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The course and trajectories of quality of life among post-COVID-19 patients in the HUS Long Covid Cohort Study

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Abstract

Patients with post-COVID condition (PCC) frequently report reduced quality of life (QoL). This study assessed QoL and health-related QoL (HRQoL) with trajectories within a prospective PCC cohort. The study included adult patients at a PCC clinic. Outcomes were collected at 0, 3, 6, and 12 months. The primary outcome was QoL by Visual Analogue Scale (VAS 0-10). Secondary outcomes included QoL by EUROHIS-QOL-8 and HRQoL by 15D, and patients' symptom perceptions by Somatic Symptom Disorder - B Criteria Scale (SSD-12). Linear mixed models analyzed temporal changes, and trajectory analysis modeled recovery patterns. At baseline, 442 patients participated, with 305 (69.0%) providing follow-up data. Most patients (92.7%) were non-hospitalized. Trajectory analysis of EUROHIS-QOL-8 identified two recovering trajectories (73.8%) and a stable group (26.2%). Stable trajectories were associated with more comorbidities and higher levels of worry-inducing symptom perceptions (mean SSD-12 score 26 out of 48), whereas marked recovery was linked to being employed and having lower SSD-12 (10–13). Mean QoL improved over 12 months from 5.2 to 6.5 on the 0-10 VAS scale and from 3.1 to 3.5 on the EUROHIS-QOL-8 scale of 1-5. HRQoL by 15D increased from 0.76 to 0.80 (scale 0-1). In conclusion, patients with comorbidities and distressing illness beliefs are the most vulnerable group in rehabilitation and require specific attention.

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1. Introduction

Post-COVID-19 condition (PCC) has been the subject of intense research, yet its clinical course and prognosis, as well as the factors affecting them, remain incompletely understood. Patients referred to specialized post-COVID clinics provide valuable insight into the outcomes among those experiencing substantial long-term impacts on daily life [1]. Both quality of life (QoL) and health-related QoL (HRQoL) have been widely monitored after acute COVID-19 and its long-term sequelae [2–5].

General QoL reflects overall well-being [6–8], while HRQoL captures physical, psychological, and social dimensions [9–11]. Approximately 59% of individuals with PCC report reduced QoL [3], influenced by persistent somatic symptoms (PSS), mental and somatic comorbidities, and social determinants like

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employment and ethnicity [12–16]. Longitudinal studies indicate heterogenous recovery patterns – rapid, gradual, stable, or worsening – shaped by not only symptom burden and comorbidities, but also pre-COVID HRQoL, and factors like age, gender and education [17–25].

While much of the existing evidence comes from hospitalized populations [26–30], emerging studies show that non-hospitalized patients can also face long-lasting illness and reduced HRQoL [31–33]. However, prospective one-year data with repeated, standardized HRQoL assessments remain scarce. We focused on a one-year follow-up period as it captures the clinically relevant early and intermediate phase of recovery in PCC, during which key rehabilitation processes take place and prognostic patterns begin to emerge[17,22].

Psychological factors appear to play an important role in shaping the course of PCC. Symptom-related worry, anxiety and negative expectations have been assessed using the Somatic Symptom Disorder-B Criteria Scale (SSD-12) and are linked to poorer outcomes and reduced QoL in PCC [34–37]. In other chronic medical conditions, health anxiety and distressing illness beliefs seem to be more decisive for QoL and healthcare utilization than the severity of somatic symptoms [36,38–41]. Psychological distress and illness beliefs are increasingly recognized as key factors in recovery, yet remain insufficiently studied [39,42–44].

A preliminary analysis of our PCC cohort of predominantly non-hospitalized patients [1] showed that one-third of patients reported good QoL at the end of a one-year follow-up. The aim of this study was to characterize trajectories of QoL and HRQoL over one year in this same cohort, and to determine factors affecting recovery or persistent impairment, including symptom perceptions.

