitive, pulmonary and physical function

Table 1 indicates the percentage of participants with symptoms and/or impaired psychological and cognitive states and reduced pulmonary and physical function at 3 months and at 6–7 months after the COVID-19 diagnosis, as well as the changes during this time. Dyspnoea and fatigue/muscle weakness were the most prevalent symptoms at 6–7 months; however, significantly fewer participants were reporting these symptoms at 6–7 months after their COVID-19 diagnosis. Approximately 30% of the sample experienced dyspnoea and fatigue/muscle weakness at 6–7 months, with no improvement in the other symptoms.

Almost half of the participants experienced impairment of their psychological state and cognitive function (PTSD < 34; HADS < 13; MoCA < 26), with slight improvement at 6–7 months (approximately 40% were still impaired in some of these variables). In fact, the mean scores on the various instruments employed to examine these variables were above or very close to the cut-off point for being considered as experiencing cognitive deficits, anxiety/depression and/or PTSD.

Pulmonary function was preserved (>80% of predicted for FEV_1 and FVC; >70% for the ratio FEV_1/FVC) in virtually the entire sample, with the lowest parameter being the FEV_1/FVC ratio, with <15% of the sample reflecting values below 70% at 6–7 months after the COVID-19 diagnosis. In terms of physical function, approximately 60% of the participants showed loss of leg and inspiratory muscle strength at 3 months, which improved statistically significant at 6–7 months. However, these improvements were slight, with 50% of participants still showing values below the 25th percentile of the baseline values for age and sex.

3.3 | Prediction of impaired health-related quality of life at six to seven months

The results of the bivariate logistic regression analysis showed that the presence at 3 months after the COVID-19 diagnosis of chest pain, dyspnoea, anxiety/depression, PTSD, fatigue/muscle weakness and/or impaired health-related quality of life (index score <25th percentile or EQ-VAS ≤ 70) were statistically significant predictors of health-related quality of life impairment at 6–7 months after the COVID-19 diagnosis. The remaining variables examined were not predictive, given that their relationship with the dependent variable was not statistically significant. Figure 3 shows the results of the bivariate logistic regression analysis.

According to the backward stepwise multivariate logistic regression, the presence at 3 months of 'impaired health-related quality of life' (EQ-5D index score <25th percentile), 'PTSD' (PCL-C ≥ 35), and 'fatigue/muscle weakness' showed a statistically significant and positive association with health-related quality of life impairment at 6–7 months after the COVID-19 diagnosis (Table 2). This model correctly predicted 82.4% of those with persistent health-related

TABLE 1 Symptoms and/or deterioration of psychological state and cognitive, pulmonary and physical function at 3 and 6–7 months after COVID-19 diagnosis, as well as the changes occurred during this time

	Post COVID-19 infection		Changes occurred
	3 months	6–7 months	McNemar's test *p*-value; [OR (95% CI)] AND/OR Mean difference (95%CI); *p*-value; Cohen's *d*
Health-related quality of life (EQ-5D-3L)			
Index score			
Impaired (<25th percentile)	60 (58.8%)	60 (58.8%)	$p = 1.00$; [1 (0.4–2.4)]
Total score			
Mean (SD)	0.82 ± 0.22	0.83 ± 0.20	−0.01 (−0.05 to 0.03); $p = .575$; $d < 0.01$
Median (1QR)	0.89 (0.72–1.00)	0.89 (0.75–1.00)	
EQ-Visual analog scale (0–100)			
Mean (SD)	70.4 ± 18.4	74.4 ± 17.9	−4 (−6.5 to −1.5); $p = .002$; $d = 0.22$
Median (1QR)	70 (55–85)	80 (64.5–90)	
Symptoms			
Dyspnoea	42 (41.2%)	30 (29.4%)	$p = .002$; [13 (1.7–99.4)]
Fatigue/muscle weakness	64 (62.8%)	36 (35.3%)	$p < .001$; [10.3 (3.2–33.8)]
Chest pain	21 (20.6%)	17 (16.7%)	$p = .344$; [2.3 (0.6–9)]
Joint pain	13 (13.8%)	11 (10.8%)	$p = .754$; [1.5 (0.4–5.3)]
Psychological status			
Post-traumatic stress disorder (PCL-C)			
Impaired (score ≥35)	41 (40.2%)	35 (34.3%)	$p = .263$; [1.9 (0.7–4.6)]
Total score			
Mean (SD)	34.2 ± 14.8	32.3 ± 14.2	1.9 (0.3–3.5); $p = .025$; $d = 0.13$
Median (1QR)	29 (23–42)	28 (21.7–39)	
Anxiety and depression (HADS)			
Moderate/Severe (score ≥13)	47 (46.1%)	46 (45.1%)	$p = 1.00$; [1.1 (0.5–2.3)]
Total score			
Mean (SD)	13.2 ± 5.8	13.3 ± 6	−0.1 (−1.0 to 0.8); $p = .822$; $d = 0.02$
Median (1QR)	12 (9–16)	11.5 (9–16.2)	
Cognitive function (MoCA)			
Impaired (score <26)	57 (55.9%)	42 (41.2%)	$p = .004$; [4 (1.5–10.7)]
Total score			
Mean (SD)	24.7 ± 3	25.8 ± 2.7	−1.1 (−1.5 to −0.7); $p < .001$; $d = 0.38$
Median (1QR)	25 (23–27)	26 (24–28)	
Pulmonary function			
FVC (% of predicted)			
Impaired (<80%)	4 (3.9%)	2 (2%)	$p = .625$; [3 (0.3–28.8)]
Total score			
Mean (SD)	114 ± 18.2	116.2 ± 18	−2.2 (−4 to −0.3); $p = .021$; $d = 0.12$
Median (1QR)	113 (103–123)	115.5 (104–125)	
FEV_1 (% of predicted)			
Impaired (<80%)	9 (8.8%)	6 (5.9%)	$p = .687$; [2 (0.4–10.9)]
Total score			
Mean (SD)	101.2 ± 20.4	105 ± 19.2	−3.8 (−6.6 to −1.1); $p = .007$; $d = 0.19$
Median (1QR)	101 (93–115)	105 (96–117.2)	

TABLE 1 (Continued)

