Master of Public Health
Master de Santé Publique

“Longitudinal impact of Post Covid-19 Condition on health related quality of life between 2 and 3 years after SARS-CoV-2 infection – results from CORFU and Long CORFU study”

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List of acronyms

CORFU	CORona Follow-Up (CORFU) study
COVID-19	Coronavirus disease 2019
EQ-5D	EuroQol- 5D
EQ VAS	EuroQol Visual Analogue Scale
HRQoL	Health related quality of life
ICU	Intensive Care Unit
PCC	Post COVID-19 Condition(s)
PROMs	Patient-reported outcome measures
PTSD	Post-traumatic stress disorder
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
WHO	World Health Organization

Abstract

Introduction: Post COVID-19 Condition (PCC) is associated with impairment of health-related quality of life (HRQoL), however there is limited long-term evidence. This study assessed the impact of PCC on changes in HRQoL between 2 and 3 years after infection and identified predictors of changes within PCC individuals.

Objectives: The objectives were to 1) assess changes in HRQoL in COVID-19 survivors with and without PCC, 2) determine the effect of PCC on changes in HRQoL, and 3) explore associations of biopsychosocial factors with changes in HRQoL among PCC individuals.

Methods: 238 participants from Dutch cohort studies of COVID-19 survivors were prospectively followed 2 and 3 years after initial SARS-CoV-2 infection. PCC at 2 years was identified based on self-reported symptoms and HRQoL was quantified at both moments with EQ-5D utility and EQ VAS scores.

Results: EQ VAS scores did not differ significantly for PCC and no-PCC. The median (IQR) for utility scores did not differ for PCC, but did for no-PCC: 0.887 (0.817, 1.0) to 0.919 (0.852, 1), *P*=0.008. The effect of PCC on change in VAS scores was 1.6 points (95% CI -2.6 , 5.8; *P*: 0.4) and on change in utility -0.03 points (95% CI -0.07,0.02; *P*=: 0.3). Social engagement was associated with change in VAS scores and an interaction between education level and ethnicity was found on change in utility scores.

Conclusions: HRQoL remained stable over time for PCC and improved for no-PCC on the utility outcome. Variation in changes within PCC individuals were not associated with sociodemographic or clinical characteristics. Higher HRQoL improvement might be expected for those with social engagement issues. PCC may be hindering improvement

of HRQoL over time. Therefore, more studies are needed to understand the variability in HRQoL changes among COVID-19 survivors.
Key words: Post COVID-19 Condition, Health related quality of life, COVID-19

1. Introduction

Evidence suggests that Post COVID-19 Condition (PCC) can persist for several years after initial infection, and that it may be affecting millions of people across the European Region (1–5). PCC refers to a broad range of new, returning or persistent symptoms present after the recovery from a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and that has no alternative explanation or diagnosis (6,7). Some populations like women, specifically of younger age, have been reported to have more severe symptoms of PCC(8–10). Higher severity of the initial acute COVID-19 illness (hospitalization or Intensive Care Unit admission) possess a higher risk of developing PCC(6), however symptoms may also appear after mild and moderate severity of the initial disease (11,12). PCC related symptoms or signs, include fatigue, shortness of breath, cough, chest pain, heart palpitations, sleep disorder, myalgia, depression, anxiety, PTSD, cognitive deficits and memory impairment, amnesia and concentration, among others (13).

The growing concern about PCC is due to its association with lower overall health status, lower health-related quality of life (HRQoL), functional impairment, negative mental health outcomes, impaired ability to work and to do daily life activities, problems with social engagement and excess burden of reported morbidities (1,4,11,12,14–19). Additionally, PCC could potentially lead to other complications over time, leading to further impairment of HRQoL. The physical limitations caused by PCC may increase the risk of permanent disabilities (20,21) and reduction of social engagement (22), which in turn relates to a higher risk of psychological distress (23). Also, adding PCC to other existing diseases may generate or magnify the burden of living with multimorbidity (24). Moreover, the financial burden due to hospitalization and care costs of COVID-19 may be worsened by the loss of income due to impaired ability to work and current costs of treatment or care of PCC (16,17). The consequences of PCC may exacerbate health inequalities among populations that are already more vulnerable, like those of advanced age, with preexisting disabilities, belonging to a racial or ethnic minority group, and having lower socioeconomic status (13,25–28). Women with PCC may face a double burden of reduced quality of life due to gender-disability related disparities (29), as they are at greater risk of developing functional impairment and role limitations due to the physical health problems and bodily pain caused by PCC (12,30).

Research suggests that while some people with PCC may recover, the timeline and extent of recovery can differ significantly amongst populations of different severity of the acute COVID-19 disease, age groups and comorbidities (31,32). The use of biopsychosocial approaches in illness recovery have shown that multiple factors interact and moderate changes in perceived quality of life(33,34). Moreover, social determinants are known to significantly influence health seeking behaviors and access to resources aimed at preventing, treating, and mitigating the effects of chronic diseases (35). Consequently, some individuals with PCC may effectively cope with their condition over time, while others may face multiple challenges that hinder their recovery process, and/or progressively worsen their quality of life. However, given the recent emergence of COVID-19 the availability of longitudinal evidence on long-term PCC is limited and thus, adequately predicting changes in HRQoL over time remains a challenge.

The first aim of this study was to assess the impact of PCC on longitudinal changes in HRQoL among COVID-19 survivors. To achieve this, two research objectives were established: 1) To assess and compare group-level changes in HRQoL, from 2 to 3 years after initial SARS-CoV-2 infection, for individuals with and without PCC, and 2) to determine the effect of PCC on individual changes in HRQoL in the period from 2 to 3 years after initial SARS-CoV-2 infection, among COVID-19 survivors who sought hospital healthcare in the Netherlands.

The second aim was to explore if variability of longitudinal changes in HRQoL among individuals with PCC is influenced by biopsychosocial factors and sociodemographic characteristics. For this, a third research objective was established: to determine the associations of acute COVID-19 illness severity, living with other preexisting morbidities, social engagement, social relationships, living arrangement, age, sex, working status, socioeconomic status, and ethnicity with individual changes in HRQoL in the period from 2 and 3 years after initial SARS-CoV-2 infection among individuals with PCC from the above-mentioned population.

Working conditions and student Contribution

The following work was carried out at the facilities of the Clinical Epidemiology & Medical Technology Assessment (KEMTA) department, at Maastricht University Medical Center (MUMC+), under the supervision of Dr Sander van Kuijk and Dr Sophie Waardenburg. Dr Sander van Kuijk is an associate professor of clinical epidemiology, and Deputy Head of KEMTA; his expertise are clinical epidemiology and biostatistics, and he teaches both at the University of Maastricht. Dr Sophie Waardenburg, is the Senior researcher on COrona Follow Up (CORFU) Study at KEMTA and her expertise is Pain Medicine. Data

was accessed through the MUMC+ platform, using validated credentials to ensure data protection. The student managed the initial manipulation and analysis of the recently collected 3-year follow-up data from the three participating cohorts of the LONG CORFU study. She was responsible for cleaning and preparing the individual datasets for integration with the existing CORFU Study dataset, which was available at the start of her work. She performed all data management tasks and analyses for this study, and drafted this article, while continuously incorporating feedback from professional supervisors at KEMTA. The merged data significantly contributed to the objectives of the LONG CORFU study, with additional analyses currently underway.

