

Quality of life, psychological and cognitive sequelae of patients with post-acute sequelae of SARS-CoV-2 infection (PASC)

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Summary

The fluidity of gender along with sexual fluidity and flexibility indicate that sexual attraction may exist and vary within a spectrum or a flux changing during the life. On the other hand, scientists distinguished two understandings of the 'self'; the self as "Me" and the self as "I". "Me" corresponds to the self as an object of experience, while "I" reflects the self as a subject of experience. The phenomenology of human sexuality provides a trans-disciplinary basis where we can create a synthesis of the various perspectival approaches to the subject. We suggested a 'Sexual-Self' model, comprised from the 'Sexual-Me' component, corresponding to 'Gender Identity', and the 'Sexual-I' component, corresponding to 'Sexuality' - including 'Sexual Preference and Orientation'. We also suggested different scientific concepts and domains that can help understanding the existence and the processes of 'Sexual-Self' throughout the life.

Background

Symptoms following SARS-CoV-2 infection of greater than or equal to 3 months duration are collectively referred to as "post-acute sequelae of SARS-CoV-2 infection" (PASC), which is a multi-organ and disabling disorder. The mental and physical health of an individual with PASC can be severely affected in the long term.

Methods

In order to determine the quality of life as well as the psychological and cognitive sequelae of patients with PASC, a presencialsurvey was designed for 38 patients with clinical symptoms of 12 months or more, evaluated in the consultation rooms of the Hospital Clínico Universitario Virgen de la Arrixaca (HCUVA) in Murcia.

Findings

Mean symptom duration was 18,18 months $\pm 6,758$. Dyspnoea was determined with the mMrc of $1,61 \pm 1,26$; self-reported quality of life using the Euroqol visual analogue scale with a mean score of $5,38 \pm 1,915$ and mean PCFS was $1, \pm 1,130$. The GAD 7 anxiety scale scored $7,18 \pm 5,306$ and PHQ-9 was $7,87 \pm 6,235$. The cognitive assessment using the PSlobtained a mean score of $40,97 \pm 32,924\%$ and the MoCA test a mean score of $25,76 \pm 3,845$.

Interpretation

PASC is not exclusively a physical affectation of patients. The mental health and self-perception of health of an individual with PASC can be severely affected in the long term.

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In December 2019 in Wuhan, China, SARS-CoV-2 emerged, which designated the 2019 coronavirus pandemic (COVID-19). It is a Betacoronavirus ¹ that can have wide-ranging complications and sequelae ². The world health organization (WHO) has identified 774,395,593 confirmed global cases of SARS-CoV-2

SARS-CoV-2 has been detected by electron microscopy in the endothelium of the lung, heart, kidney, brain and skin ⁶. Multiple organ involvement⁷⁸.



NICE (National Institute for Health and Care Excellence) guidelines state that 'post-SARS-CoV-2 syndrome' can be diagnosed if symptoms persist beyond 12 weeks, a definition supported by the WHO^{19,18}. The term 'Long COVID' was originally coined by a patient⁹ and by social media¹⁰. It has been called by many names until the consensus of the Spanish-based Multidisciplinary Collaborative Group for the Scientific Monitoring of SARS-CoV-2 (GCMSC) coined the term Post-Acute SARS-CoV-2 Syndrome (or PACS)¹¹. PACS is a multi-organ disorder ranging from mild symptoms to a disabling state⁸. They are a wide range of new, recurrent or ongoing health problems that people may experience¹².

According to the Americans with Disabilities Act (ADA)¹³, PASC can be an incapacitating condition, a "physical or mental" impairment that "substantially limits" one or more major life activities.

Material and methods

Primary objective

Assessing the functional status and quality of life, psychological impact and conduct an assessment of the cognitive sequelae of the patients with PASC.

Secondary objective

Describe persistent symptoms of patients with PASC.

Study design

A descriptive study was designed to include all adult patients over 15 years of age following SARS-CoV-2 infection assessed in the infectious diseases department of the HUVA after acute hospitalisation or who have been referred to them from primary care due to persistent symptomatology in the period from September 2020 to March 2022. To ensure that persistent symptoms are related to SARS-CoV-2 infection, those with previous dyspnea determined by the modified Medical Research Council (mMRC) dyspnea scale, the presence of sequelae, the baseline situation that limits the completion of the same or refusal to carry out the survey. Those who persist with symptoms for more than 12 months will be evaluated in the survey.

Variables

1. Clinical and demographic variables are collected in the questionnaire (**Annex 1**).
2. Respiratory function: Modified Medical Research Council (mMRC) dyspnoea scale (**Annex 2**).
3. Health-related quality of life: EuroQol-5D (EQ-5D), a generic instrument that contains five dimensions of health and its visual analogue scale (EQ-EVA) which consists of a numerical thermometer where the patient self-assesses their health status (0 being the worst and 10 being the best self-perception of health). (**Annex 3**).
4. Post-COVID-19 Functional Scale (PCFS)¹⁴ (**Annex 4**), which ranges from 0 (no limitation) to 4 (worst state of health).

This is an ordinal scale that emerged during the SARS-CoV-2 pandemic that categorizes the impact on patients' daily lives with the aim of capturing the heterogeneity of the impact and being a monitoring tool. It goes from 0 (no limitation) to 4 (worst state of health).

5. Psychological assessment: Patient health questionnaire-9 (PHQ-9) (**Annex 5**) and the General Anxiety Disorder-7 (GAD-7) (**Annex 6**) that evaluate the presence and severity of depression and anxiety, respectively.
6. Cognitive assessment: Prefrontal Symptom Inventory (PSI) (**Annex 1.1**) and the Montreal (MoCA) test (**Annex 1.2**). PSI assesses symptoms of prefrontal malfunction in daily life, has shown good psychometric properties and has been applied in the general population and clinical samples from Spain and Latin America. The MoCA test evaluates executive and visuospatial function, identification, memory, attention, language, abstraction, memory and orientation.

All variables are reflected in the questionnaire.

Results

Description of the cohort

The initial cohort is made up of a total of 551 patients. A total of 147 (26,7%) patients have been excluded for various reasons: 1) Due to cardiorespiratory or thromboembolic complications after the infection that avoid the correctly discerning whether the symptoms would be secondary to them; 2) Due to the patient's baseline situation or previous pathologies that did not allow us to differentiate whether the symptoms are secondary consequence of the SARS-CoV-2 infection or the progression of their diseases; 3) Due to cognitive impairment that prevents clinical assessment or completion of the questionnaire; and 4) Patients who did not attend the appointment. Finally, the number of patients included was 404.