	Post COVID-19 infection		Changes occurred
	3 months	6–7 months	McNemar's test *p*-value; [OR (95% CI)] AND/OR Mean difference (95%CI); *p*-value; Cohen's *d*
FEV_1/FVC (%)			
Impaired (<70%)	20 (19.6%)	15 (14.7%)	$p = .227$; [2.7 (0.7–10)]
Total score			
Mean (SD)	74 ± 9.7	75.5 ± 9.1	−1.5 (−3 to 0.1); $p = .067$; $d = 0.15$
Median (1QR)	76.7 (71.4–79.9)	77.4 (72.8–80.1)	
Physical function/strength			
Inspiratory strength (MIP, % of predicted)			
Impaired (<80%)	68 (66.7%)	56 (54.9%)	$p = .017$; [3.4 (1.3–9.2)]
Total score			
Mean (SD)	74.7 ± 22.6	77.2 ± 22.5	−2.5 (−5.2 to 0.2); $p = .070$; $d = 0.11$
Median (1QR)	72 (59.5–87.5)	77.6 (61.9–88.2)	
Right handgrip strength (kg)			
Decreased (<25th percentile)	7 (6.9%)	2 (2%)	$p = .063$; [1 (0.7–49.8)]
Total score			
Mean (SD)	32.4 ± 11.8	33.7 ± 11.9	−1.3 (−2.1 to −0.4); $p = .004$; $d = 0.11$
Median (1QR)	28 (24–40.3)	30.5 (25–42)	
Left handgrip strength (kg)			
Decreased (<25th percentile)	7 (6.9%)	3 (2.9%)	$p = .219$; [5 (0.6–42.8)]
Total score			
Mean (SD)	30.8 ± 11.6	31.6 ± 11.8	0.8 (−1.7 to −0.1); $p = .034$; $d = 0.04$
Median (1QR)	28 (21–39)	28 (23–39)	
Lower limb strength (1 min STS)			
Decreased (<25th percentile)	61 (59.8%)	46 (45.1%)	$p = .001$; [6 (1.8–20.4)]
Total score			
Mean (SD)	31.7 ± 9.7	34.7 ± 11.9	−3 (−4.5 to −1.6)**; $p < .001$; $d = 0.28$
Median (1QR)	31 (25–39.5)	36 (26.5–42.5)	

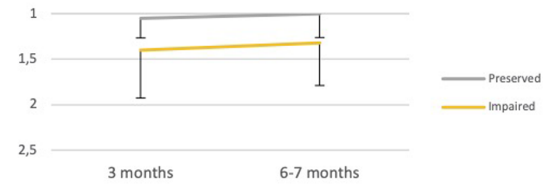
Abbreviations: 1QR, interquartile range; CI, confidence interval; EQ, EuroQol; FEV_1, forced expiratory volume at the first second; FVC, forced vital capacity; HADS, hospital anxiety and depression scale; MIP, maximal inspiratory pressure; MoCA, montreal cognitive assessment; OR, odds ratio; PCL-C, post-traumatic stress disorder checklist – Civilian version; SD, standard deviation.

quality of life impairment. Furthermore, the ROC analysis supported the model's acceptable diagnostic precision (AUC, 0.90 [0.84–0.96]; $p < .001$; Figure 4), presenting a sensitivity of 86.7% and a specificity of 83.3% (Youden index, 0.70) for identifying individuals whose health-related quality of life will be impaired at 6–7 months post-COVID-19 when the probability proposed by the model (*p* [impaired QoL at 6–7 months]) is ≥.57 (Table 2).

4 | DISCUSSION

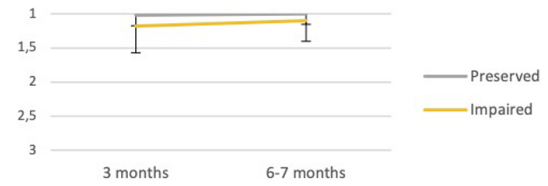
To the best of our knowledge, this is the first study to investigate the influence of COVID-19 on the long-term outcomes of nonhospitalised COVID-19 survivors and to follow them over time to track the progression of their symptoms. The most striking finding is the high proportion (60%) of nonhospitalised patients with COVID-19 with health-related quality-of-life impairment 6–7 months after the first symptoms. We also observed a high level of self-reported symptoms, such as dyspnoea, fatigue/muscle weakness, PTSD, anxiety, depression, cognitive deficits and a decrease in physical function among survivors. The bivariate regression analysis indicated that chest pain, dyspnoea, anxiety/depression, PTSD and/or fatigue/muscle weakness were risk factors for developing impaired health-related quality of life. This study therefore confirms the long-term repercussions of COVID-19 on nonhospitalised patients, suggesting that many of these deficits are likely ongoing consequences of COVID-19, given that they did not return to normal over time. Increased knowledge regarding the significant predictors of health-related quality-of-life impairment in the long term due to COVID-19 is imperative to develop preventive measures for patients at risk.

MOBILITY



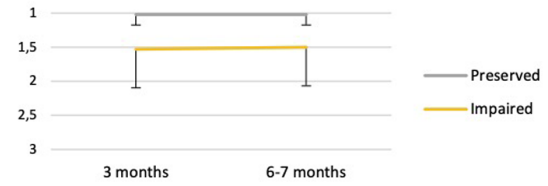
3 months		
No problems	Some problems	Unable to
77 (75.5%)	24 (23.5%)	1 (1%)
6–7 months		
No problems	Some problems	Unable to
80 (78.4%)	22 (21.6%)	—

SELF-CARE



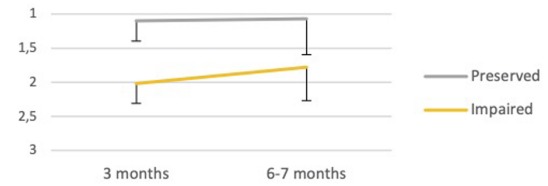
3 months		
No problems	Some problems	Unable to
90 (88.2%)	12 (11.8%)	—
6–7 months		
No problems	Some problems	Unable to
95 (93.1%)	7 (6.9%)	—

USUAL ACTIVITIES



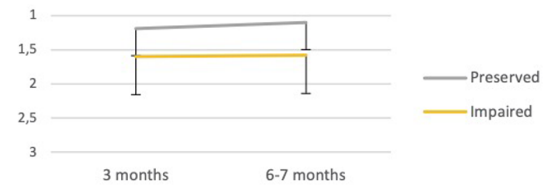
3 months		
No problems	Some problems	Unable to
71 (69.6%)	29 (28.4%)	2 (2%)
6–7 months		
No problems	Some problems	Unable to
73 (71.6%)	27 (26.4%)	2 (2%)

PAIN / DISCOMFORT



3 months		
No problems	Some problems	Unable to
40 (39.2%)	59 (57.9%)	3 (2.9%)
6–7 months		
No problems	Some problems	Unable to
44 (43.2%)	55 (53.9%)	3 (2.9%)

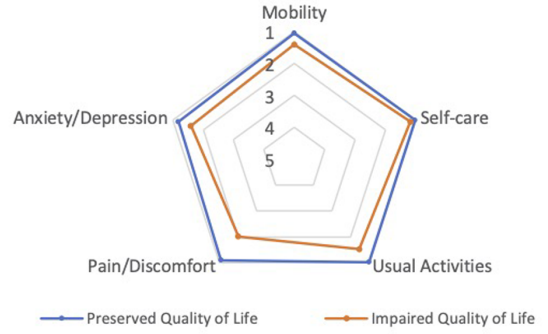
ANXIETY / DEPRESSION



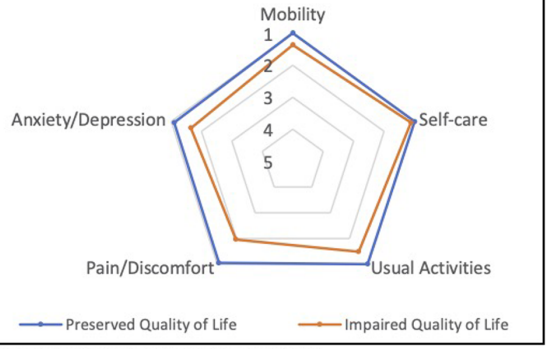
3 months		
No problems	Some problems	Unable to
60 (58.8%)	40 (39.2%)	2 (2%)
6–7 months		
No problems	Some problems	Unable to
61 (59.8%)	39 (38.2%)	2 (2%)

EQ-5D-3L DESCRIPTIVE SYSTEM

3 months



6–7 months



In all plots, scores of 1 indicate perfect/optimal health status, while a score of 3 indicates severe health status.