2. Methods

2.1 Study design and data source

We conducted a longitudinal prospective cohort study by merging the data of the CORona Follow-Up (CORFU) study and the subsequent Long CORFU study. CORFU is a longitudinal multiple cohort study that aggregated data of six existing COVID-19 cohorts from the Netherlands, and a national survey assessed in the general Dutch population, prospectively complemented with routinely collected outcome data on PCC-related symptoms and a selection of patient-reported outcome measures (PROMs) for several follow up moments up to 2 years after acute SARS-CoV-2 infection(36). Long CORFU was a subsequent study that added a 3 year follow-up on all these complementary data. Three of the six CORFU cohorts (“Bernhoven early detection of vascular damage after COVID-19 (COVAS) cohort”, “MaastrICCht” cohort and “ZuydErLand COVID-19 regiStry (ELVIS)” cohort) contributed to the 3 year follow-up data for Long CORFU.

2.2 Study population and inclusion criteria

Patients were included in one of the COVID-19 cohorts if they had a confirmed or suspected infection of SARS-CoV-2 during the period of March-December of 2020 (first COVID-19 waves), if they were at least 18 years of age and had good knowledge of Dutch language. The SARS-CoV-2 infection was assessed by a positive PCR or a positive scored CT scan of the chest (4 or 5on CO-RADS by a radiologist). The MaastriCCht” cohort included patients admitted to the Intensive Care Unit (ICU). Both the COVAS and ELVIS cohorts included patients admitted to the Ward, UCI or at the Emergency room but subsequently sent home for recovery. All participants from the separate cohort studies were considered eligible and were asked to participate in the CORFU and Long CORFU studies. More information on individual cohort description is available elsewhere (36). For the current study, only those who participated in the 2-year

follow-up were considered eligible, and from those, only participants who participated in the 3- year follow-up were included.

2.3 Data collection and measurement

Initial infection and illness details and baseline characteristics, including age and ethnicity were collected at the time of hospital admission and assessed through medical records. The complementary follow-up data (including PCC related symptom severity, PROMs, living arrangement, working status, education level and preexisting morbidities) was collected through digital or paper-based CORFU questionnaires sent to participants at each follow-up moment. Participants completed the questionnaires individually or assisted by caregivers. The questionnaire consisted, among other domains, of a modified version of EuroQol's 5Q-5D-5L instrument in Dutch language, where participants were asked to rate the severity of each item using a Likert scale (1-5): 1-No problems, 2-slight problems, 3-moderate problems, 4-severe problems, 5-unable to /extreme problems. The questions included, among others, problems with 13 PCC-related symptoms (cognition, fatigue, sleep, appetite, smell and taste, cough, breathing/shortness of breath, pain when breathing, chest pain and discomfort, palpitations, dizziness, swollen ankles/feet, muscle weakness/soreness), problems with 5 health dimensions (mobility, self-care, usual activities, pain and discomfort, and anxiety and depression), problems with social engagement and problems with social relationships. It also included a Visual Analogue Scale (VAS) where participants were asked to score their perceived present health in a graphic scale with marks from 0 to 100. Instructions were included for each question.

2.4 Definition of Variables

The exposure of PCC in this study was determined using the WHO definition (2): at least one symptom that persists after initial acute disease or develops after recovery and can't explained by other causes. PCC was considered present if in the 2-year follow-up questionnaire: 1) the participant scored at least one symptom with a severity level 3 or higher on the scale of 1 to 5, and 2) if the participant indicated that the symptom was not present before initial SARS-CoV-2 infection. When the definition was not met, the participant was categorized as not having PCC (comparison group).

The main outcome was the change of perceived HRQoL, between 2 and 3-years after initial SARS-CoV-2 infection. For this study, two EQ-5D-5L measures of HRQoL were used: the EQ-5D utility and the EQ VAS score. The EQ-5D utility is a score of health state calculated with a set of weights that reflect the health preferences from the Dutch population and with the reported scores from the 5 dimensions of health. EQ-5D Utility

scores could range from less than 0 (where 0 is the value of a health state equivalent to dead; negative values representing values as worse than dead) to 1 (the value of full health), with higher scores indicating higher health utility. The EQ VAS score is the participant's perceived overall current HRQoL, where 0 is the worst imaginable health and 100 the best imaginable health, with higher VAS score indicating higher current health(37).

Potential confounders included sex, age at time of initial SARS-CoV-2 infection, ethnicity, working status at 2-year follow-up, living arrangement at 2-year follow-up and level of education at 2 year-follow-up. The latter was used as a proxy for Socioeconomic status, where "Low level" education was considered if the highest education achieved was Primary or Secondary, and "High level" education was considered if the highest education achieved was Higher Vocational Education or Scientific/academic. Severity of acute COVID-19 illness was determined by the place of treatment (ICU, hospital ward, home). The number of preexisting morbidities (before initial SARS-CoV-2 infection) were grouped by the presence of none, at least one, and more than one reported morbidity. Problems related to social engagement and problems with social relationships reported at 2- year follow-up, were both used as psycho-social factors, and they were considered as present if the participant reported a severity of 3 or higher on the scale of 1 to 5 at 2-year follow-up.

2.5 Addressing Potential sources of bias

To account for any possible bias due to attrition, a description of counts and frequencies for sociodemographic characteristics was done for participants lost to follow-up (participants who completed 2-year follow up questionnaires who did not complete 3-year questionnaire) and were compared to the characteristics of the participants of the final sample. Additionally, associations between characteristics of the participants and the event on participating on the 3-year follow-up questionnaire were analyzed using a logistic regression model.

2.6 Statistical methods

Missing data was reported in count and frequency for each variable. Descriptive summary of sociodemographic, clinical characteristics and reported difficulties with social engagement and social relationships was done using count and frequency of responses for categorical variables and, mean and Standard Deviation (SD) for continuous variables, and presented stratified by PCC status (PCC or no PCC). Between PCC status group differences were tested with Pearson's Chi-squared test, Wilcoxon rank sum test or Fisher's exact test. Variables with more than 50% of missing data were

not imputed and not included in the analysis and, for the rest, missing at random was determined and Multiple imputation using chained equations (MICE) was used to avoid introduction of bias and loss of statistical power compared to using only complete cases. Categories with low counts (< 3) were grouped where possible.