Out of a total of 60 patients who were still symptomatic $\geq$ 12 months, 38 patients attended for a face-to-face questionnaire. Women predominated (21 vs 17), with a mean age of $54,92 \text{ years} \pm 10,65$, of Spanish nationality ($n = 34, 89,5\%$); most were unvaccinated (27 vs 11), requiring hospital admission (78,9%) with only 2 patients (5,3%) requiring ICU admission. A total of 20 patients (52,6%) had at least one CVRF including: Hypertension (10 patients, 26,3%), dyslipidaemia (8 patients, 21,05%), diabetes (4 patients, 10,52%), smoking (1 patient, 2,63%). The mean BMI was 28.95, concluding that the majority had at least one CVRF, the most frequent being obesity ($\text{BMI} > 30$). The mean duration of symptoms was $18,18 \text{ months} \pm 6,758$ (table 1, graphs 1 and 2).

Table 1. Baseline characteristics of the study population.

Characteristics (n = 38 patients)	Value
Demographics	
Age (Mean and SD)	Overall: 54,92 (10,650), Men: 55,41 (8,761), Women: 54,52 (12,168)
Male sex (n,%)	17 (44,7%)
Female sex (n,%)	21 (55,3%)
Country of Birth (n,%)	Spain: 34 (89,5%) Sweden: 1 (2,6%) Costa Rica: 1 (2,6%) Ecuador: 2 (5,3%)
Vaccination (n,%)	Yes: 11 (28,9), No: 27 (71,1)
Maximum attention received	
Hospital admission (n,%)	Yes: 30 (78,9%); No: 21 (21,1%)
Uci (n,%)	Yes: 2 (5,3%); No: 36 (94,7%)
Cardiovascular risk factors (CVRFs)	
At least 1 CVRF	Yes: 20; No: 18
Weight (Mean and SD)	80,21 (12,377)
BMI (Mean and SD)	28,95 (5,16)
BMI men (Mean and SD); BMI women (Mean and SD)	29,27 (2,77); 28,68 (6,55419)
BMI Normal (18,5 - 24,99)	10
BMI Overweight (25 - 29,99)	11
BMI Obesity (≥ 30)	17
HTA (n,%)	10 (26,3%)
Diabetes (n,%)	4 (10,52%)
Dyslipidaemia (n,%)	8 (21,05%)
Smoking (n,%)	1 (2,63%)
Depression (n,%)	7 (18,42%)

Persistent symptomatology

Table 2 shows the presence of 21 persistent symptoms and their frequency of occurrence, the most frequent being asthenia (32 patients, 84,2%), followed by myalgia (25 patients, 65,8%), mental dullness (23 patients, 60,5%), insomnia (19 patients, 50%) and malaise 18 (47,4%).

Table 2. Persistent symptoms.

Patients with clinic (n = 38)	
Clinic	(n, %)
Asthenia	32 (84,2%)
Myalgia	25 (65,8%)
Mental dullness	23 (60,5%)
Insomnia	19 (50%)
General malaise	18 (47,4%)
Excessive sweating	17 (44,7%)
Headache	15 (39,5%)
Tachycardia	12 (31,6%)
Dyspnoea	11 (28,9%)
Anosmia	11 (28,9%)
Hair loss	11 (28,9%)
Cough	10 (26,3%)
Dizziness	10 (26,3%)
Rhinitis	9 (23,7%)
Diarrhoea	9 (23,7%)
Ageusia or dysgeusia	7 (18,4%)
Skin alterations	6 (15,8%)
Fever	5 (13,2%)
Nausea	4 (10,5%)
Arthralgias	1 (2,6%)
Aphonia	1 (2,6%)

Quality of life of PASC patients

In order to analyse health-related quality of life, the mMRC dyspnoea scale, the Euroqol questionnaire and the PFCS were used.

mMRC scale

According to the mMRC, the majority of patients have dyspnoea when walking uphill (36,8%) and when keeping pace with people of the same age (23,7%), leaving only 18,4% with a dyspnoea grade of 0, 13,2% had dyspnoea when going out of the house. The mean and SD for this scale is 1,61 (SD 1,26). Table 3.

Table 3. Modified Medical Research Council (mMRC) dyspnoea scale.

mMRC 0	mMRC 1	mMRC 2	mMRC 3	mMRC 4	Total
Intense exercise	When climbing slopes	At the pace of people my age	At 100 metres on the flat	When leaving the house or with the toilet	
7 (18,4%)	14 (36,8%)	9 (23,7%)	3 (7,9%)	5 (13,2%)	38

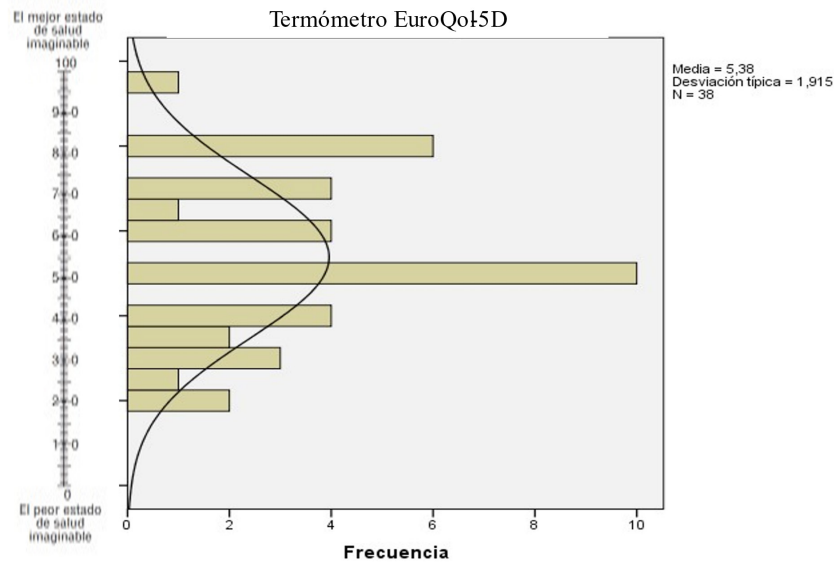
Euroqol

In the Euroqol quality questionnaire, pain/discomfort (73,7%) and limited mobility (55,2%), activities of daily living (50%) and with some respect for self-care capacity (21%) predominate. The Euroqol analogue scale includes a numerical thermometer on the self-perception of health status, with 0 being the worst and 10 the healthiest, obtaining an average of $5,38 \pm 1,915$. Graph 3.

Table 4. Euroqol.

Category	Score			
Intense exercise	When climbing slopes	At the pace of people my age	At 100 metres on the flat	When leaving the house or with the toilet
7 (18,4%)	14 (36,8%)	9 (23,7%)	3 (7,9%)	5 (13,2%)

Category	Score			
	No problems	Some problems	Unable/Much pain or discomfort	Total problems
Mobility	17 (44,7%)	20 (52,6%)	1 (2,6%)	55,2%
Self-care	30 (78,9%)	7 (18,4%)	1 (2,6%)	21%
Day-to-day activities	19 (50%)	16 (42,1%)	3 (7,9%)	50%
Pain or Discomfort	10 (26,3%)	22 (57,9%)	6 (15,8%)	73,7%



Graph 1. Euroqol Thermometer.