2. Materials and methods

2.1. Study population and design

The Long Covid Cohort Study is a prospective, single-site cohort study registered at www.clinicaltrials.gov (NCT05699512) [1,45]. Recruitment occurred from June 1, 2021, to October 18, 2023, and the study included adult patients (≥18 years) referred to the Helsinki University Hospital (HUS) Clinic for Long-Term Effects of COVID-19 due to persistent symptoms following a COVID-19 infection. The diagnosis of post-COVID-19 condition was based on the World Health Organization (WHO) case definition [46]. Referrals came from university hospital clinics and primary care when symptoms could not be attributed to a somatic disease or psychiatric disorder. Patients with ongoing diagnostic evaluations for alternative causes

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were typically not accepted until these had been completed. Patients with lung alterations or other organ damage due to COVID-19 were managed at specialized units and not referred to the Long-Term Effects Clinic. The clinic provided multidisciplinary rehabilitation for patients with PCC, and referrals were assessed based on whether such rehabilitation was likely to be beneficial.

The clinic was able to accept only about half of all referrals. The most common reason for non-acceptance was the assessment that the patient's condition could be more appropriately managed within primary care, as existing measures had not been fully utilized, or rehabilitation was unlikely to provide additional benefit because of a chronic presentation with extensive multimorbidity. Other cases of non-acceptance were due to concurrent specialized care, and the timing of multidisciplinary rehabilitation was not considered optimal. Decisions regarding referral acceptance were based on clinical judgement within the team of physicians and were not guided by strictly predefined criteria. In some cases, patients whose referrals were initially declined were later accepted if recommended primary care interventions had been implemented without sufficient benefit and multidisciplinary rehabilitation was then considered appropriate.

For the cohort study, eligibility criteria included a confirmed COVID-19 diagnosis (PCR or antibody test) at least three months prior and willingness to participate via signed informed consent. Exclusion criteria were inability to complete study forms in Finnish, participation being unreasonably burdensome (e.g., patients on bed rest), or ongoing drug abuse.

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2.2. Study phases

The study comprised baseline assessment followed by a series of follow-ups. During the baseline phase, eligible patients were identified and recruited, and their sociodemographic and clinical histories were collected via electronic and paper surveys. Before their initial outpatient clinic visit, patients received patient-reported outcome measures (PROMs) questionnaires along with the study consent and information leaflet. During the baseline visit, clinicians addressed any questions about the study and drafted an individualized treatment plan based on clinical assessment. The collected PROM data were stored in a pseudonymized format in the HUSeCRF system (HUS electronic Case Report Form).

The follow-up phase was conducted at 3, 6, and 12 months post-enrollment, with participants receiving digital questionnaires linked to the HUSeCRF

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system. If a patient did not respond within a week, two weekly reminders were sent via email and text messages. Participants who did not respond to follow-up questionnaires despite reminders were not excluded from the study; however, those with only baseline data could not be included in trajectory analyses requiring repeated measurements but were retained in other analyses where appropriate.

2.3. Treatment at the Clinic

The clinic's interdisciplinary team comprised physicians specialized in general and occupational medicine, a psychologist, a social worker, a nurse, and psychosomatically oriented physiotherapists. Treatment followed WHO recommendations for long COVID rehabilitation [47] and was delivered through individualized combinations of pharmacological management, physiotherapy, and group-based rehabilitation. Care was tailored to patient needs and was not strictly standardized. In addition to symptom-based treatment, psychological aspects were addressed through providing information on the biopsychosocial model of illness [43,48–51] and addressing illness-related beliefs and concerns with the aim of reducing distress and supporting recovery. Comorbidities were managed within the clinic or through referral as appropriate.

2.4. Outcome measures

The primary outcome of the study was change in self-reported QoL. Secondary outcomes included additional measures of QoL and HRQoL, as well as factors potentially associated with recovery.

The primary outcome measure was self-reported QoL using a Visual Analogue Scale (VAS 0-10) at baseline and during follow-ups at 3, 6, and 12 months. Patients were instructed: "Mark your quality of life on the line between 0 (poor) and 10 (excellent)". The VAS scale was chosen for its simplicity, patient-friendliness, and feasibility in a clinical setting [52,53].