We described count and frequency of severity of problems for each of the EQ-5D-5L dimensions of health for both groups at 2 and 3 years after infection. Differences between 2 and 3 year frequencies for each dimension were compared with Wilcoxon signed-rank test. For the first objective, we computed the EQ-5D utility scores and described these and the EQ VAS scores for 2 and 3-years as median and Interquartile Range (IQR) stratified by PCC status. Differences between 2- and 3-year scores for each PCC status groups were tested using the Wilcoxon signed-rank test. Also, differences of 2-year EQ VAS scores and EQ-5D utility scores between PCC status groups were tested with Wilcoxon rank-sum test, and the same was done for the 3-year scores between both groups.

For the second objective, for each participant we computed their change score for both EQ-5D utility scores [Utility score $_{(3\text{-year follow-up})}$ – Utility score $_{(2\text{-year follow-up})}$], and EQ VAS scores [VAS score $_{(3\text{-year follow-up})}$ – VAS score $_{(2\text{-year follow-up})}$]. Next, the mean (SD) of individual change scores was calculated, and the comparison between PCC status groups was done using Welch's Two Sample t-test. The median and IQR of individual change scores were calculated to further explore variability of individual changes.

We used directed acyclic graphs to determine the structure of the multivariable regression models. Linear multivariable regression was used for the individual “changes of EQ-5D utility scores” outcome, and adjustment was done for potential confounders (age, sex, ethnicity, education level, severity of initial disease, living arrangement and number of pre-existing morbidities). We used the same regression model for the “changes in EQ VAS score” outcome. For the third objective, the same regression analysis method was used, but only individuals from the group with PCC were included. Covariates included age, sex, ethnicity, working status, education level, severity of initial disease, number of preexisting morbidities, problems with social relationships and social engagement. Relevant interactions between covariates were tested using cross product terms. Interaction terms were retained in the model if they were statistically significant and if enough representation was available between subgroups, to avoid introduction of bias. Results of regression analysis were reported as unadjusted and adjusted regression coefficients (betas), with their 95% Confidence Interval (95% CI), and p-value (*P*). Based on the results obtained on the multivariate regressions, additional subgroup

analysis was done to explore direction of changes. Comparison of mean(SD) between groups was done with using Welch's Two Sample t-test.

In accordance with standard statistical conventions, statistical significance was defined as p-values less than 0.05. RStudio version 4.3.1 was used for data analysis.

2.7 Ethical approval

Approval was obtained from the medical research ethics committee of Maastricht University Medical Center+ and Maastricht University (CORFU study: METC 2021-2990; Long CORFU study: METC 2021-2990-A-2) and local committees of the participating cohorts. The project is supported by ZonMW and EuroQol Research Foundation and is registered with the trial registration number: NCT05240742.

3. Results

3.1 Description of participants

The 364 individuals who completed the 2-year follow-up were invited to participate in the 3-year follow up, of those, a total of 238 participants were included in the study for analysis (*Figure 1*). The counts for each reason for non-participation were unknown for this study, as data collection depended on individual cohorts. The characteristics of participants loss to follow up can be found in *Supplementary Table S1*. Those loss to follow-up were more likely to be female, less likely to have problems with social relationships, more likely to have been treated at Home during the acute COVID-19 illness, less likely to be treated at ICU, compared to the final sample. No association was found for PCC status and for HRQoL outcomes at 2-year follow-up. After adjustment, only being treated in the ICU was significantly associated with likeliness of participation in the study (*Supplementary Table S 2).*

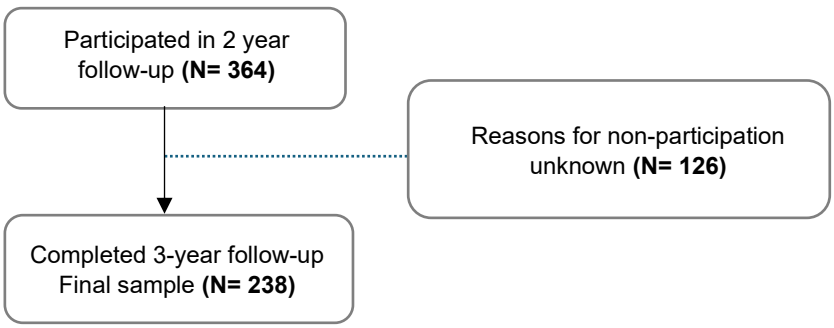

Figure 1. Flow diagram of study sample inclusion

A description of sociodemographic, psychosocial problems and clinical characteristics of participants, stratified by PCC status, is shown in *Table 1*. Participants from the final sample were mostly male (173/238, 73%), the age at time of initial infection ranged between 22 and 91 years, with a mean (SD) age of 64(11). Most participants were of Dutch ethnicity (231/234, 97%), retired (108/214, 50%), living with a partner (192/237, 81%), did not report problems with social engagement(187/217, 86%), and did not report problems with social relationships (194/219, 89%). More than half of the participants (144/238, 61%) reported at least one preexisting morbidity, and belonged to the groups: “home” (32/238, 13%), “hospital ward” (142/238, 60%) or “ICU” (64/238, 27%).

A total of 158 participants (66%) had at least one symptom that met the definition for PCC. The most frequent PCC symptoms were fatigue, muscle pain and weakness, and sleeping problems. A complete description of symptom frequency can be found in *Supplementary Table S 3*. Differences in characteristics between those with and without PCC were found in sex, working status, initial severity of disease, number of preexisting morbidities, presence of social engagement and social relationship problems.

Table 1 Characteristics of study participants by Post COVID-19 Condition (PCC) status classification.

Characteristic	**Missing[1]**	**Overall, N = 238[2]**	**PCC status**		**p-value[3]**
			No PCC, N = 80[2]	**PCC, N = 158[2]**	
Sex	0 (0%)				0.016
Female		65 (27%)	14 (18%)	51 (32%)	
Male		173 (73%)	66 (83%)	107 (68%)	
Age (at inclusion)	0 (0%)	64 (11)	65 (10)	64 (12)	0.481
Ethnicity	1 (0.4%)				0.667
Dutch		231 (97%)	79 (99%)	152 (97%)	
Non-Dutch		6 (2.5%)	1 (1.3%)	5 (3.2%)	
Level of education	3 (1.3%)				0.900
High		54 (23%)	18 (23%)	36 (23%)	
Low		181 (77%)	62 (78%)	119 (77%)	
Working status	24 (10%)				<0.001
Employed		63 (29%)	28 (41%)	35 (24%)	
Household/Caretaker		2 (0.9%)	1 (1.5%)	1 (0.7%)	
Partially due to health		17 (7.9%)	1 (1.5%)	16 (11%)	
Retired		108 (50%)	36 (53%)	72 (49%)	
Sick leave, incapacity, unemployed		24 (11%)	2 (2.9%)	22 (15%)	
Living arrangement	1 (0.4%)				0.200
Alone		35 (15%)	7 (8.8%)	28 (18%)	
Alone, with children		6 (2.5%)	3 (3.8%)	3 (1.9%)	
Parents or other		4 (1.7%)	1 (1.3%)	3 (1.9%)	
Partner, with or without children		192 (81%)	69 (86%)	123 (78%)	
Number of preexisting morbidities	0 (0%)				0.030
None		94 (39%)	41 (51%)	53 (34%)	