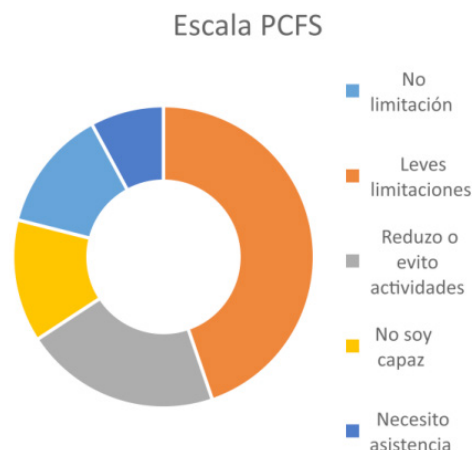
PCFS Scale

The PCFS scale emerged during the pandemic as an optimal instrument intended as an ordinal scale that assesses the full range of limitations. Ordinal scales classify patients into meaningful categories, do not differentiate between underlying causes, and can be used for follow-up¹⁴. It ranges from 1 (no limitation) to 5 (worst health status).

In our sample the mean PCFS is $1,58 \pm 1,130$. We found that the majority (17, 44,7%) have slight limitations, followed by 8 patients (21,1%) who need to reduce activities, 5 patients (13,2%) have no limitations and only 3 (7,9%) need assistance to carry out their activities. Table 5 and graph 4.

Table 5 and Graph 2. PCFS

PCFS. Score	Number of patients (n, %)
No limitation	5 (13,2)
Slight limitations	17 (44,7)
I reduce or avoid activities	8 (21,1%)
I am not able to	5 (13,2)
I need assistance	3 (7,9%)
Total	38



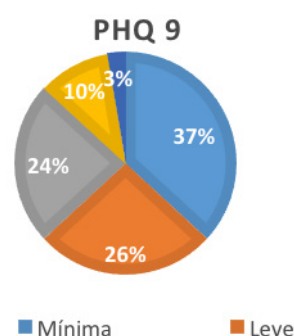
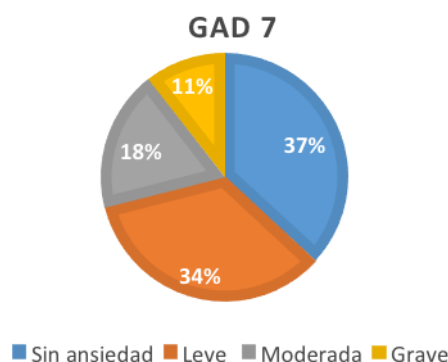
Mental health assessment

In our sample, 7 patients (18,42%) had a history of depression prior to infection. For psychological assessment (table 6 and graph 5), the GAD-7 scales were used with a mean score of $7,18 \pm 5,306$, with 14 patients (36,8%) not meeting anxiety criteria versus 24 (63,2%) patients who did meet criteria (13 mild, 7 moderate and 4 severe anxiety, being 34,2%, 18,4% and 10,5% respectively).

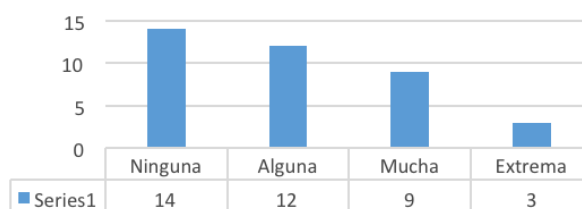
A mean score of $7,87 \pm 6,235$ was obtained on the PHQ-9 scale, showing 14 patients (36,8%) with minimal or absent depression criteria, 10 patients presenting mild depression, 9 moderate, 4 moderately severe and 1 patient with severe depression (26,3%, 23,7%, 10,5% and 2,6% respectively). The majority had mild impact or difficulty (31,6%).

Table 6. Mental health.

Anxiety. GAD 7	No anxiety	Slight	Moderate	Serious	
	14 (36,8%)	13 (34,2%)	7 (18,4%)	4 (10,5%)	
Depression PHQ-9	Minima	Slight	Moderate	Moderately severe	Serious
	14 (36,8%)	10 (26,3%)	9 (23,7%)	4 (10,5%)	1 (2,6%)
Difficulty	None	Some	Much	Extreme	
	14 (36,8%)	12 (31,6%)	9 (23,7%)	3 (7,9%)	



Difficulty in day-to-day life of GAD 7 and PHQ 9



Graph 3. Mental Health.

Cognitive assessment

PSI

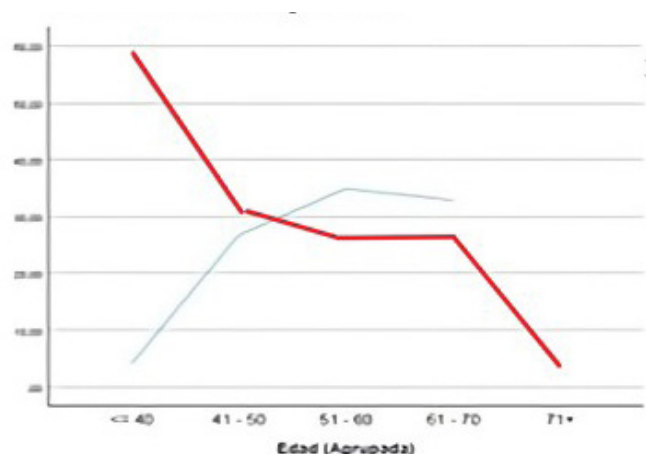
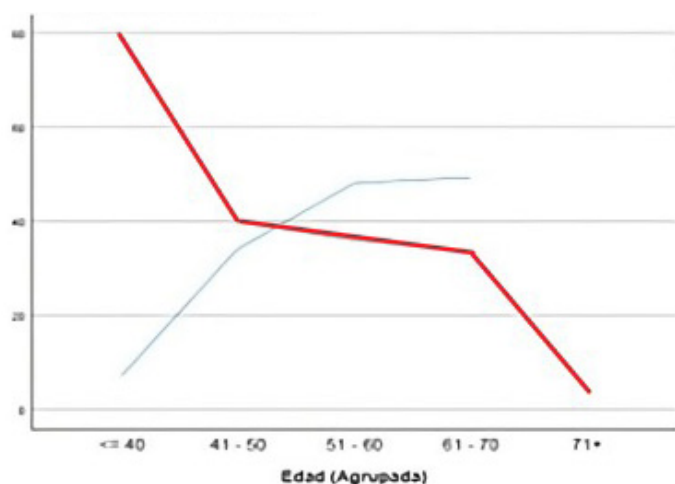
This questionnaire investigates symptoms of poor prefrontal functioning in everyday life. It has shown good psychometric properties and has been applied in general population and clinical samples in Spain and other Spanish-speaking countries. Table 7 shows the different scores obtained by men and women in the different sections and in the total score of the PSI. The executive control score was $12,47 \pm 12,47$; the attention score was $9,76 \pm 7,332$; the motivational score was $8,13 \pm 5,878$; the emotional score was $6,08 \pm 6,373$; the behavioural score was $4,63 \pm 5,479$ and the overall score was $40,97 \pm 32,924\%$. In the table we can see that males score higher in problems in attentional, motivational, emotional and social behavioural control, while females obtain higher scores in problems in executive control.