FIGURE 2 Change in EQ-5D-3L dimensions in participants with and without impaired health-related quality of life

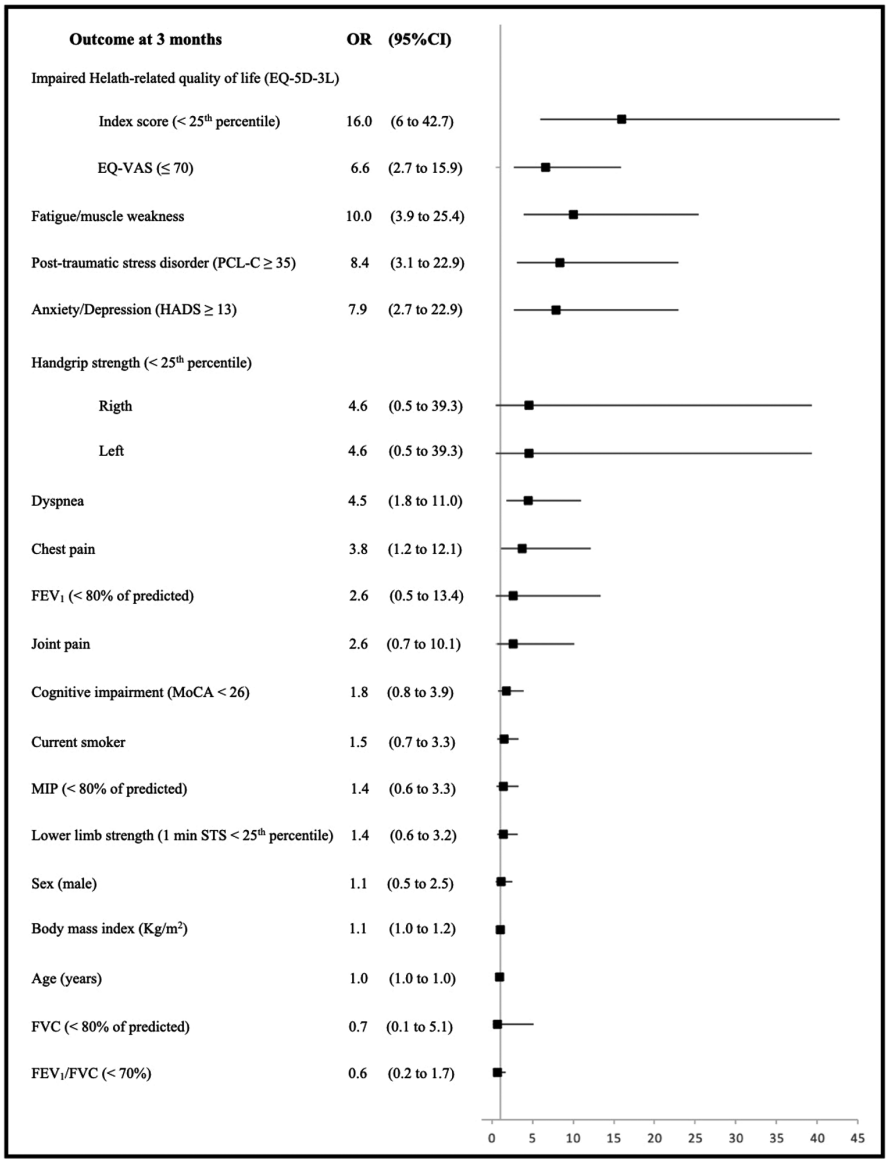


FIGURE 3 Results of bivariate logistic regression analysis showing factors associated with presence of impaired health-related quality of life at 6–7 months after COVID-19 diagnosis. CI, confidence interval; EQ, EuroQol; FEV_1, forced expiratory volume at the first second; FVC, forced vital capacity; HADS, hospital anxiety and depression scale; MIP, maximal inspiratory pressure; MoCA, montreal cognitive assessment; OR, odds ratio; PCL-C, post-traumatic stress disorder checklist – Civilian version; VAS, visual analog scale

4.1 | Health-related quality of life

In our cohort, 60% of the patients who had not been admitted to the hospital demonstrated an EQ-5D index below the 25th percentile of normative values, indicating that their health-related quality of life did not return to normal, even long after the infection had ended. The patients with impaired health-related quality of life reported problems in all EuroQol dimensions that remained virtually unchanged 6–7 months after the COVID-19 infection, except for mobility and pain/discomfort. The dimensions that were primarily associated with the deterioration in health-related quality of life were pain/discomfort, anxiety/depression and the inability to perform usual activities. Comparing our data with a representative sample of the general population, the frequency with which the coronavirus survivors reported certain quality-of-life problems was substantially higher than the Spanish norm (König et al., 2009). For the mean EQ-VAS scores, a statistically significant increase was observed at 6–7 months compared with those obtained at 3 months; however, this increase does not appear to be clinically relevant, given that it was only four points on a scale ranging from 0 to 100. Therefore, the statistically significant difference found in our study could be explained by the large sample size, given that in samples considered large ($n > 40$) any small change is more likely to be statistically significant (Thiese et al., 2016). These findings were consistent with previous studies of medium-term outcomes of patients with COVID-19 after hospital discharge (Meys et al., 2020; Qu et al., 2021; Rass et al., 2021; van der Sar - van der Brugge et al., 2021; Willi et al., 2021; Wong et al., 2020) and at 6 months of follow-up (Walle-Hansen et al., 2021). The quality of life of nonhospitalised Belgian patients after 3 months was affected in 40% of the cases, with a mean EQ-5D index and EQ-VAS score of 0.62 and 51, respectively, results lower than those of our cohort, perhaps due to the fifth percentile of normative values used as the cut-off (Meys et al., 2020). Even in the long term, the quality of life of patients with COVID-19 is as affected as that of

TABLE 2 Results of backwards stepwise multivariate logistic regression analysis showing factors associated with presence of impaired health-related quality of life at 6–7 months after COVID-19 diagnosis