One		68 (29%)	19 (24%)	49 (31%)	
>1		76 (32%)	20 (25%)	56 (35%)	
Social Engagement problems	21 (8.8%)	30 (14%)	1 (1.4%)	29 (20%)	<0.001
Social Relationships problems	19 (8.0%)	25 (11%)	1 (1.4%)	24 (16%)	0.002
Severity of acute COVID-19 illness	0 (0%)				0.032
Home		32 (13%)	17 (21%)	15 (9.5%)	
Hospital Ward		142 (60%)	41 (51%)	101 (64%)	
ICU		64 (27%)	22 (28%)	42 (27%)	

[1] N Missing (% Missing)
[2] n (%); Mean (SD)
[3] Pearson's Chi-squared test; Wilcoxon rank sum test; Fisher's exact test
*Sex, age, ethnicity, number of preexisting morbidities and severity of acute COVID-19 illness are at baseline(at the time of the initial acute disease). Level of education, working status, living arrangement, problems with social engagement and problems with social relationships are at 2-year follow-up.

3.2 HRQoL outcomes at 2 and 3 years after initial infection

EQ VAS scores at 2-years between PCC and No PCC were significantly different (*P*=<0.001), and similar results were found for EQ VAS scores at 3-years between both groups (*P*=<0.001).

The response distribution for each of the EQ-5D-5L dimensions at 2-year follow-up, were similar to the distribution at 3-year follow-up, for both PCC status groups (*Supplementary Table S 4)*.

EQ-5D utility scores at 2-years between PCC and No PCC were significantly different (*P*=<0.001), and similar results were found for EQ-5D utility scores at 3-years between both groups (*P*=<0.001).

For the PCC group, median (IQR) EQ VAS scores at 2- and 3-year were 64 (50, 75) and 64 (50.25, 73.75), respectively, (*P*=0.671). For the No PCC group median (IQR) EQ VAS scores at 2 and 3 years were 80 (75, 79.8) and 80 (73, 90), respectively, (*P*= 0.664).

For the PCC group, the EQ-5D utility scores median (IQR) at both follow-ups were of 0.739 (0.596 , 0.821) and 0.743 (0.592 , 0.817) respectively, (*P*=0.596). For the No PCC, EQ-5D utility scores median (IQR) for 2 and 3 years were of 0.887 (0.817, 1.0) and 0.919 (0.852, 1), respectively, (*P*=0.008).

3.3 Individual change scores of HRQoL outcomes (from 2 to 3 years after initial infection)

The mean (SD) change in VAS scores was for the PCC of 0.91 points (15.60), and for the No PCC group of 0.16 points (12.01), *P*=0.685. Additionally, the changes median (IQR), in EQ VAS scores was for the PCC group of 0.00 points (-9.0 , 9.75) and for No PCC group of 0.00 points (-5.25, 5.00).

The mean change in EQ-5D utility scores, was for the PCC group of 0.008 points (0.18) and for the No PCC of 0.032 points (0.10), *P*=0.20. The change median (IQR) in EQ-5D utility scores was for the PCC group of 0.00 points (-0.076, 0.084) and for the No PCC group of 0.00 points (0.00 , 0.105).

Difference in mean change of EQ VAS scores between those with and without PCC was 0.74 points (CI 95% -3.2, 4.7; *P*= 0.7) and after adjustment 1.6 points (95% CI -2.6 , 5.8; *P*: 0.4) (*Table 2*). The difference in mean change of EQ-5D utility scores between those with and without PCC was -0.02 points (95% CI -0.07, 0.02; *P*=: 0.3) and after adjustment -0.03 points (95% CI -0.07,0.02; *P*=: 0.3) (*Table 3*).

Table 2. Unadjusted and adjusted regression coefficients (Betas), changes in EQ VAS score

Characteristic	Unadjusted				Adjusted *		
	N	Beta	95% CI[1]	p-value	Beta	95% CI[1]	p-value
PCC Status	238						
PCC		0.74	-3.2, 4.7	0.7	1.6	-2.6, 5.8	0.4

[1] CI = Confidence Interval

*****Adjusted for sex, age, ethnicity , education level, severity of acute COVID-19 illness, and presence of preexisting morbidities. “No PCC” is the reference.

Table 3. Unadjusted and adjusted regression coefficients (Betas), changes in EQ-5D Utility scores

Characteristic	Unadjusted				Adjusted *		
	N	Beta	95% CI[1]	p-value	Beta	95% CI[1]	p-value
PCC Status	238						
PCC		-0.02	-0.07, 0.02	0.3	-0.03	-0.07, 0.02	0.3

[1] CI = Confidence Interval

*****Adjusted for sex, age, ethnicity , education level, severity of acute COVID-19 illness, and presence of preexisting morbidities. “No PCC” is the reference.

3.4 Multivariate analysis: individual changes within the PCC group

Not many statistically significant associations were observed between sociodemographic, clinical or psychosocial characteristics and mean changes in EQ VAS scores within those with PCC. After adjustment for other covariates, an association was found for social engagement problems, where the difference in mean change in VAS scores between those with social engagement problems compared to those without was of 11 points (95% CI 2.8- 20; *P*=0.003). For all other covariates, no significant associations were found, neither were there significant interaction terms using cross products (*Table 4*).

Also, not many statistically significant associations were observed between sociodemographic, clinical, or psychosocial characteristics and mean changes in EQ-5D utility scores within those with PCC after adjustment. However, a significant interaction

was found for ethnicity and education level (0.37 points , *P*=0.024), the effect of having low education on change was greater for those with non-Dutch ethnicity than for those with Dutch ethnicity. Interaction term for sex and number of pre-existing morbidities was of 0.10 (*P*=0.057) (*Table 5).*

Table 4. Regression coefficients, 2 to 3 year changes in EQ VAS score within the PCC group