The graphical representation of the score obtained grouped by age and compared by sex has been made for the values

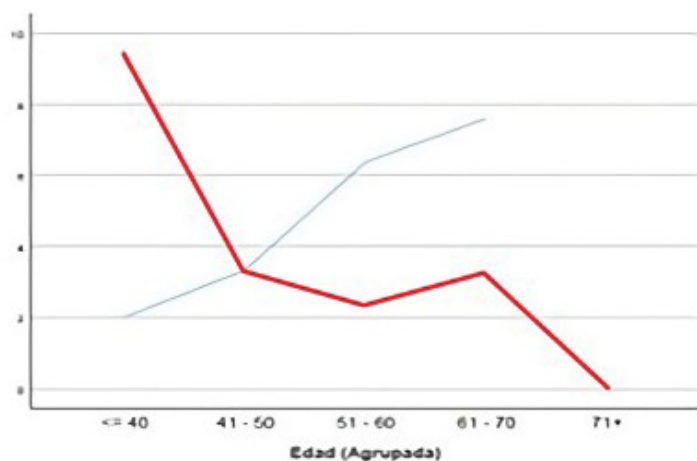
of the total PSI score, the executive PSI score (which includes execution, attentional and motivational), the behavioural PSI score and the emotional PSI score. Graph 6.

Table 7. PSI.

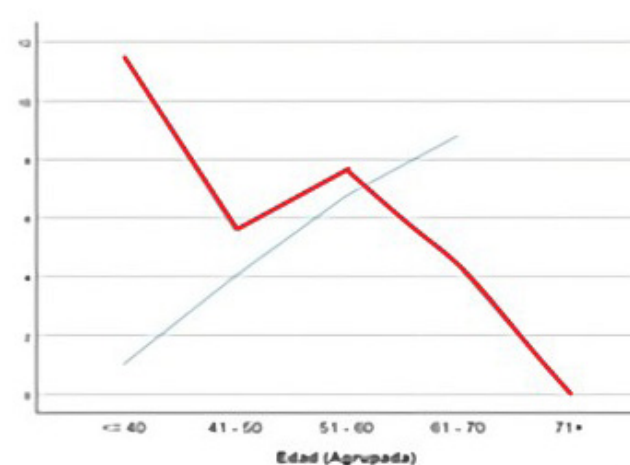
Scope	Overall (Mean, SD)	Men (Mean, SD)	Women (Mean, SD)
Executive Control	12,47 (12,47)	12,29 (11,815)	12,62 (11,668)
Attentional	9,76 (7,332)	9,94 (6,995)	9,62 (7,762)
Motivational	8,13 (5,878)	8,76 (5,739)	7,62 (6,078)
Emotional behaviour	6,08 (6,373)	6,53 (6,520)	5,71 (6,389)
Behavioural	4,63 (5,479)	5,94 (6,628)	3,57 (4,214)
Total score	40,97 (32,924%)	43,47 (33,690)	38,95 (32,981)



Puntuación ISP Conductual



Puntuación ISP Emocional



Graph 6. Men are represented by the blue line and women by the red line, both grouped by age ranges.

Patients who reported persistent cognitive symptoms had a higher PSI score (therefore, a higher number of self-reported prefrontal symptoms) than those who did not, and this association was statistically significant. Table 8.

Table 8. PSI and cognitive symptoms.

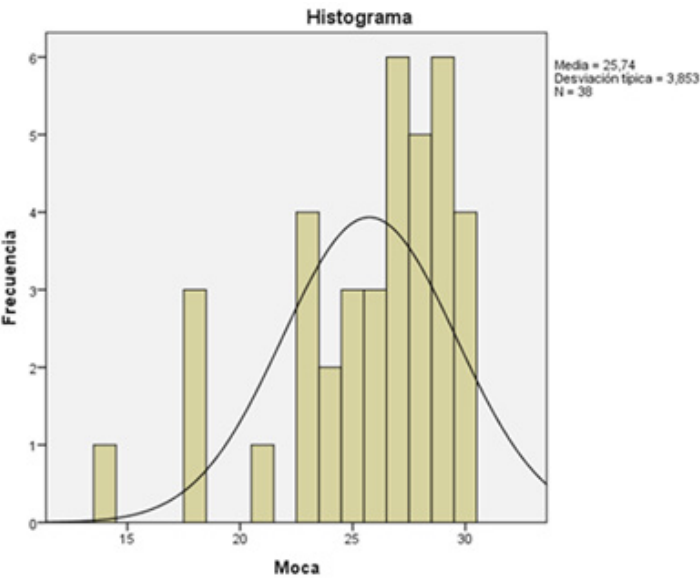
Total score of PSI	Presence of cognitive symptoms	Media and DT	p value
	No	25,53 (24,413)	
	Yes	51,04 (34,282)	

Moca

The results of the Moca test are shown in table 9. Attention problems stand out with the worst overall score with a mean of $4,82 \pm 1,486$ and delayed recall with a mean of $3,84 \pm 1,405$, while animal identification and orientation are the best preserved. In the total score, all items are added together and an extra point is added for patients with a level of education ≤ 12 years, as this is a requirement for validation of the Moca test. The normal score is greater than or equal to 26, so it is striking that the mean score was $25,76 \pm 3,845$ (below normal) (Figure 7). The score was low in 14 patients (36,8%) compared to 24 (63,2%) who scored normal.

Table 9. Moca test.

Paragraphs	Maximum score	Mean (DT)	Score
Executive and visuo-spatial	5	4,11 (1,226)	≤ 4 (47,4%) y ≤ 3 (21,1%)
Identification	3	2,92 (0,273)	≤ 2 (7,9 %)
Attention	6	4,82 (1,486)	≤ 4 (26,3%) y ≤ 3 (15,8%)
Language	3	2,29 (0,984)	≤ 2 (42,1%)
Abstraction	2	1,76 (0,431)	≤ 1 (23,7 %)
Delayed recall	5	3,84 (1,405)	≤ 4 (52,6%) y ≤ 3 (34,2%)
Orientation	6	5,92 (0,273)	≤ 5 is 7,9 %.
Total score	30	25,76 (3,845)	Low (< 25) = 14 (36,8%) Normal (≥ 26) = 24 (63,2%)



Graph 7. Moca.