Outcomes at 3 months	B	SE	Wald test	*p*-value	OR (95% CI)
Predictor variables					
Impaired QoL (EQ-5D-3L < 25th percentile)	2.46	0.58	17.61	<.001	11.7 (3.7–36.8)
Post-traumatic stress disorder (PCL-C ≥ 35)	1.79	0.63	8.02	.005	6.0 (1.7–20.7)
Fatigue/muscle weakness	1.73	0.59	8.57	.003	5.7 (1.8–18.1)
Excluded variables (at each step)					
Dyspnoea	−0.06	0.75	0.01	.939	0.9 (0.2–4.1)
Chest pain	0.23	0.96	0.06	.809	1.3 (0.2–8.3)
Impaired QoL (EQ-VAS ≤ 70)	−0.80	0.78	1.04	.307	0.5 (0.1–2.1)
Anxiety/depression (HADS ≥ 13)	1.28	0.71	3.22	.073	3.6 (0.9–14.6)
Probability of the presence of impaired quality of life at 6–7 months					
Formula proposed by the model for calculating the probability of the presence of impaired quality of life:					

$$\text{Probability (impaired QoL at 6 – 7 months)} = \frac{1}{1+e^{-(2.46\times[\text{Impaired QoL}]+1.79\times[\text{Posttraumatic stress disorder}]+1.73\times[\text{Fatigue/muscle weakness}]-2.68)}}$$

Note: The initial model included the following variables assessed at 3 months after COVID-19 diagnosis: (1) chest pain, dyspnoea; (2) anxiety/depression; (3) post-traumatic stress disorder; (4) fatigue/muscle weakness; and (5) impaired health-related quality of life (5.1: index score <25th percentile; and 5.2: EQ-VAS ≤ 70).

Abbreviations: CI, confidence interval; EQ, EuroQol; HADS, hospital anxiety and depression scale; OR, odds ratio; PCL-C, post-traumatic stress disorder checklist – Civilian version; QoL, quality of life; SE, standard error; VAS, visual analog scale.

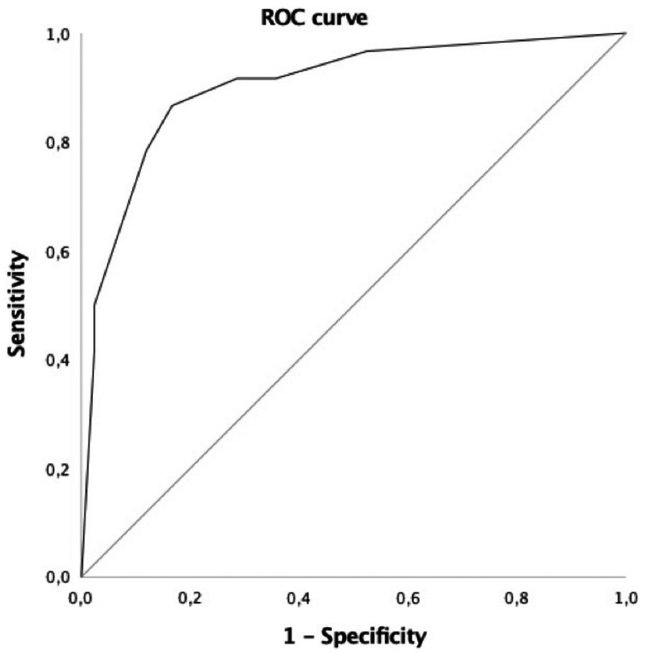


FIGURE 4 ROC analysis to determine the diagnostic accuracy of the model for identifying patients with quality of life impairment at 6–7 months after COVID-19 diagnosis

patients with chronic respiratory diseases such as asthma (mean EQ-5D index, 0.77–0.88) (Hernandez et al., 2019; Szentes et al., 2020), which permanently detracts from their quality of life, due possibly to the incomplete recovery of pulmonary function (Zheng et al., 2020) or psychological problems (Yuan et al., 2020). It is therefore important for health professionals to be aware of the relationships between the psychological factors and health-related quality of life, given these relationships can identify possible targets for interventions to improve these aspects.

4.2 | Symptoms and psychological state

At 6–7 months after the COVID-19 infection, the nonhospitalised patients were mainly troubled by dyspnoea and fatigue/muscle weakness. In the medium term, 41% and 63% reported dyspnoea and muscle fatigue, respectively, which agrees with other studies on hospitalised patients (Carfì et al., 2020; González et al., 2021; Qi et al., 2020; Raman et al., 2021; Willi et al., 2021; Wong et al., 2020). In the long term, Huang et al. (2021) observed a prevalence of muscle fatigue of 63%, which is higher than in our report; however, their sample consisted of hospitalised patients who were severely ill, who might have had more severe muscle weakness due to immobilisation during their hospital stay (Aarden et al., 2019). The assessment of the psychological state revealed long-term PTSD and symptoms of anxiety/depression in 34% and 45%, respectively, with the post-traumatic stress slightly improving over time but the anxiety and depression remaining constant. PTSD was considerably more prevalent in the medium term in our cohort than those from other studies (Bellan et al., 2021; Bonazza et al., 2020; Mazza et al., 2020; Qi et al., 2020; Rass et al., 2021; Tarsitani et al., 2021), as was anxiety and depression in the long term (Huang et al., 2021; Qi et al., 2020; Taquet et al., 2021). These differences might be due to sample size, methodology (e.g. assessment tools and cut-offs) and management of the pandemic (e.g. health system collapse and prolonged confinement). Close attention should therefore be paid to patients' mental health after a COVID-19 infection due to the negative psychosocial consequences of their isolation.

4.3 | Cognitive, pulmonary and physical function

Cognitive and physical function are among the most important factors for health-related quality of life and the patients' perception of the impact of the disease and their disability (Fusco et al., 2012; Saraçli et al., 2015). In our study, long-term cognitive deficits were frequent (41%) after the COVID-19 diagnosis, which is in line with other study (Miskowiak et al., 2021), although the deficits slightly improved over time. Impaired lung function was observed in a small proportion of the sample in the long term, indicating that the preserved pulmonary function of the nonhospitalised patients with COVID-19 might be due to the critical illness showing a higher incidence of major long-term sequelae in the lungs (Anastasio et al., 2021; Bellan et al., 2021; González et al., 2021; Huang et al., 2021; Huang et al., 2020; van der Sar - van der Brugge et al., 2021). However, more than half of the participants experienced a reduction in respiratory muscle strength in the long term, a finding in line with other studies (Anastasio et al., 2021; Huang et al., 2020). Leg strength showed the same tendency consistent with the evidence (Bellan et al., 2021; Belli et al., 2020; Núñez-Cortés et al., 2021; Raman et al., 2021), although it slightly improved over time, and these improvements could be considered clinically important as almost 15% of patients improved. However, 45% of patients still had impaired leg strength at 6–7 months after the COVID-19 diagnosis. The main reasons for the reduction in physical function might lie in the fact that the lockdowns heavily limited people's exercise possibilities, promoting sedentary lifestyles due to the hesitation to go outside (Constandt et al., 2020); in fact, most of the patients in our sample gained weight in the long term. The result from our study highlights a clear need for rehabilitative interventions after a COVID-19 infection.