Secondary outcomes were assessed using the validated instruments EUROHIS-QOL-8 [54] and the 15D [55], that capture the multidimensional impact of PCC.

EUROHIS-QOL-8 (European Health Interview Survey-Quality of Life) is an 8-item index, a shortened version of the WHOQOL-BREF (World Health Organization Quality of Life Instrument-Abbreviated Version). Patients respond using a 1-5 Likert scale, with the total score expressed as a mean, where 5 reflects the best possible QoL. Changes in EUROHIS-QOL-8 scores

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are interpreted as reflecting changes in overall perceived QoL, with higher scores indicating better QoL.

The 15D is a generic measure assessing physical, mental, and social well-being across 15 dimensions including mobility, vision, hearing, breathing, sleep, speech, depression, and complaints and symptoms. A set of population-based preference weights is used to generate the 15D score, a single index number ranging from 0 to 1, with 1 representing full health and 0 representing the state of being dead. A meaningful difference in health status corresponds to a change of 0.015 on the 15D scale between measurements, and a change of 0.035 is considered major [56].

To assess modifying factors of QoL, we applied the Somatic Symptoms Disorder-B Criteria Scale (SSD-12) [37]. It is used to assess the patient's perceptions of their symptom-related thoughts, feelings, and behaviors, according to the B criteria of The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) somatic symptom disorder [57]. It consists of 12 items rated on a 0–4 Likert scale, with total scores ranging from 0 to 48, where higher scores indicate greater symptom-related psychological distress.

2.5. Data sources

Baseline data included registry and clinical data from the HUS Data Lake on the HUS Acamedic platform. Comorbidity data from patients' healthcare records covered the past five years of tertiary care and HUS acute departments. Follow-up data consisted of patient-reported outcomes collected via digital questionnaires and stored in the HUSeCRF system. Data from other primary or occupational healthcare sources were not included, as these were not comprehensively available through the national registry databases accessed for this study.

2.6. Statistical analysis

Baseline characteristics were summarized as frequencies and percentages for categorical variables and as means with standard deviations for continuous variables. Symptom duration was estimated as the time from the date of confirmed SARS-CoV-2 infection (PCR or antibody test) to the baseline visit, expressed in months. As precise onset of symptoms was not systematically recorded, the date of positive testing was used as a proxy for symptom onset. Comorbidities included in the analyses were selected based on their frequency in the study population; those with very low prevalence ($n < 8$) were not analyzed separately to avoid unreliable estimates.

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Between-group comparisons were conducted using chi-squared tests for categorical variables and Kruskal-Wallis tests for continuous variables. Missing data were handled as described for each analysis.

Trajectory clustering

EUROHIS-QOL-8 trajectories were clustered using agglomerative hierarchical clustering with Dynamic Time Warping (DTW) distance. Intermittently missing values were linearly interpolated before clustering. DTW allows comparison of time series that may vary in timing and length and is well suited for longitudinal data with irregular follow-up patterns. Patients with at least one follow-up measurement (n = 305) were included, meaning that both full and partial responders contributed to the analyses. Clusters were derived in a data-driven manner and were not based on predefined cut-offs for change in QoL.

Attrition analysis

An attrition analysis was performed to assess potential bias due to loss to follow-up. Participants were categorized as non-responders (no follow-up data, not included in trajectory clustering), partial responders (some but not all follow-up measurements) and full responders (completed all follow-up assessments). Baseline characteristics were compared between these groups.

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Linear mixed models

We employed linear mixed models (LMMs) to analyze changes in QoL over time, as they allow for both fixed and random effects. In this model, fixed effects estimate the overall trends across the study cohort, while random effects capture participant-specific variations.

Covariates considered in the analyses included demographic and clinical variables such as sex, body-mass index (BMI), living arrangements, and employment status. Factors associated with follow-up participation were explored and considered when specifying the final models. Marginal means and standard errors (SE) were reported at each time point.