Discussion

a) Assessing the quality of life of patients with PASC mMRC scale

PASC can potentially cause unexplained and persistent dyspnoea (in the absence of cardiopulmonary problems). The mean score of our sample was $1,61 \pm 1,26$. In the study by George Alba *et al.*¹⁵ study of 18 patients with PASC and compared to controls obtained an mMRC score of 1,6

$\pm 0,9$ vs $1,4 \pm 0,9$. The cohort of 58 patients by Stephan Nopp *et al.*¹⁶ had a median mMRC score of 1 (interquartile range 0-1). Other cohorts had worse dyspnoea scores, such as Rehab M. Hamdy *et al.*¹⁷ which included 60 patients, obtained an mMRC score of $2,4 \pm 0,7$; Garrigues E,*et al.*¹⁸ 35 patients (29%) had an mMRC grade ≥ 2 ; Grace Y, Lamet *al*¹⁹ with 165 patients, the mean mMRC was $2,0 \pm 0,8$. Of the 156 patients surveyed by Tabacof L, *et al.*²⁰ 63 patients (40%) reported a score of 3 or more on the mMrc Scale, suggesting moderate to severe disability due to dyspnoea. Unfortunately they do not indicate the mean score for comparison with our data.

Euroqol

Our mean score on the EQ-5D-5L visual (EQ-EVA) analogue scale was $5,8 \pm 1,915$, lower than that reflected in the literature where the score ranges from 6,0 to 7,03.

Ayham Daher *et al*²¹ with 33 patients obtained a EQ-EVA score of $6,00 \pm 1$; Nopp *et al*.¹⁶ obtained a VAS-QS of $6,37 \pm 1,79$.

In the survey carried out by Tabacof *et al*.²⁰ which included 156 patients, the visual analogue scale EQ-5D-5L was 6,4 (not reflecting standard deviation). In the study by Grace Y. Lamet *et al*¹⁹ with 165 patients obtained an EQ-EVA score of $6,5 \pm 2,06$.

Finally, the highest scores were obtained in the 150 patients of Garrigues *et al*.¹⁸ with a EQ-EVA score of $7,03 \pm 2,15$ and in the 91-patient cohort of Taboada *et al*,²² with a score of $8,758 \pm 1,168$.

PCFS Scale

On the PCFS scale, most of our patients had a mild PCFS limitation of $1,58 \pm 1,130$, which is similar to other studies that have used this scale: score around 2 or 2,5, in other words, a higher functional limitation than that obtained in our sample.

In the study by Rehab M. Hamdy *et al*.¹⁷ study of 60 patients with PASC resulted in a PCFS score of $2,5 \pm 0,7$. Grace Y. Lamet *et al*¹⁹ of 165 patients report that those with exertional tolerance also reported greater functional impairment with higher PCFS scores (between 1 and 3) and lower health-related quality of life scores. Nopp *et al*¹⁶ who included 58 patients reported dysfunction graded by the PCFS scale with a median score of 2 (Interquartile range, 2-3).

Psychological evaluation

Schou *et al*²³ suggest that survivors are at risk of psychiatric sequelae (depression and/or anxiety up to >30% at follow-up). Taquet *et al*²⁴ report twice the risk of psychiatric illness compared to patients diagnosed with pathologies other than SARS-CoV-2. In another publication by Taquet *et al*²⁵ the estimated incidence of neuropsychiatric diagnosis in the following six months was 33,62%.

The meta-analysis by Lopez-Leon *et al*²⁶ which assess anxiety and depression and report a frequency of 13 and 14% respectively. In the meta-analysis by O'Mahoney *et al*.²⁷ they put depression at 13,29% and anxiety at 10,67%.

In our sample of 38 patients, 24 patients (63,2%) met criteria for anxiety and 24 patients (63,2%) had mild to severe depression. These figures are higher than in the literature reviewed. The mean GAD-7 anxiety score was $7,18 \pm 5,306$ and in PHQ-9 a mean score of $7,87 \pm 6,235$ was obtained.

In the study of Ayham Daher *et al*²¹ with a follow-up of 33 patients, according to the PHQ-9 and GAD-7 questionnaires, the patients suffered mostly from mild depression and anxiety (PHQ-9: median = 7 {ICR: 4-11}, GAD-7: median = 4 {IRC 1-9}, respectively). When compared to our study, the results of the PHQ-9 are similar, on the contrary, in the GAD-7 we obtained a higher score than in this study.

In the study by Stephen J. Ferrando *et al*²⁸ with 75 participants, we agreed on the GAD-7 score (mean $7,3 \pm 5,5$), but differed on the PHQ-9 score (mean $10,1 \pm 6,3$).

On the other hand, our study differs from the following studies:

In the assessment by Munam Raza Jafri *et al*²⁹ which included 70 people in the PHQ-9 questionnaire, only 8 (11,4%) had no depression, 17 (24,28%) had minimal depression, 27 (38,5%) had mild depression and the remaining 18 (40,4%) had moderate depression, moderately severe depression and severe depression. This study does not indicate the mean score, so we cannot compare data, but it does highlight that, unlike this study, where mild depression predominates, in our sample, minimal or absent depression predominates.

In the cross-sectional study by Hasan *et al*³⁰ conducted in Bangladesh with 237 patients, the overall prevalence of anxiety and depression was 55,7% and 87,3%, respectively. The mean score of the GAD-7 was $5,79 \pm 4,95$ and the mean score of the PHQ-9 was $5,64 \pm 5,15$. Among the depressed patients, 38,4% were predominantly mildly depressed and 32,1% moderately depressed, Likewise, 37,1%, 10,5% and 8% presented mild, moderate and severe anxiety levels, respectively. If we compare it with our data, our mean score on both scales is lower and on the other hand, in our study there is no predominance of mild depression but minimal or absent depression, but we do coincide in the predominance of mild anxiety.

In the survey of Tabacof L, *et al*.²⁰ of 156 patients, 19% of the patients scored 10 or more on the GAD-7 (as the mean score is not included we cannot compare with our study).

Assessment of cognitive sequelae.

Our PSI data gives an overall score of $40,97 \pm SD 32,924\%$, and for the MOCA scale, the mean score was $25,76 \pm 3,845$.

We agree on the MoCa score in the following studies:

Stephen J. Ferrando *et al*²⁸ analysed neurocognitive symptoms of 75 patients with a mean MoCA total score of $25,7 \pm 2,7$. They conclude that all patients with PASC should be screened for neuropsychiatric complications. Sean Lynch *et al*³¹ obtained a mean MoCA score of 26,1 (one third below the cut-off score of 26). In the study of Jacqueline E. Shanley *et al*³² with 44 participants the mean MoCA score was 26 ± 2 .

With respect to the PSI, we point out that it is a useful instrument for research and clinical use in acquired brain injury, degenerative dementias, chronic pain, fibromyalgia, addictive behaviours or personality disorders, widely used both in Spain and in Spanish-speaking countries³³. The challenge is to validate a version in English and probably this fact has conditioned the fact that we have not found any study that has related it to SARS-CoV-2 or PASC, making our study the first to evaluate it.

Limitations and strengths

As the survey was voluntary and face-to-face, some patients refused to take the survey for personal reasons.