Characteristic	Unadjusted			Adjusted		
	Beta	**95% CI[1]**	**p-value[2]**	**Beta**	**95% CI[1]**	**p-value[2]**
Sex			0.372			0.300
Female	—	—		—	—	
Male	2.4	-2.9, 7.6		3.0	-2.7, 8.7	
Age	-0.16	-0.37, 0.05	0.134	0.01	-0.30, 0.33	0.926
Ethnicity			0.477			0.203
Dutch	—	—		—	—	
Non-Dutch	-5.1	-19, 9.0		-9.4	-24, 5.1	
Working status			0.721			0.890
Employed	—	—		—	—	
Household/Caretaker	0.98	-30, 32		-12	-46, 22	
Partially due to health	1.7	-7.3, 11		-4.2	-14, 5.5	
Retired	-3.0	-8.8, 2.8		-2.0	-9.6, 5.7	
Sick leave, incapacity, unemployed	0.66	-7.4, 8.7		-3.0	-12, 6.2	
Level of education			0.526			0.538
High	—	—		—	—	
Low	-1.9	-7.7, 4.0		-2.1	-8.9, 4.7	
Living arrangement			0.223			0.344
Alone	—	—		—	—	
Alone, with children	11	-7.5, 30		15	-5.3, 36	
Parents or other	4.8	-14, 23		0.68	-20, 21	
Partner, with or without children	6.5	0.08, 13		5.1	-1.9, 12	
Severity of acute COVID-19 illness			0.694			0.671
Home	—	—		—	—	
Hospital Ward	-3.6	-12, 4.9		-4.3	-14, 5.6	
ICU	-3.7	-13, 5.7		-4.6	-15, 5.9	
Number of preexisting morbidities			0.567			0.753
None	—	—		—	—	
One	0.77	-5.3, 6.9		0.60	-5.8, 7.0	
>1	-2.3	-8.3, 3.6		-1.7	-8.1, 4.6	
Social engagement problems	10	3.8, 16	**0.002**	11	2.8, 20	**0.010**
Social relationships problems	5.5	-1.2, 12	0.104	1.7	-6.5, 9.9	0.687

[1] CI = Confidence Interval

[2] Global p-value, p-values < 0.05 are in bold

Sex, age, ethnicity, number of preexisting morbidities and severity of acute COVID-19 illness are at baseline(at the time of the initial acute disease). Level of education, working status, living arrangement, problems with social engagement and problems with social relationships are at 2-year follow-up.

Table 5. Regression coefficients, 2-to-3-year individual changes in EQ-5D utility scores among the PCC group

Characteristic	Unadjusted			Adjusted		
	Beta	95% CI[1]	p-value[2]	Beta	95% CI[1]	p-value[2]
Sex			0.167			0.42
Female	—	—		—	—	
Male	0.04	-0.02, 0.10		-0.04	-0.15, 0.06	
Age	0.00	0.00, 0.00	0.154	0.00	0.00, 0.00	0.721
Ethnicity			0.004			0.568
Dutch	—	—		—	—	
Non-Dutch	0.23	0.08, 0.39		0.06	-0.15, 0.27	
Working status			0.1635			0.442
Employed	—	—		—	—	
Household/Caretaker	0.17	-0.18, 0.52		0.27	-0.11, 0.64	
Partially due to health	0.06	-0.04, 0.16		0.00	-0.11, 0.11	
Retired	-0.01	-0.07, 0.06		-0.01	-0.10, 0.07	
Sick leave, incapacity, unemployed	0.08	-0.01, 0.17		0.06	-0.04, 0.16	
Level of education			0.870			0.900
High	—	—		—	—	
Low	0.01	-0.06, 0.07		0.00	-0.07, 0.08	
Living arrangement			0.707			0.508
Alone	—	—		—	—	
Alone, with children	0.08	-0.14, 0.29		0.10	-0.13, 0.32	
Parents or other	-0.09	-0.30, 0.13		-0.09	-0.31, 0.14	
Partner, with or without children	0.01	-0.07, 0.08		-0.03	-0.11, 0.04	
Severity of acute COVID-19 illness			0.4473			0.505
Home	—	—		—	—	
Hospital Ward	0.04	-0.06, 0.14		0.06	-0.05, 0.17	
ICU	0.07	-0.04, 0.17		0.07	-0.05, 0.18	
Number of preexisting morbidities			0.766			0.122
None	—	—		—	—	
One	-0.01	-0.08, 0.06		-0.13	-0.25, 0.00	
>1	-0.03	-0.09, 0.04		-0.09	-0.21, 0.03	
Social engagement problems	0.12	0.05, 0.19	<0.001	0.06	-0.03, 0.15	0.183
Social relationships problems	0.09	0.01, 0.17	0.020	0.06	-0.03, 0.15	0.209
Sex * Number of preexisting morbidities						0.057
*Male * One*				0.19	0.04, 0.35	
*Male * >1*				0.10	-0.05, 0.24	
Ethnicity * Level of education						**0.024**
*Other * Low*				0.37	0.05, 0.68	

[1] CI = Confidence Interval

[2] Global p-value, p-values < 0.05 are in bold

Sex, age, ethnicity, number of pre-existing morbidities and severity of acute COVID-19 illness are at baseline(at the time of the initial acute disease). Level of education, working status, living arrangement, problems with social engagement and problems with social relationships are at 2-years after initial acute disease.

3.5 Additional analysis, exploration of direction of individual changes

Withing the PCC group, mean (SD) change of VAS score for those with and without social engagement problems was of 9.07 (20.57) and -0.93 (13.69) respectively, (*P*=0.018). Within the subgroup of PCC people with low education, mean (SD) change in utility scores of non-Dutch ethnicity was 0.45, while for Dutch was 0 (0.18) , P=0.3.

4. Discussion

4.1 Interpretation of main findings

The first aim of this study was to assess the long-term impact of PCC on longitudinal changes in HRQoL by comparing group-level HRQoL outcomes 2 and 3 years after acute COVID-19 illness and finding an association of the presence of PCC with individual changes in HRQoL over time. In this study, we followed COVID-19 survivors from the Dutch population from 2 to 3 years after initial SARS-CoV-2 infection. HRQoL was quantified with EQ VAS and EQ 5D utility measurements. Our findings show that the significant difference of HRQoL between PCC and No PCC groups, observed at 2 years, remained one year later, indicating that those with PCC still have significant lower HRQoL 3 years after initial infection. When analyzing group-level changes from 2 to 3 years, HRQoL quantified with EQ VAS scores, did not change significantly. This held for both COVID-19 survivors with and without PCC. This lack of longitudinal change was also observed when looking at the EQ-5D-5L dimensions in the PCC and no PCC group, no differences were found between the 2-year and 3-year distributions. This result partly aligns to a study that measured the effects of PCC on HRQoL between 1 and 2 years after initial infection, where distributions of the EQ-5D-5L dimensions: anxiety and depression, mobility, and self-care at year 1 were similar to those at 2 years after initial infection. However their study did find that although the difference was not significant, the dimensions on the ability to perform usual activities and pain/discomfort, showed a slight improvement (4). However, participants of this study were mostly females and of younger average age.

A similar study that followed COVID-19 survivors 2 to 3 years after initial infection, found a significant improvement in the HRQoL Mental Components Scale scores (from the standardized 36-item Short Form Survey SF-36 questionnaire) over that year period for COVID-19 survivors with and without PCC(38). Interestingly, in our study, EQ-5D Utility scores did not change on a group level between 2-and 3 years for the group with PCC, but it did show a significant improvement for the group without PCC. An improvement in the EQ-5D utility suggests an improvement in at least one of the five health dimensions for this group, and not a decrease in any other. This improvement of the group without PCC contrasts with the stability found for the PCC group, suggesting that the presence of PCC at 2 years may impede improvement in HRQoL over time.