4.4 | Prediction of impaired health-related quality of life at six to seven months

The results of the bivariate logistical regression indicated that the health-related quality of life at 6–7 months after the COVID-19 diagnosis was affected by certain factors, such as chest pain, dyspnoea, anxiety/depression, PTSD and/or fatigue/muscle weakness and, especially, the quality of life at 3 months. The proposed model for calculating the probability of impaired health-related quality of life in the long term predicted 82.4% of the cases based on an EQ-5D index score <25th percentile, PTSD and fatigue/muscle weakness. These results are in line with emerging evidence showing that PTSD leads to a higher risk of developing serious events and poorer outcomes in COVID-19 (Chang & Park, 2020; Tarsitani et al., 2021). Physical symptoms are closely related to an increased psychological burden, as well as impaired physical function, ultimately impacting on the quality of life (Nunes et al., 2017; Storm van's Gravesande et al., 2019). The quality of life 3 months after the COVID-19 infection appears to be the most important predictor of the patient's quality of life at 6–7 months, which is consistent with the predictive models of disability established in other diseases in which the assessment of medium-term disability itself is the best indicator of the degree of disability in the long term (Ritchie et al., 2013, 2015). Future studies are warranted to examine the multidisciplinary interventions aimed at improving patients' psychological and physical state, which will presumably lead to an increase in the quality of life for post-COVID-19 patients.

5 | LIMITATIONS

The first limitation of the current study is its limited external validity due to the fact that our sample was limited to a single geographic location. Although a larger sample size from different areas would be ideal for this type of study, ours is a diverse cohort from a catchment area that represents the diversity of Spain and is located in the early epicenter of the COVID-19 outbreak (Madrid). Thus, the generalisation of our results is facilitated by the well-characterised and prospective nature of our cohort. Although this probably overestimates the actual impact on the quality of life of general nonhospitalised COVID-19 survivors, it might also be a reliable representation of the current population of nonhospitalised COVID-19 survivors with persistent symptoms. In addition, some symptoms that are highly prevalent in COVID-19 survivors and could influence on quality of life, such as sense of smell disorders, were not assessed. Thus, it is possible that there are other symptoms relevant to predict poor quality of life at 6–7 months in COVID-19 patients. Lastly, we only recorded the relevant clinical findings that were self-reported by the participants or by their physicians through a physical examination during medium and long-term follow-up periods.

6 | CLINICAL IMPLICATIONS

Our findings highlight the long-term impact of COVID-19 on patients, even after their reported recovery from the acute manifestations of this disease. Our results emphasise the need for a comprehensive multidisciplinary approach that is aligned with patient needs to deliver the most appropriate care to these patients. It is important that health practitioners focus on improving the psychological state and reducing the fatigue/muscle weakness of post-COVID-19 patients to improve the patients' health-related quality of life. More longitudinal studies with larger samples are needed to determine the causal relationships and identify the effects of time. Long-term follow-up of patients with COVID-19 is needed to determine the dynamic recovery of their health-related quality of life.

7 | CONCLUSION

In conclusion, a considerable number of nonhospitalised patients with COVID-19 experience an impaired health-related quality of life and symptoms such as dyspnoea, fatigue/muscle weakness, PTSD, anxiety, depression, cognitive deficits and reduced physical

function at long-term. Poor health-related quality of life was significantly associated with chest pain, dyspnoea, anxiety/depression, PTSD and/or fatigue/muscle weakness in the long term. This adds further evidence that patients who have not been admitted to the hospital with COVID-19 continue to struggle after recovering from the acute phase of this disease, with a diverse range of impairments.

AUTHOR CONTRIBUTIONS

ILUV and TDC designed the study. NMR, SFV, CRD, and SAZ supervised the collection of the data. ILUV analysed the data. ILUV and TDC interpreted the data. All authors did the literature search. All authors prepared the figures, tables, and wrote the first draft of the manuscript. All authors critically reviewed and edited the manuscript.

ACKNOWLEDGMENTS

The authors thank the Centro Superior de Estudios Universitarios La Salle for its services in editing this manuscript.

CONFLICT OF INTEREST

The authors have stated that they had no interests which might be perceived as posing a conflict or bias.

ORCID

Tamara del Corral https://orcid.org/0000-0002-3144-5411
Ibai López-de-Uralde-Villanueva https://orcid.org/0000-0001-7474-5257

REFERENCES

Aarden, J. J., Van Der Schaaf, M., Van Der Esch, M., Reichardt, L. A., Van Seben, R., Bosch, J. A., Twisk, J. W. R., Buurman, B. M., & Engelbert, R. H. H. (2019). Muscle strength is longitudinally associated with mobility among older adults after acute hospitalization: The Hospital-ADL study. *PLoS One*, *14*(7), e0219041. https://doi.org/10.1371/journal.pone.0219041

Anastasio, F., Barbuto, S., Scarnecchia, E., Cosma, P., Fugagnoli, A., Rossi, G., Parravicini, M., & Parravicini, P. (2021). Medium-term impact of COVID-19 on pulmonary function, functional capacity and quality of life. *European Respiratory Journal*, *58*(3), 2004015. https://doi.org/10.1183/13993003.04015-2020

Badia, X., Roset, M., Montserrat, S., Herdman, M., & Segura, A. (1999). The Spanish version of EuroQol: A description and its applications. European Quality of Life scale. *Medicina Clinica*, *112*(Suppl), 79–85.

Bellan, M., Soddu, D., Balbo, P. E., Baricich, A., Zeppegno, P., Avanzi, G. C., Baldon, G., Bartolomei, G., Battaglia, M., Battistini, S., Binda, V., Borg, M., Cantaluppi, V., Castello, L. M., Clivati, E., Cisari, C., Costanzo, M., Croce, A., Cuneo, D., … Pirisi, M. (2021). Respiratory and psychophysical sequelae among patients with COVID-19 four months after hospital discharge. *JAMA Network Open*, *4*(1), e2036142. https://doi.org/10.1001/jamanetworkopen.2020.36142

Belli, S., Balbi, B., Prince, I., Cattaneo, D., Masocco, F., Zaccaria, S., Bertalli, L., Cattini, F., Lomazzo, A., Dal Negro, F., Giardini, M., Franssen, F. M. E., Janssen, D. J. A., & Spruit, M. A. (2020). Low physical functioning and impaired performance of activities of daily life in COVID-19 patients who survived hospitalisation. *The European Respiratory Journal*, *56*(4), 2002096. https://doi.org/10.1183/13993003.02096-2020

Bonazza, F., Borghi, L., di San Marco, E. C., Piscopo, K., Bai, F., d'Arminio Monforte, A., & Vegni, E. (2020). Psychological outcomes after hospitalization for COVID-19: Data from a multidisciplinary follow-up screening program for recovered patients. *Research in Psychotherapy: Psychopathology, Process and Outcome*, *23*(3), 247–255. https://doi.org/10.4081/ripppo.2020.491

Carfì, A., Bernabei, R., & Landi, F. (2020). Persistent symptoms in patients after acute COVID-19. *JAMA - Journal of the American Medical Association*, *324*(6), 603–605. https://doi.org/10.1001/jama.2020.12603

Chang, M. C., & Park, D. (2020). Incidence of post-traumatic stress disorder after coronavirus disease. *Healthcare*, *8*(4), 373. https://doi.org/10.3390/healthcare8040373

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (Vol. *18*, Issue 2, pp. 131–132). Lawrence Erlbaum Associates Inc.