Strengths include that it is a tertiary hospital where both hospitalized and outpatients patients have been evaluated in real clinical practice. Data and cognitive assessment were obtained personally by the principal investigator. Finally, we are the first study to evaluate the PSI in PASC.

Conclusions

1. Patients with PASC in our cohort present impairment in their health-related quality of life in different areas: the majority present a grade 1 or 2 on the mMRC scale, specifically 36,8% of them suffer from dyspnea when climbing, hills and 23,7% when walking with people of the same age; on the Euroqol scale, it predominates pain/discomfort (73,7%) and difficulty in mobility (55,2%) with an average score on the EQ-VAS of 5,38 +/- 1,915; finally, the mean PCFS was 1,58 +/- 1,13, which indicates limitations in their daily activities and involves reducing or avoiding activities to avoid symptoms.
2. Regarding the psychological affectation of the PASC patients evaluated in the questionnaire, we obtained an average score on the GAD-7 anxiety scale of 7,18 +/- 5,30, in which 24 patients (63,2%) presented anxiety at different levels with a predominance of mild grade 34,2%. On the PHQ-9 depression scale, an average score of 7,87 +/- 6,235 was obtained, with 14 patients (36,8%) meeting criteria for minimal or absent depression and 10 patients (26,3%) with mild depression.
3. Regarding the neurological evaluation, patients who reported cognitive alterations presented a higher PSI score (more self-reported prefrontal symptoms). In this scale we observe that men present more problems in attentional and motivational control, while women present them in executive control. The overall mean score of the MoCA scale was 25,76 +/- 3,845, being below normal in 14 patients (36,8%) and with predominance of involvement in the attention area.
4. It is important to note that the use of standardized clinical, neurological and functional scales is essential for the initial evaluation and follow-up of patients.
5. PASC can be a disabling illness resulting in physical limitations, neuropsychiatric sequelae and impairment of individuals' functionality. Therefore, multidisciplinary assessment, planning of rehabilitation therapies, strengthening of mental health services and resources are necessary.

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ANNEX 1. SURVEY

SARS-COV-2 AFFECTATION ASSESSMENT SURVEY

Instructions

Please take a few minutes to complete this survey about your overall health. We value your feedback and your answers will be kept confidential. Thank you for your input.

Clinical information

Name (Optional)	Date of diagnosis or onset of symptoms of SARS-CoV-2	(/ /)
Age:	Were you vaccinated at the time of infection?	Yes/No. Dosage: 1/2/3
Gender:	Have you been admitted to hospital?	Yes/No.
Weight: Size:	Has he/she been admitted to the ICU?	Yes/No.
Country of birth:		

Mark with an **X** if you have or take medication for the following conditions.

Diabetes	☐	Rheumatoid arthritis,	☐
Hypertension	☐	Rheumatological disease or lupus	☐
Cholesterol	☐	Tobacco	☐
Renal insufficiency	☐	Asthma	☐
Haemodialysis	☐	Disease	☐
Thyroid	☐	chronic pulmonary	☐
Ictus	☐	Liver disease	☐
Cardiac infarction	☐	or cirrhosis	☐
Thrombosis (PET/PVT)	☐	Transplant (Specify)	☐
Cancer (Specify) _____	☐	(Renal/Liver/Pancreas/Lung/Heart)	☐
Lymphoma, leukaemia	☐	Depression	☐
Immunosuppression	☐	Other (Specify)	☐

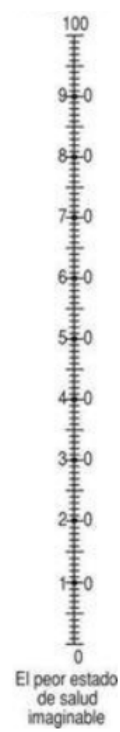
SYMPTOMS: **Mark** with an **X** if you are CURRENTLY experiencing the following symptoms DUE TO SARS-CoV-2 infection.

Fever	☐	Nasal itching or runny nose	☐
Fatigue	☐	Muscle pain	☐
Coughing (or increased their usual cough)	☐	Nausea/vomiting	☐
Palpitations	☐	Diarrhoea	☐
Sweating	☐	Headache	☐
Skin blemishes	☐	Dullness, problems of memory or concentration	☐
Hair loss	☐	Dizziness	☐
Loss of taste	☐	Insomnia	☐
Olfactory impairment	☐	Other (Specify) _____	☐
General malaise	☐		

General symptoms. I have had shortness of breath or difficulty breathing. Please circle one answer.				
With intense exercise	When going uphill or fast on the flat	Walking with people my age	At 100 metres on the flat	When I leave the house, when I get dressed or undress me

General symptoms. Please circle one answer.			
Mobility	I have no problem walking	I have some problems walking	I have to be in bed
Personal care	I have no problems	Some problems	Unable to perform personal care
Daily activities (work, study, household chores, family activities, leisure time)	I have no problems	Some problems	I am incapable.
Pain or discomfort	I have no pain	Moderate pain or discomfort	A lot of pain or discomfort

EUROQOL health self-assessment thermometer. We would like you to tell us on this scale, in your opinion, how good or how bad your state of health is TODAY.



In the last 2 weeks, how often have you been bothered by the following. Please place one cross in each row.	No. Not at all	Several days	More than half of the days	Almost every day
1. I have felt nervous or anxious.				
2. Unable to stop or control the worry.				
3. Worried too much about different things				
4. Difficulty relaxing				
5. I am so tired that it is even difficult to sit down				
6. I get angry or irritable easily				
7. I am afraid that something bad might happen				
8. Little interest or pleasure in doing things				
9. I feel low, depressed or hopeless.				
10. I have difficulty falling asleep or I sleep too much.				
11. Feeling tired or low in energy				
12. Little or too much appetite				
13. I feel bad about myself or that I will let myself or my family down.				
14. Difficulty in concentrating on things like reading the newspaper or watching television.				
15. I move or speak so slowly that other people have noticed - or conversely, so energetically that I have moved more than usual.				
16. Thoughts of wishing you dead or wanting to harm you in some way.				
If you have had a problem, how difficult was it for you to work, do homework or socialise with friends?	No difficulties	Some difficulty	Much difficulty	Extremely difficult

How are you CURRENTLY affected by SARS-CoV-2 in your day-to-day life?	Mark X in ONLY ONE of the following boxes
No limitations in my daily life and no covid-related symptoms, pain, anxiety or depression.	
I have SLIGHT limitations in my life and can carry out tasks and activities although I still have covid-related symptoms, pain, anxiety or depression.	
Because of the symptoms, I SUFFER LIMITATIONS in my daily life and occasionally I AVOID OR REDUCE daily activities or need to space them out. But I am able to do them.	
I SUFFER LIMITATIONS in my daily life and I AM NOT ABLE to perform daily activities because of symptoms, pain, anxiety or depression, but I can take care of myself without help.	
I SUFFER SEVERE LIMITATIONS in my daily life: I AM NOT ABLE to perform daily activities and NEED ASSISTANCE or care from another person because of symptoms, pain, depression or anxiety.	