The analysis on individual changes showed that PCC was not associated with greater decreasing changes compared to the group without PCC. However, much heterogeneity in direction and magnitude of change scores was observed for the PCC group. About 25% show negative changes above 9 points and about 25% show positive changes

above 9.75 points. Something similar was observed for the group without PCC, but with less heterogeneity. This confirms our hypothesis that a high variability in recovery process is present among PCC patients and supports the importance of the second aim of this study.

The second aim was to identify factors influencing a variability in changes of HRQoL among individuals with PCC. We found that, contrary to what was expected, those with social engagement problems on average, have a larger increase in EQ VAS score over time. Because of its association with higher risk of developing disabilities and mental health issues, people with social engagement problems were expected to be associated with greater negative changes or at least less improvement in their HRQoL compared to those who did not exhibit these problems. An explanation for this might be that people with social engagement problems at 2 years could be more likely to cope with their disease over time and thus more likely to show improvement and those who did not have these problems stayed relatively stable. An analysis of changes in coping mechanisms, lifestyle and receiving treatment from 2 to 3 years among those having problems with social engagement problems could help clarify this result. This result may also be explained by regression to the mean. If some participants with problems with social engagement had extreme values at baseline, in this case at 2 years, they were likely to move closer to the average in the following measurement.

Additionally, we found that among the PCC group, the level of education showed no significant effect on change, however an interaction took place between education and ethnicity in which low education and non-Dutch ethnicity had on average a greater positive change in EQ-5D utility scores. All participants of the non-Dutch ethnicity group were of male sex. So, this result should be taken with caution as it is not generalizable to both sexes of non-Dutch population. Ethical minorities of low education are populations known to be more vulnerable to health inequities, so this result is opposite to what would be expected in our hypothesis. Regression to the mean could possibly explain this result.

Sex, and the interaction of age and sex were not significant in both EQ VAS and EQ-5D Utility change scores, which is contrary to what was hypothesized, as younger aged women with PCC have been identified by previous studies as more vulnerable (8). This could be because of lack of variability in the distribution of age among those with PCC to detect significant differences. Moreover, the absence of significant differences in HRQoL changes between sexes in our study might be explained by the findings of García et al(39). In this study the EQ-5D-5L instrument was also used to measure HRQoL in

PCC patients. Authors suggest that women's health self-perception is impacted by social and personal factors intrinsic to women, beyond biological and socio-economic influences, and that those factors may not be fully captured with the current tools.

4.2 Strengths and limitations

The main strength of this study is the long 3-year follow-up period, which allows for a thorough analysis of the long-term effects of PCC as they develop over time. To our knowledge, few studies have such extended data on COVID-19 survivors. Being a multicenter study conducted in the Netherlands allows applicability of results to a broader population. The use of the EQ-5D utility allows for comparison of the impact of PCC with other diseases in clinical and burden of disease analysis. Also, the inherent advantage of the design, a prospective cohort study reduces the likelihood of recall bias during the exposure and outcome ascertainment. Furthermore, in this case self-reported data is potentially better than assessment of exposure using Medical Records, considering that knowledge and diagnostic protocols of PCC are still limited in healthcare settings. Also, exposed and unexposed groups were selected within the same cohort, they all had the same potential risk of outcome and allowed to control any other confounding variables that might otherwise influence the outcomes.

A limitation of the study is that the distribution of the initial disease severity does not reflect that of the general population of former COVID-19 patients who sought medical attention in 2020. Due to the combination of three sources of data that included mostly hospitalized patients, our study had a higher proportion of hospitalized patients compared to those who managed their infection at home during the acute phase. Also, our sample consisted of mostly people who were retired, and half were over 65 years at the moment of initial disease, so generalization of this results must be taken with discretion.

The source of systematic attrition was identified by a higher change of participating if treated in the ICU. We accounted for this potential bias by controlling for the variable of severity of initial acute COVID-19 disease in our regression analysis. The reason for this attrition could be explained by the differences in the follow-up techniques used by individual cohorts mostly because this relationship was observed only in one of the cohorts that included all three levels of severity of initial disease. This explains the overrepresentation of male participants and people with social engagement problems in the final sample, as most patients admitted to ICU were male and compared to other severity groups had more people with social engagement problems. As attrition was not differential on exposure (PCC), results are not likely to be biased.

Results from a study in the Netherlands evidenced that ethnic minority groups were more likely to be affected by SARS-CoV-2 infection than native Dutch population(27). However, as participants of non-Dutch ethnicity represent only 2.5% (6/238) of our total sample, the results of our study may not be generalizable to all ethnic minority patients hospitalized due to COVID-19. Another study showed that risk of PCC was higher among patients with a migration background compared to Dutch origin patients (40). In our study, 5/6 (83%) non-Dutch participants were categorized as having PCC, which somehow aligns to their result.

Although severity of symptoms was asked prospectively, when determining if symptoms were not present before initial SARS-CoV-2 infection, possibility of recall bias 2-years after the event can't be discarded. If present, misclassification of exposure may occur, as this was part of the criteria used to define the presence of PCC. If recall bias was present, it could lead to non-differential misclassification of exposure, which could bias effects towards the null.

Other confounders not considered in this study, which could have affected health, are major life events, comorbidities that may have developed after initial infection, and SARS- CoV-2 re-infection. However, a study found that although re-infection was associated with higher prevalence of PCC and lower EQ-5D VAS scores, it was not associated with further impairment of daily activities at 3 years after infection (41).

There was limited possibility to detect interactions due to low or null representation of several subgroups. Also, high variability (thus large Confidence Intervals) and low stability of results could be explained by the sample size.

Relying solely on two reference points over a brief period of one year may not provide adequate insight into detecting consistent patterns of changes of HRQoL among individuals. However, a study testing Self-adjustment approach based-interventions on patients with PCC (42), found significant changes of quality of life (using EuroQol-5D-5L), and symptom severity of PCC after 6 weeks of intervention compared to control group, which indicates that changes may be detected in a short period of time with this tool.

4.3 Recommendations and future directions

It is still important to note that 2 and 3 years after initial infection average scores of HRQoL for VAS and Utility scores, were both statistically lower than those of the group without PCC. Long term impact of PCC in HRQoL is still evident 3 years after initial

infection and should therefore still be a concern for public health and healthcare professionals.

As our study can't determine whether the magnitudes of the differences of change score between groups reflect a clinical significance for PCC related symptoms, so an important next step is to conduct research to establish sex specific cut-off points for clinically significant changes of EQ5D outcomes among PCC patients of this population. Additionally, an important following step would be to evaluate the responsiveness properties of the EQ-5D-5L tool to measure changes in HRQoL among in this population. For epidemiological monitoring of the impact of PCC, another possible step after this study, would be to analyze all possible outcomes related to sudden or progressive negative changes of HRQoL among people with PCC, as they could be predictors of higher use of healthcare services, and mortality, like has been evidenced for other illnesses (43).