Statistical software

Statistical analyses were performed with R inside the HUS Acamedic environment. The package *lmer* was used for LMMs, and *dtwclust* for

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clustering. Statistical significance was set at $p<0.05$. No formal adjustments for multiple testing were performed.

2.7. Ethical approval

All methods were performed in compliance with relevant guidelines and regulations. The study was approved by the Helsinki University Hospital Research Ethics Committee (ID HUS/1493/2021; approval date 3 June 2021) and conducted in accordance with the Declaration of Helsinki[58]. All participants provided written informed consent.

3. Results

3.1. Baseline data and trajectory patterns of recovery

Patient flow is depicted in the flow chart (Figure 1). The total number of study participants at baseline was 442, of which 305 patients (69.0%) provided at least one follow-up measurement and were included in the trajectory analysis. Their mean age was 46.4 years (SD 10.7) and 211 (69.2%) were female. Most patients (92.7%) had not been hospitalized due to acute COVID-19.

Figure 1. Flow chart of recruitment and attrition at the Outpatient Clinic of Long-Term Effects of COVID-19. Patients were included if they had a confirmed COVID-19 diagnosis (PCR or antibody test) at least three months prior and willingness to participate via signed informed consent. Reasons for loss to follow-up and detailed exclusion criteria were not systematically recorded.

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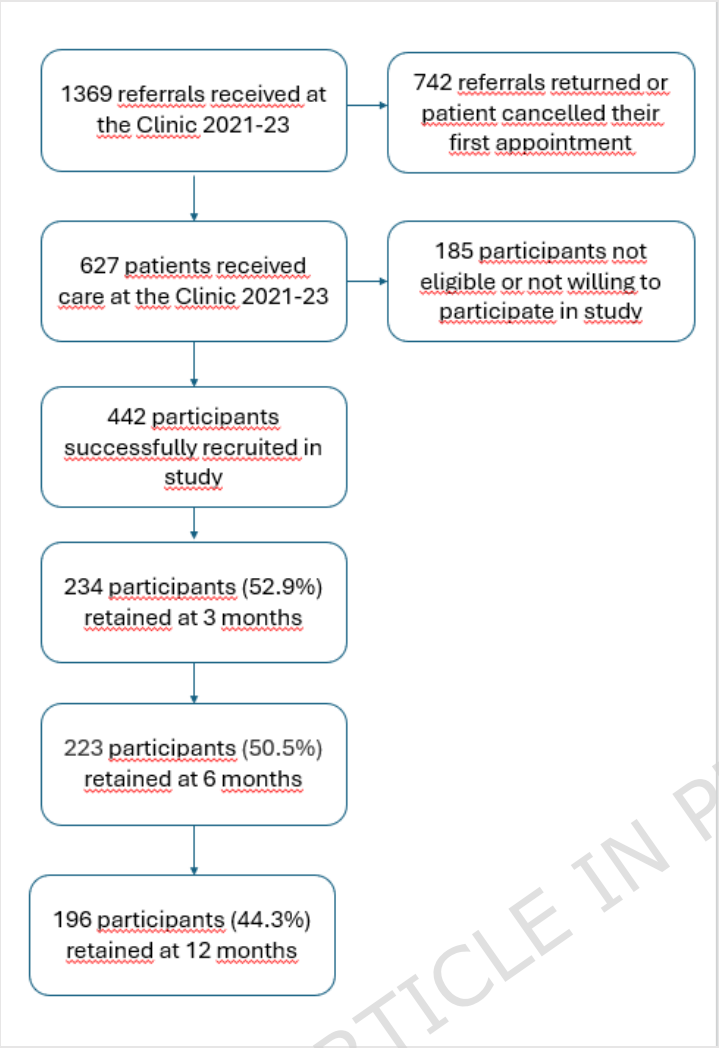

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Table 1 shows the baseline characteristics of three trajectory clusters according to EUROHIS-QOL-8 QoL prognosis: (1) *Stable*, characterized by persistently low EUROHIS-QOL-8 scores; (2) *Partial Recovery*, improving modestly over time; and (3) *Marked Recovery*, improving substantially during follow-up (Figure 2). Among participants, 73.8% belonged to recovering clusters, while 26.2% showed little or no improvement during follow-up at 3, 6, and 12 months.