ANNEX 1.1. PSI INVENTORY OF THE SURVEY³⁴

INVENTARIO DE SÍNTOMAS PREFRONTALES (ISP)

INSTRUCCIONES

A continuación se le plantearán 46 afirmaciones sobre cuestiones de la vida cotidiana que usted puede experimentar o no. Marque en la opción que mejor le represente. Señale con una X sobre la casilla NUNCA O CASI NUNCA si cree que esa afirmación no es correcta sobre usted; POCAS VECES si es algo que le ha pasado, pero en contadas ocasiones; A VECES SÍ Y A VECES NO, si le sucede o no le sucede con la misma frecuencia; MUCHAS VECES si es algo que le pasa a menudo; y SIEMPRE O CASI SIEMPRE si la afirmación define su modo habitual de pensar o actuar.

POR FAVOR, RESPONDA A TODAS LAS PREGUNTAS.

		NUNCA O CASI NUNCA	POCAS VECES	A VECES SÍ Y A VECES NO	MUCHAS VECES	SIEMPRE O CASI SIEMPRE
1	Tengo problemas para empezar una actividad. Me falta iniciativa					
2	Me resulta difícil concentrarme en algo					
3	No puedo hacer dos cosas al mismo tiempo (por ejemplo, preparar la comida y hablar)					
4	Río o lloro con demasiada facilidad					
5	Me enfado mucho por cosas insignificantes. Me irrito con facilidad					
6	Tengo poca capacidad para resolver problemas					
7	Mezclo algunos episodios de mi vida con otros. Me confundo al intentar ponerlos por orden					
8	Llego tarde a mis citas					
9	Me cuesta adaptarme a los cambios de mis rutinas					
10	Hablo con desconocidos como si les conociera					
11	Me distraigo con facilidad					
12	Tengo problemas para cambiar de tema en las conversaciones					
13	Ciertas cosas me cabrean demasiado y en esos momentos me paso de la raya					
14	Estoy como aletargado, como adormecido					
15	Tengo dificultades para tomar decisiones					
16	Hablo fuera de turno interrumpiendo a los demás en las conversaciones					
17	Me olvido de que tengo que hacer cosas pero me acuerdo cuando me lo recuerdan					
18	Se me echa la hora encima con mucha facilidad					
19	No hago las cosas sin que alguien me diga que las tengo que hacer					
20	Tengo dificultades para seguir el argumento de una película o un libro					
21	Tengo dificultad para pensar cosas con antelación o para planificar el futuro.					

		NUNCA O CASI NUNCA	POCAS VECES	A VECES SÍ Y A VECES NO	MUCHAS VECES	SIEMPRE O CASI SIEMPRE
22	Puedo pasar de la risa al llanto con facilidad					
23	Descuido mi higiene personal					
24	No me entusiasmo con las cosas. No me interesa ninguna actividad					
25	Corro riesgos sólo por el placer de hacerlo aunque me meta en líos por ello					
26	Me cuesta cambiar de planes cuando las cosas están saliendo mal					
27	Cuento chistes inapropiados en situaciones inapropiadas					
28	Actúo como si las demás personas no existieran					
29	Me cuesta ponerme en marcha. Me falta energía					
30	Repito los mismos errores. No aprendo de la experiencia					
31	Cuando hay ruido en la calle tengo problemas para pensar con claridad					
32	Me cuesta planificar las cosas con antelación					
33	Toco o abrazo a la gente aunque no los conozca demasiado					
34	Doy portazos, golpeo muebles o lanzo cosas por el aire cuando me cabreo					
35	Me cuesta encontrar la solución a los problemas					
36	Hago las cosas impulsivamente					
37	Hago comentarios sobre temas muy personales delante de los demás					
38	Tengo ganas de hacer algunas cosas, pero luego no las hago					
39	Hago o digo cosas embarazosas					
40	Me confundo cuando estoy haciendo cosas en un orden					
41	Tengo explosiones emocionales sin una razón importante					
42	Tengo problemas para entender lo que otros quieren decir					
43	Me manifiesto ante los demás de una manera sensual. Coqueteo demasiado					
44	Hago o digo cosas que no debo cuando estoy con otras personas.					
45	Hago comentarios sexuales inapropiados					
46	Todo me resulta indiferente. Me dan igual las cosas					

ANNEX 1.2. MOCHA SURVEY INVENTORY³⁵

MONTREAL COGNITIVE ASSESSMENT (MOCA) (EVALUACIÓN COGNITIVA MONTREAL)

NOMBRE:
Nivel de
estudios:
Sexo:

Fecha de nacimiento:
FECHA:

VISUOESPACIAL / EJECUTIVA		Copiar el cubo		Dibujar un reloj (Once y diez) (3 puntos)		Puntos		
				☐ Contorno ☐ Números ☐ Agujas		___/5		
IDENTIFICACIÓN								
						___/3		
MEMORIA	Lea la lista de palabras, el paciente debe repetirlas. Haga dos intentos. Recuérdese las 5 minutos más tarde.		ROSTRO	SEDA	IGLESIA	CLAVEL	ROJO	Sin puntos
	1er intento							
	2º intento							
ATENCIÓN	Lea la serie de números (1 número/seg.) El paciente debe repetirla. ☐ 2 1 8 5 4 El paciente debe repetirla a la inversa. ☐ 7 4 2						___/2	
	Lea la serie de letras. El paciente debe dar un golpecito con la mano cada vez que se diga la letra A. No se asignan puntos si ≥ 2 errores. ☐ FBACMNAAJKLBAFAKDEAAAJAMOFAB						___/1	
	Restar de 7 en 7 empezando desde 100. ☐ 93 ☐ 86 ☐ 79 ☐ 72 ☐ 65 4 o 5 sustracciones correctas: 3 puntos, 2 o 3 correctas: 2 puntos, 1 correcta: 1 punto, 0 correctas: 0 puntos.						___/3	
LENGUAJE	Repetir: El gato se esconde bajo el sofá cuando los perros entran en la sala. ☐ Espero que él le entregue el mensaje una vez que ella se lo pida. ☐						___/2	
	Fluidez del lenguaje. Decir el mayor número posible de palabras que comiencen por la letra "P" en 1 min. ☐ _____ (N ≥ 11 palabras)						___/1	
ABSTRACCIÓN	Similitud entre p. ej. manzana-naranja = fruta ☐ tren-bicicleta ☐ reloj-regla ☐						___/2	
RECUERDO DIFERIDO	Debe acordarse de las palabras SIN PISTAS	ROSTRO	SEDA	IGLESIA	CLAVEL	ROJO	Puntos por recuerdos SIN PISTAS únicamente	___/5
		☐	☐	☐	☐	☐		
Optativo	Pista de categoría							
	Pista elección múltiple							
ORIENTACIÓN	☐ Día del mes (fecha) ☐ Mes ☐ Año ☐ Día de la semana ☐ Lugar ☐ Localidad						___/6	
© Z. Nasreddine MD Versión 07 noviembre 2004 www.mocatest.org						Normal ≥ 26 / 30 TOTAL ☐ /30 Añadir 1 punto si tiene ≤ 12 años de estudios		

ANNEX 2. mMRC

Modified Medical Research Council Scale (mMRC)³⁶

Grade 0	I just get out of breath with the intense exercise.
Grade 1	I get short of breath when rushing on flat terrain or when walking uphill.
Grade 2	On flat terrain, I walk slower than people of the same age due to lack of air, or I have to stop to breathe when I walk at my own pace on the flat.
Grade 3	I stop to breathe after walking about 100 metres or after a few minutes on flat terrain.
Grade 4	I am too short of breath to leave the house or I am out of breath when I get dressed.