Future studies should consider a more comprehensive inclusion of biopsychosocial factors, like objective biomarker and psychological measurements, and analysis of lifestyle and behavioral changes over time. Additionally, they should aim for study designs that allow the analysis of intersectional disparities in health, with particular attention in gender, disability, and migration status. This approach could improve the understanding of factors that interact, influence, and explain changes in perception of general health and quality of life over time for certain populations.

5. Conclusions

In conclusion, among adult COVID-19 survivors of the Dutch population, particularly those who were hospitalized at initial acute COVID-19 illness during the first waves, the HRQoL at 2 years remained stable 1 year after for the group with PCC and showed a significant improvement the EQ 5D utility outcome for the group without PCC. Individual decreasing changes were not associated with the presence of PCC at 2 years. Our findings suggest that although the presence of PCC at 2 years is not triggering a decrease of HRQoL over time, it may be impeding improvement over time.

Although some individuals with PCC showed divergent changes in HRQoL in direction and magnitude, disparities could not be attributed to sociodemographic or clinic characteristics. However, a potential higher improvement of HRQoL could be expected over time for those with problems with social engagement. Most importantly, our study showed that overall, those with PCC continue to have a poor HRQoL over time. Therefore, further studies with a comprehensive inclusion of biopsychosocial factors are necessary to understand what is influencing the individual variability of improvement and

decline of HRQoL among COVID-19 survivors living with PCC. Continued follow-up of HRQoL is recommended to identify long-term health threats and to facilitate targeted monitoring, intervention, and management of PCC.

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Supplementary information

Supplementary Table S1. Characteristics of participants that were Loss to Follow-up and those who were included in the Final sample

Characteristic	**Overall**, N = 364[1]	**Loss to follow-up**, N = 126[1]	**Sample**, N = 238[1]	**p-value**[2]
Sex				0.023
Female	114 (31%)	49 (39%)	65 (27%)	
Male	250 (69%)	77 (61%)	173 (73%)	
Age at inclusion				>0.9
<67	207 (57%)	72 (57%)	135 (57%)	
>= 67	157 (43%)	54 (43%)	103 (43%)	
Ethnicity				0.7
Dutch	355 (98%)	124 (98%)	231 (97%)	
Non-Dutch	8 (2.2%)	2 (1.6%)	6 (2.5%)	
Working status				0.3
Employed	93 (29%)	30 (29%)	63 (29%)	
Household/Caretaker	7 (2.2%)	5 (4.9%)	2 (0.9%)	
Partially due to health	25 (7.9%)	8 (7.8%)	17 (7.9%)	
Retired	156 (49%)	48 (47%)	108 (50%)	
Sick leave, incapacity, unemployed	36 (11%)	12 (12%)	24 (11%)	
Level of education				0.4
High	78 (22%)	24 (19%)	54 (23%)	
Low	283 (78%)	102 (81%)	181 (77%)	
Living arrangement				0.8
Alone	56 (15%)	21 (17%)	35 (15%)	
Alone, with children	10 (2.8%)	4 (3.2%)	6 (2.5%)	
Parents or other	7 (1.9%)	3 (2.4%)	4 (1.7%)	
Partner, with or without children	289 (80%)	97 (78%)	192 (81%)	
Severity of initial COVID-19 illness				0.2
Home	57 (16%)	25 (20%)	32 (13%)	
Hospital Ward	216 (59%)	74 (59%)	142 (60%)	
ICU	91 (25%)	27 (21%)	64 (27%)	
Social Engagement problems	39 (12%)	9 (8.4%)	30 (14%)	0.2
Social Relationship problems	28 (8.6%)	3 (2.8%)	25 (11%)	0.009
Pre-existing morbidities				0.2
None	136 (37%)	42 (33%)	94 (39%)	
One	115 (32%)	47 (37%)	68 (29%)	
>1	113 (31%)	37 (29%)	76 (32%)	
EQ-5D Utility at 2-year Follow-up	0.81 (0.70, 0.89)	0.81 (0.74, 0.89)	0.81 (0.68, 0.89)	0.2
EQ VAS score at 2-year Follow-up	70 (60, 80)	70 (60, 80)	70 (60, 80)	0.5
PCC at 2-year Follow-up				0.7
No	125 (34%)	45 (36%)	80 (34%)	
Yes	239 (66%)	81 (64%)	158 (66%)	

[1] n (%); Median (IQR)
[2] Pearson's Chi-squared test; Fisher's exact test; Wilcoxon rank sum test
Cell counts may differ due to missing data

Supplementary Table S 2. Associations of all variables with Participating in 3-year Follow-up

Characteristic	N	Unadjusted			Adjusted		
		OR[1]	95% CI[1]	p-value	OR[1]	95% CI[1]	p-value
Sex	364						
Female		—	—		—	—	
Male		1.69	1.07, 2.68	0.024	1.34	0.75, 2.36	0.3
Age at inclusion	364						
<67		—	—		—	—	
>= 67		1.02	0.66, 1.58	>0.9	0.80	0.33, 1.82	0.6
Ethnicity	363						
Dutch		—	—		—	—	
Non-Dutch		1.61	0.36, 11.1	0.6	1.15	0.22, 8.72	0.9
Working status and health impact	317						
Employed		—	—		—	—	
Household/Caretaker		0.19	0.03, 0.94	0.055	0.22	0.03, 1.35	0.12
Partially due to health		1.01	0.40, 2.72	>0.9	0.87	0.30, 2.63	0.8
Retired		1.07	0.61, 1.86	0.8	1.29	0.53, 3.31	0.6
Sick leave, incapacity, unemployed		0.95	0.42, 2.21	>0.9	0.68	0.26, 1.83	0.4
Level of education	361						
High		—	—		—	—	
Low		0.79	0.45, 1.34	0.4	0.99	0.51, 1.90	>0.9
Living arrangement	362						
Alone		—	—		—	—	
Alone, with children		0.90	0.23, 3.86	0.9	1.37	0.26, 8.23	0.7
Parents or other		0.80	0.16, 4.39	0.8	1.00	0.14, 8.75	>0.9
Partner, with or without children		1.19	0.65, 2.14	0.6	1.19	0.58, 2.40	0.6
Severity of initial COVID-19 illness	364						
Home		—	—		—	—	
Hospital Ward		1.50	0.82, 2.71	0.2	1.43	0.74, 2.74	0.3
ICU		1.85	0.93, 3.71	0.080	2.92	1.18, 7.61	0.023
Social Engagement problems	324	1.75	0.83, 4.04	0.2	1.43	0.50, 4.41	0.5
Social Relationship problems	327	4.51	1.54, 19.3	0.016	4.50	1.11, 25.1	0.053
Pre-existing morbidities	364						
None		—	—		—	—	
One		0.65	0.38, 1.09	0.10	0.69	0.37, 1.29	0.2
>1		0.92	0.54, 1.57	0.8	0.74	0.38, 1.45	0.4
EQ-5D Utility Score at 2-year Follow-up	361	0.77	0.27, 2.08	0.6	1.82	0.28, 12.0	0.5
EQ VAS Score at 2-year Follow-up	363	1.0	0.98, 1.01	0.4	0.99	0.97, 1.01	0.6
PCC at 2-year Follow-up	364						
No		—	—		—	—	
Yes		1.10	0.70, 1.72	0.7	1.08	0.58, 2.02	0.8

[1] OR = Odds Ratio, CI = Confidence Interval

Supplementary Table S 3. Frequency of PCC related symptoms at 2-year follow-up, not present before initial acute COVID-19 illness.