Constandt, B., Thibaut, E., De Bosscher, V., Scheerder, J., Ricour, M., & Willem, A. (2020). Exercising in times of lockdown: An analysis of the impact of COVID-19 on levels and patterns of exercise among adults in Belgium. *International Journal of Environmental Research and Public Health*, *17*(11), 1–10. https://doi.org/10.3390/ijerph17114144

Delgado, C., Araneda, A., & Behrens, M. I. (2019). Validation of the Spanish-language version of the Montreal Cognitive Assessment test in adults older than 60 years. *Neurologia*, *34*(6), 376–385. https://doi.org/10.1016/j.nrl.2017.01.013

Disser, N. P., De Micheli, A. J., Schonk, M. M., Konnaris, M. A., Piacentini, A. N., Edon, D. L., Toresdahl, B. G., Rodeo, S. A., Casey, E. K., & Mendias, C. L. (2020). Musculoskeletal consequences of COVID-19. *Journal of Bone and Joint Surgery*, *102*(14), 1197–1204. https://doi.org/10.2106/JBJS.20.00847

Esakandari, H., Nabi-Afjadi, M., Fakkari-Afjadi, J., Farahmandian, N., Miresmaeili, S. M., & Bahreini, E. (2020). A comprehensive review of COVID-19 characteristics. *Biological Procedures Online*, *22*(1), 19. https://doi.org/10.1186/s12575-020-00128-2

EuroQol Research Foundation. (2018). EQ-5D-3L user guide. https://euroqol.org/publications/user-guides

Fusco, O., Ferrini, A., Santoro, M., Lo Monaco, M. R., Gambassi, G., & Cesari, M. (2012). Physical function and perceived quality of life in older persons. *Aging Clinical and Experimental Research*, *24*(1), 68–73. https://doi.org/10.1007/BF03325356

Gibson, G. J., Whitelaw, W., Siafakas, N., Supinski, G. S., Fitting, J. W., Bellemare, F., Loring, S. H., Troyer, A. D., & Grassino, A. E. (2002). ATS/ERS Statement on respiratory muscle testing. *American Journal of Respiratory and Critical Care Medicine*, *166*(4), 518–624. https://doi.org/10.1164/rccm.166.4.518

González, J., Benítez, I. D., Carmona, P., Santisteve, S., Monge, A., Moncusí-Moix, A., Gort-Paniello, C., Pinilla, L., Carratalá, A., Zuil, M., Ferrer, R., Ceccato, A., Fernández, L., Motos, A., Riera, J., Menéndez, R., Garcia-Gasulla, D., Peñuelas, O., Bermejo-Martin, J. F., … Barbé, F. (2021). pulmonary function and radiological features in survivors of critical COVID-19: A 3-month prospective cohort. *Chest*, *160*(1), 187–198. https://doi.org/10.1016/j.chest.2021.02.062

Hernandez, G., Garin, O., Dima, A. L., Pont, A., Pastor, M. M., Alonso, J., Van Ganse, E., Laforest, L., De Bruin, M., Mayoral, K., Serra-Sutton, V., & Ferrer, M. (2019). EuroQol (EQ-5D-5L) validity in assessing the quality of life in adults with asthma: Cross-sectional study. *Journal of Medical Internet Research*, *21*(1), e10178. https://doi.org/10.2196/10178

Herrero, M. J., Blanch, J., Peri, J. M., De Pablo, J., Pintor, L., & Bulbena, A. (2003). A validation study of the hospital anxiety and depression scale (HADS) in a Spanish population. *General Hospital Psychiatry*, *25*(4), 277–283. https://doi.org/10.1016/S0163-8343(03)00043-4

Huang, C., Huang, L., Wang, Y., Li, X., Ren, L., Gu, X., Kang, L., Guo, L. I., Liu, M., Zhou, X., Luo, J., Huang, Z., Tu, S., Zhao, Y., Chen, L. I., Xu, D., Li, Y., Li, C., Peng, L. U., … Cao, B. (2021). 6-month consequences of COVID-19 in patients discharged from hospital: A cohort study. *The Lancet*, *397*(10270), 220–232. https://doi.org/10.1016/S0140-6736(20)32656-8

Huang, Y., Tan, C., Wu, J., Chen, M., Wang, Z., Luo, L., Zhou, X., Liu, X., Huang, X., Yuan, S., Chen, C., Gao, F., Huang, J., Shan, H., & Liu, J. (2020). Impact of coronavirus disease 2019 on pulmonary function in early convalescence phase. *Respiratory Research*, *21*(1), 163. https://doi.org/10.1186/s12931-020-01429-6

König, H. H., Bernert, S., Angermeyer, M. C., Matschinger, H., Martinez, M., Vilagut, G., Haro, J. M., De Girolamo, G., De Graaf, R., Kovess, V., & Alonso, J. (2009). Comparison of population health status in six European countries results of a representative survey using the EQ-5D questionnaire. *Medical Care*, *47*(2), 255–261. https://doi.org/10.1097/MLR.0b013e318184759e

Lamprecht, B. (2020). Is there a post-COVID syndrome? *Pneumologe*, *17*(6), 398–405. https://doi.org/10.1007/s10405-020-00347-0

Lauer, S. A., Grantz, K. H., Bi, Q., Jones, F. K., Zheng, Q., Meredith, H. R., Azman, A. S., Reich, N. G., & Lessler, J. (2020). The incubation period of coronavirus disease 2019 (CoVID-19) from publicly reported confirmed cases: Estimation and application. *Annals of Internal Medicine*, *172*(9), 577–582. https://doi.org/10.7326/M20-0504

Long, J. S. (1997). *Regression models for categorical and limited dependent variables*. SAGE Publications.

Mao, L., Jin, H., Wang, M., Hu, Y., Chen, S., He, Q., Chang, J., Hong, C., Zhou, Y., Wang, D., Miao, X., Li, Y., & Hu, B. (2020). Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurology*, *77*(6), 683–690. https://doi.org/10.1001/jamaneurol.2020.1127

Mateo Lázaro, M. L., Penacho Lázaro, M. A., Berisa Losantos, F., & Plaza Bayo, A. (2008). New tables on hand strength in the adult population from Teruel. *Nutricion Hospitalaria*, *23*(1), 35–40.