ANNEX 3. EUROQOL

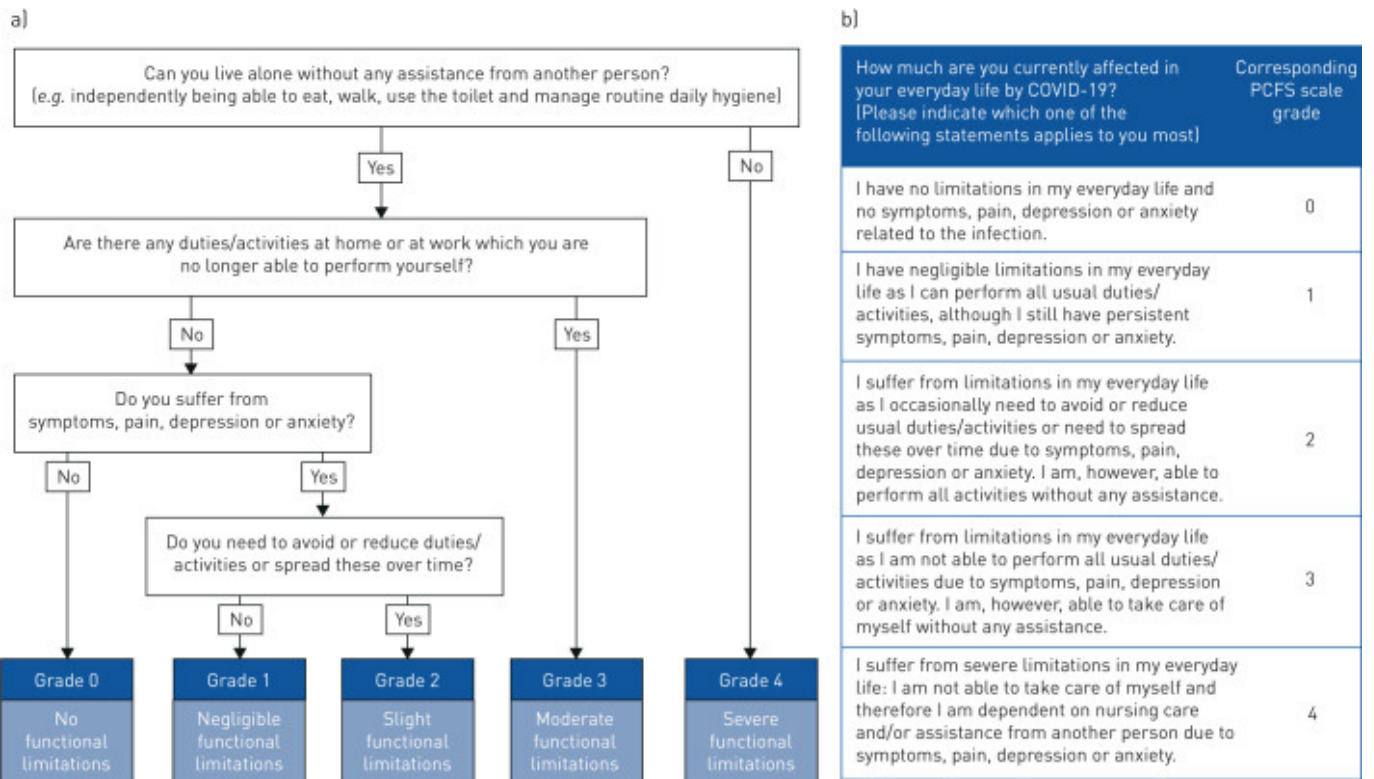
EUROQOL scale³⁷ and self-assessment health status thermometer.

Mobility.	I have no problems	Some problems	I have to be in bed
Personal care	I have no problems	Some problems	Unable to perform personal care
Day-to-day activities	I have no problems	Some problems	I am incapable.
Pain or discomfort	I have no pain	Moderate pain or discomfort	A lot of pain or discomfort



ANNEX 4. PCFS

Patient self-report methods for the post-COVID-19 functional status scale (PCFS) .¹⁴. A flow chart.



ANNEX 5. PHQ-9

The Patient Health Questionnaire (PHQ-9)³⁸

In the last 2 weeks, how often have you had discomfort due to the following problems?	No day	Several days	More than half of the days	Almost every day
1. Little interest or pleasure in doing things	0	1	2	3
2. I feel low in mood, depressed or hopeless.	0	1	2	3
3. I have difficulty falling asleep or I sleep too much.	0	1	2	3
4. Feeling tired or low in energy	0	1	2	3
5. Little or too much appetite	0	1	2	3
6. I feel bad about myself or that I will disappoint myself or my family.	0	1	2	3
7. Difficulty concentrating on things like reading the newspaper or watching TV.	0	1	2	3
8. I move or speak so slowly that other people have noticed - or conversely, so energetically that I have moved more than usual.	0	1	2	3
9. Thoughts of wishing you dead or wanting to harm you in some way.	0	1	2	3

The severity of depression symptoms can be organized into 4 categories:

- 0-4 (Minimum Depression)
- 5-9 (Mild depression)
- 10-14 (Moderate depression)
- 15-19 (Moderately severe depression)
- 20-27 (Severe depression)

ANNEX 6. GAD-7

The Generalised Anxiety Disorder Scale (GAD-7)³⁹

In the last 2 weeks, how often have you been bothered by the following?	Not at all	Several days	More than half of the days	Almost every day
1. I have felt nervous or anxious.	0	1	2	3
2. Unable to stop or control the worry.	0	1	2	3
3. Worried too much about different things	0	1	2	3
4. Difficulty relaxing	0	1	2	3
5. I am so tired that it is even difficult to sit down	0	1	2	3
6. I get angry or irritable easily	0	1	2	3
7. I am afraid that something bad might happen	0	1	2	3

Each of the 7 items is scored from 0 to 3, providing a severity score from 0 to 21.

Interpretation:

- 5-9 = Mild Anxiety
- 10-14 = Moderate anxiety
- 15-21 = Severe anxiety