Symptoms	**Missing**[1]	**N = 158**[2]
Fatigue	7 (4.4%)	84 (56%)
Dizziness	3 (1.9%)	24 (15%)
Muscle pain and weakness	1 (0.6%)	75 (48%)
Cough	0 (0%)	26 (16%)
Breathing/shortness of breath	5 (3.2%)	55 (36%)
Pain when breathing	1 (0.6%)	5 (3.2%)
Chest Pain (angina)	4 (2.5%)	8 (5.2%)
Heart Palpitations	2 (1.3%)	17 (11%)
Cognition	1 (0.6%)	53 (34%)
Loss of Smell and taste	0 (0%)	28 (18%)
Sleeping problems	0 (0%)	60 (38%)
Loss of Appetite	0 (0%)	7 (4.4%)
Swollen Feet and ankles	3 (1.9%)	23 (15%)

[1] N Missing (% Missing)
[2] n (%)

Supplementary Table S 4. Distribution of frequency of severity of problems for the EQ-5D-5L dimensions by PCC status

	PCC Status					
	PCC (N=158)			No PCC (N=80)		
Dimension	**2-year**	**3-year**	**p-value[1]**	**2-year**	**3-year**	**p-value[1]**
Mobility			0.586			1
No problems	47 (30%)	43 (27%)		48 (60%)	52 (65%)	
Slight problems	33 (21%)	43 (27%)		27 (34%)	22 (28%)	
Moderate Problems	53 (34%)	49 (31%)		3 (3.8%)	6 (7.5%)	
Severe Problems	24 (15%)	23 (15%)		2 (2.5%)	0 (0%)	
Extreme problems	1 (0.6%)	0 (0%)		0 (0%)	0 (0%)	
Self-care			1			1
No problems	110 (70%)	112 (71%)		77 (96%)	77 (96%)	
Slight problems	32 (20%)	30 (19%)		3 (3.8%)	2 (2.5%)	
Moderate Problems	11 (7.0%)	11 (7.0%)		0 (0%)	0 (0%)	
Severe Problems	1 (0.6%)	3 (1.9%)		0 (0%)	1 (1.3%)	
Extreme problems	4 (2.5%)	2 (1.3%)		0 (0%)	0 (0%)	
Usual Activities			0.892			1
No problems	31 (20%)	43 (27%)		55 (69%)	59 (74%)	
Slight problems	62 (39%)	40 (25%)		23 (29%)	19 (24%)	
Moderate Problems	47 (30%)	57 (36%)		1 (1.3%)	2 (2.5%)	
Severe Problems	16 (10%)	18 (11%)		1 (1.3%)	0 (0%)	
Extreme problems	2 (1.3%)	0 (0%)		0 (0%)	0 (0%)	
Pain and Discomfort			1			1
No problems	35 (22%)	42 (27%)		41 (51%)	58 (73%)	
Slight problems	59 (37%)	49 (31%)		34 (43%)	17 (21%)	
Moderate Problems	56 (35%)	55 (35%)		5 (6.3%)	5 (6.3%)	
Severe Problems	6 (3.8%)	10 (6.3%)		0 (0%)	0 (0%)	
Extreme problems	2 (1.3%)	2 (1.3%)		0 (0%)	0 (0%)	
Anxiety and Depression			1			1
No problems	85 (54%)	94 (59%)		66 (83%)	70 (88%)	
Slight problems	43 (27%)	34 (22%)		11 (14%)	9 (11%)	
Moderate Problems	23 (15%)	27 (17%)		3 (3.8%)	1 (1.3%)	
Severe Problems	7 (4.4%)	3 (1.9%)		0 (0%)	0 (0%)	
Extreme problems	0 (0%)	0 (0%)		0 (0%)	0 (0%)	

[1] Wilcoxon Signed Rank Test

Abstract in french

Titre : « L'impact longitudinal du Syndrome post-COVID-19 (SPC) sur la qualité de vie liée à la santé (QVLS) entre 2 et 3 ans après l'infection par le SARS-CoV-2 - résultats de l'étude CORFU et Long CORFU »

Introduction : Syndrome post-COVID-19 (SPC) est associé à une altération de la qualité de vie liée à la santé (QVLS), mais les preuves de recherche à long terme sont limitées. Cette étude a évalué l'impact du SPC sur les changements de QVLS entre 2 et 3 ans après l'infection et a identifié des prédicteurs de changements chez les individus SPC. Les objectifs étaient de 1) évaluer les changements dans la QVLS chez les survivants de la COVID-19 avec et sans SPC, 2) déterminer l'effet du SPC sur les changements dans la QVLS, et 3) explorer les associations de facteurs biopsychosociaux avec les changements dans la QVLS parmi les individus SPC.

Méthodes : 238 participants d'études de cohorte néerlandaises portant sur des survivants du COVID-19 ont été suivis de manière prospective 2 et 3 ans après l'infection initiale par le SARS-CoV-2. Le SPC à 2 ans a été identifié sur la base des symptômes autodéclarés et la QVLS a été quantifiée aux deux moments avec l'utilité EQ-5D et les scores EQ VAS.

Résultats : Les scores VAS ne différaient pas significativement pour SPC et no- SPC. La médiane (IQR) des scores d'utilité ne différait pas pour le SPC, mais pour no-SPC: 0,887 (0,817, 1,0) à 0,919 (0,852, 1), P = 0,008. L'effet du SPC sur changements des scores VAS était de 1,6 point (IC à 95 % -2,6, 5,8 ; P : 0,4) et sur la modification de l'utilité -0,03 point (IC à 95 % -0,07, 0,02 ; P= : 0,3). L'engagement social était associé à l'évolution des scores VAS et une interaction entre le niveau d'éducation et l'origine ethnique a été constatée sur l'évolution des scores d'utilité.

Conclusions : La QVLS est restée stable au fil du temps pour le SPC et s'est améliorée pour no-SPC sur le résultat d'utilité. La variation des changements au sein des individus SPC n'était pas associée à des caractéristiques sociodémographiques ou cliniques. Une amélioration plus élevée de la QVLS pourrait être attendue pour les personnes avec des problèmes d'engagement social. Le SPC peut entraver l'amélioration de la QVLS au fil du temps. Par conséquent, davantage d'études sont nécessaires pour comprendre la variabilité des changements de QVLS parmi les survivants du COVID-19.

Mots clés : Syndrome post-COVID-19, qualité de vie liée à la santé, COVID-19