Mazza, M. G., De Lorenzo, R., Conte, C., Poletti, S., Vai, B., Bollettini, I., Melloni, E. M. T., Furlan, R., Ciceri, F., Rovere-Querini, P., & Benedetti, F. (2020). Anxiety and depression in COVID-19 survivors: Role of inflammatory and clinical predictors. *Brain, Behavior, and Immunity*, *89*, 594–600. https://doi.org/10.1016/j.bbi.2020.07.037

Meys, R., Delbressine, J. M., Goërtz, Y. M. J., Vaes, A. W., Machado, F. V. C., Van Herck, M., Burtin, C., Posthuma, R., Spaetgens, B., Franssen, F. M. E., Spies, Y., Vijlbrief, H., van't Hul, A. J., Janssen, D. J. A., Spruit, M. A., & Houben-Wilke, S. (2020). Generic and respiratory-specific quality of life in non-hospitalized patients with COVID-19. *Journal of Clinical Medicine*, *9*(12), 3993. https://doi.org/10.3390/jcm9123993

Miles, J. N. V., Marshall, G. N., & Schell, T. L. (2008). Spanish and English versions of the PTSD Checklist-Civilian Version (PCL-C): Testing for differential item functioning. *Journal of Traumatic Stress*, *21*(4), 369–376. https://doi.org/10.1002/jts.20349

Miller, M. R., Crapo, R., Hankinson, J., Brusasco, V., Burgos, F., Casaburi, R., Coates, A., Enright, P., van der Grinten, C. P. M., Gustafsson, P., Jensen, R., Johnson, D. C., MacIntyre, N., McKay, R., Navajas, D., Pedersen, O. F., Pellegrino, R., Viegi, G., Wanger, J., & ATS/ERS Task Force. (2005). General considerations for lung function testing. *The European Respiratory Journal*, *26*(1), 153–161. https://doi.org/10.1183/09031936.05.00034505

Miskowiak, K. W., Johnsen, S., Sattler, S. M., Nielsen, S., Kunalan, K., Rungby, J., Lapperre, T., & Porsberg, C. M. (2021). Cognitive impairments four months after COVID-19 hospital discharge: Pattern, severity and association with illness variables. *European Neuropsychopharmacology: The Journal of the European College of Neuropsychopharmacology*, *46*, 39–48. https://doi.org/10.1016/j.euroneuro.2021.03.019

Morales, P., Sanchis, J., Cordero, P. J., & Díez, J. L. (1997). Maximum static respiratory pressures in adults. Reference values for a Caucasian Mediterranean population. *Archivos De Bronconeumologia*, *33*(5), 213–219. https://doi.org/10.1016/s0300-2896(15)30609-8

Nunes, M. D. R., Jacob, E., Bomfim, E. O., Lopes-Junior, L. C., de Lima, R. A. G., Floria-Santos, M., & Nascimento, L. C. (2017). Fatigue and health related quality of life in children and adolescents with cancer. *European Journal of Oncology Nursing*, *29*, 39–46. https://doi.org/10.1016/j.ejon.2017.05.001

Núñez-Cortés, R., Rivera-Lillo, G., Arias-Campoverde, M., Soto-García, D., García-Palomera, R., & Torres-Castro, R. (2021). Use of sit-to-stand test to assess the physical capacity and exertional desaturation in patients post COVID-19. *Chronic Respiratory Disease*, *18*. https://doi.org/10.1177/14799731211999205

Pascarella, G., Strumia, A., Piliego, C., Bruno, F., Del Buono, R., Costa, F., Scarlata, S., & Agrò, F. E. (2020). COVID-19 diagnosis and management: A comprehensive review. *Journal of Internal Medicine*, *288*(2), 192–206. https://doi.org/10.1111/joim.13091

Peduzzi, P., Concato, J., Kemper, E., Holford, T. R., & Feinstein, A. R. (1996). A simulation study of the number of events per variable in logistic regression analysis. *Journal of Clinical Epidemiology*, *49*(12), 1373–1379. https://doi.org/10.1016/S0895-4356(96)00236-3

Peolsson, A., Hedlund, R., & Oberg, B. (2001). Intra- and inter-tester reliability and reference values for hand strength. *Journal of Rehabilitation Medicine: Official Journal of the UEMS European Board of Physical and Rehabilitation Medicine*, *33*(1), 36–41. https://doi.org/10.1080/165019701300006524

Qi, R., Chen, W., Liu, S., Thompson, P. M., Zhang, L. J., Xia, F., Cheng, F., Hong, A., Surento, W., Luo, S., Sun, Z. Y., Zhou, C. S., Li, L., Jiang, X., & Lu, G. M. (2020). Psychological morbidities and fatigue in patients with confirmed COVID-19 during disease outbreak: Prevalence and associated biopsychosocial risk factors. *MedRxiv*. https://doi.org/10.1101/2020.05.08.20031666

Qu, G., Zhen, Q. I., Wang, W., Fan, S., Wu, Q., Zhang, C., Li, B., Liu, G., Yu, Y., Li, Y., Yong, L., Lu, B., Ding, Z., Ge, H., Mao, Y., Chen, W., Xu, Q., Zhang, R., Cao, L. U., … Sun, Y. (2021). Health-related quality of life of COVID-19 patients after discharge: A multicenter follow-up study. *Journal of Clinical Nursing*, *30*(11-12), 1742–1750. https://doi.org/10.1111/jocn.15733

Raman, B., Cassar, M. P., Tunnicliffe, E. M., Filippini, N., Griffanti, L., Alfaro-Almagro, F., Okell, T., Sheerin, F., Xie, C., Mahmod, M., Mózes, F. E., Lewandowski, A. J., Ohuma, E. O., Holdsworth, D., Lamlum, H., Woodman, M. J., Krasopoulos, C., Mills, R., McConnell, F. A. K., … Neubauer, S. (2021). Medium-term effects of SARS-CoV-2 infection on multiple vital organs, exercise capacity, cognition, quality of life and mental health, post-hospital discharge. *EClinicalMedicine*, *31*, 100683. https://doi.org/10.1016/j.eclinm.2020.100683

Rass, V., Beer, R., Josef Schiefecker, A., Kofler, M., Lindner, A., Mahlknecht, P., Heim, B., Limmert, V., Sahanic, S., Pizzini, A., Sonnweber, T., Tancevski, I., Loeffler-Ragg, J., Scherfler, C., Zamarian, L., Bellmann-Weiler, R., Weiss, G., Djamshidian, A., Kiechl, S., … Helbok, R. (2021). Neurological outcome and quality of life three months after COVID-19: A prospective observational cohort study. *European Journal of Neurology*, *28*(10), 3348–3359. https://doi.org/10.1111/ene.14803

Ritchie, C., Hendrikz, J., Jull, G., Elliott, J., & Sterling, M. (2015). External validation of a clinical prediction rule to predict full recovery and ongoing moderate/severe disability following acute whiplash injury. *Journal of Orthopaedic and Sports Physical Therapy*, *45*(4), 242–250. https://doi.org/10.2519/jospt.2015.5642

Ritchie, C., Hendrikz, J., Kenardy, J., & Sterling, M. (2013). Derivation of a clinical prediction rule to identify both chronic moderate/severe disability and full recovery following whiplash injury. *Pain*, *154*(10), 2198–2206. https://doi.org/10.1016/j.pain.2013.07.001

Saraçli, Ö., Akca, A. S. D., Atasoy, N., Önder, Ö., Senormanci, Ö., Kaygisiz, I., & Atik, L. (2015). The relationship between quality of life and cognitive functions, anxiety and depression among hospitalized elderly patients. *Clinical Psychopharmacology and Neuroscience*, *13*(2), 194–200. https://doi.org/10.9758/cpn.2015.13.2.194

Singer, S., Kuhnt, S., Götze, H., Hauss, J., Hinz, A., Liebmann, A., Krauß, O., Lehmann, A., & Schwarz, R. (2009). Hospital anxiety and depression scale cutoff scores for cancer patients in acute care. *British Journal of Cancer*, *100*(6), 908–912. https://doi.org/10.1038/sj.bjc.6604952

Storm van's Gravesande, K., Blaschek, A., Calabrese, P., Rostásy, K., Huppke, P., Kessler J, J., Kalbe, E., & Mall, V. (2019). Fatigue and depression predict health-related quality of life in patients with pediatric-onset multiple sclerosis. *Multiple Sclerosis and Related Disorders*, *36*, 101368. https://doi.org/10.1016/j.msard.2019.08.010

Strassmann, A., Steurer-Stey, C., Lana, K. D., Zoller, M., Turk, A. J., Suter, P., & Puhan, M. A. (2013). Population-based reference values for the 1-min sit-to-stand test. *International Journal of Public Health*, *58*(6), 949–953. https://doi.org/10.1007/s00038-013-0504-z

Swets, J. A. (1988). Measuring the accuracy of diagnostic systems. *Science Science*, *240*(4857), 1285–1293. https://doi.org/10.1126/science.3287615

Szende, A., Janssen, B., & Cabasés, J. (2014). *Self-reported population health: An international perspective based on EQ-5D*. Springer. https://doi.org/10.1007/978-94-007-7596-1

Szentes, B. L., Schultz, K., Nowak, D., Schuler, M., & Schwarzkopf, L. (2020). How does the EQ-5D-5L perform in asthma patients compared with an asthma-specific quality of life questionnaire? *BMC Pulmonary Medicine*, *20*(1), 168. https://doi.org/10.1186/s12890-020-01205-8

Taquet, M., Geddes, J. R., Husain, M., Luciano, S., & Harrison, P. J. (2021). 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records. *The Lancet Psychiatry*, *8*(5), 416–427. https://doi.org/10.1016/S2215-0366(21)00084-5

Tarsitani, L., Vassalini, P., Koukopoulos, A., Borrazzo, C., Alessi, F., Di Nicolantonio, C., Serra, R., Alessandri, F., Ceccarelli, G., Mastroianni, C. M., & d'Ettorre, G. (2021). Post-traumatic stress disorder among COVID-19 survivors at 3-month follow-up after hospital discharge. *Journal of General Internal Medicine*, *36*(6), 1702–1707. https://doi.org/10.1007/s11606-021-06731-7

Thiese, M. S., Ronna, B., & Ott, U. (2016). P value interpretations and considerations. *Journal of Thoracic Disease*, *8*(9), E928–E931. https://doi.org/10.21037/jtd.2016.08.16

Turner, D., Schünemann, H. J., Griffith, L. E., Beaton, D. E., Griffiths, A. M., Critch, J. N., & Guyatt, G. H. (2009). Using the entire cohort in the receiver operating characteristic analysis maximizes precision of the minimal important difference. *Journal of Clinical Epidemiology*, *62*(4), 374–379. https://doi.org/10.1016/j.jclinepi.2008.07.009

van der Sar - van der Brugge, S., Talman, S., Boonman - de Winter, L., de Mol, M., Hoefman, E., van Etten, R. W., & De Backer, I. C. (2021). Pulmonary function and health-related quality of life after COVID-19 pneumonia. *Respiratory Medicine*, *176*, 106272. https://doi.org/10.1016/j.rmed.2020.106272

von Elm, E., Altman, D. G., Egger, M., Pocock, S. J., Gøtzsche, P. C., & Vandenbroucke, J. P. (2008). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. *Journal of Clinical Epidemiology*, *61*(4), 344–349. https://doi.org/10.1016/j.jclinepi.2007.11.008

Walle-Hansen, M. M., Ranhoff, A. H., Mellingsæter, M., Wang-Hansen, M. S., & Myrstad, M. (2021). Health-related quality of life, functional decline, and long-term mortality in older patients following hospitalisation due to COVID-19. *BMC Geriatrics*, *21*(1), 199. https://doi.org/10.1186/s12877-021-02140-x

Willi, S., Lüthold, R., Hunt, A., Hänggi, N. V., Sejdiu, D., Scaff, C., Bender, N., Staub, K., & Schlagenhauf, P. (2021). COVID-19 sequelae in adults aged less than 50 years: A systematic review. *Travel Medicine and Infectious Disease*, *40*, 101995. https://doi.org/10.1016/j.tmaid.2021.101995

Wong, A. W., Shah, A. S., Johnston, J. C., Carlsten, C., & Ryerson, C. J. (2020). Patient-reported outcome measures after COVID-19: A prospective cohort study. *European Respiratory Journal*, *56*(5), 2003276. https://doi.org/10.1183/13993003.03276-2020

Yeager, D. E., Magruder, K. M., Knapp, R. G., Nicholas, J. S., & Frueh, B. C. (2007). Performance characteristics of the posttraumatic stress disorder checklist and SPAN in veterans affairs primary care settings. *General Hospital Psychiatry*, *29*(4), 294–301. https://doi.org/10.1016/j.genhosppsych.2007.03.004

Yuan, B., Li, W., Liu, H., Cai, X., Song, S., Zhao, J., Hu, X., Li, Z., Chen, Y., Zhang, K., Liu, Z., Peng, J., Wang, C., Wang, J., & An, Y. (2020). Correlation between immune response and self-reported depression during convalescence from COVID-19. *Brain, Behavior, and Immunity*, *88*, 39–43. https://doi.org/10.1016/j.bbi.2020.05.062

Zheng, Z., Yao, Z., Wu, K., & Zheng, J. (2020). Patient follow-up after discharge after COVID-19 pneumonia: Considerations for infectious control. *Journal of Medical Virology*, *92*(11), 2412–2419. https://doi.org/10.1002/jmv.25994

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: del Corral, T., Menor-Rodríguez, N., Fernández-Vega, S., Díaz-Ramos, C., Aguilar-Zafra, S., & López-de-Uralde-Villanueva, I. (2022). Longitudinal study of changes observed in quality of life, psychological state cognition and pulmonary and functional capacity after COVID-19 infection: A six- to seven-month prospective cohort. *Journal of Clinical Nursing*, *00*, 1–14. https://doi.org/10.1111/jocn.16352