Table 1. The baseline characteristics of three trajectory clusters according to EUROHIS—QOL-8 QoL prognosis. Green lines indicate statistically significant differences between groups ($p < 0.05$).

	Total	**Trajectory clusters**			**p-value**
		Stable cluster	**Partial recovery cluster**	**Marked recovery cluster**	

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Total, n (% of total)	305 (100.0)	85 (27.9)	131 (43.0)	89 (29.2)	NA
Patient characteristics					
Female, n (%)	211 (69.2)	59 (69.4)	87 (66.4)	65 (73.0)	0.58
Age (years), mean (SD)	46.4 (10.7)	47.0 (9.6)	46.1 (11.2)	46.3 (10.9)	0.77
BMI (kg/m2), mean (SD)	27.6 (5.9)	28.7 (6.1)	27.5 (6.2)	26.8 (5.0)	0.15
Living alone, n (%)	80 (26.2)	25 (29.4)	34 (26.0)	21 (23.6)	0.70
Tertiary education, n (%)	183 (60.8)	44 (51.8)	82 (64.6)	57 (64.0)	0.13
Employed, N (%)	213 (69.8)	48 (56.5)	90 (68.7)	75 (84.3)	< .001
Monthly doses of alcohol, mean (SD)	7.1 (10.0)	5.1 (5.4)	7.7 (10.2)	8.0 (12.4)	0.40
Smoking, n (%)	17 (5.6)	6 (7.1)	7 (5.4)	4 (4.5)	0.78
PCC-related variables					
Symptom duration (months), mean (SD)	10.8 (7.2)	10.8 (6.0)	10.8 (7.2)	10.8 (8.4)	0.94
Hospitalization during acute COVID-19, n (%)	22 (7.3)	7 (8.3)	9 (7.0)	6 (6.7)	0.91
Intensive care during acute COVID-19, n (%)	11 (3.6)	1 (1.2)	5 (3.9)	5 (5.6)	0.32
Comorbidities					
Number of comorbidities, mean (SD)	1.1 (1.4)	1.7 (1.7)	1.0 (1.2)	0.7 (1.0)	< .001
At least one comorbidity, n (%)	163 (54.0)	56 (66.7)	71 (55.0)	36 (40.4)	0.004
Asthma, n (%)	53 (17.5)	20 (23.8)	25 (19.4)	8 (9.0)	0.03
Antidepressant medication, n (%)	34 (11.3)	15 (17.9)	14 (10.9)	5 (5.6)	0.04
Musculoskeletal pain, n (%)	28 (9.3)	13 (15.5)	11 (8.5)	4 (4.5)	0.04
Sleep apnea, n (%)	27 (8.9)	15 (17.9)	8 (6.2)	4 (4.5)	0.004
Hypertension, n (%)	27 (8.9)	10 (11.9)	9 (7.0)	8 (9.0)	0.48
Anxiety disorder, n (%)	19 (6.3)	10 (11.9)	5 (3.9)	4 (4.5)	0.04
Migraine, n (%)	19 (6.3)	8 (9.5)	6 (4.7)	5 (5.6)	0.35
Depression, n (%)	16 (5.3)	8 (9.5)	7 (5.4)	1 (1.1)	0.05
Hypothyroidism, n (%)	15 (5.0)	3 (3.6)	6 (4.7)	6 (6.7)	0.59
Diabetes, n (%)	11 (3.6)	4 (4.8)	2 (1.6)	5 (5.6)	0.24
Long term insomnia, n (%)	10 (3.3)	3 (3.6)	6 (4.7)	1 (1.1)	0.38
Irritable bowel syndrome (IBS), n (%)	8 (2.6)	3 (3.6)	4 (3.1)	1 (1.1)	0.61

BMI = body mass index, PCC=post-covid condition, SD = standard deviation.

Figure 2. Trajectory clusters of quality of life (EUROHIS-QOL-8) during follow-up. Three recovery clusters identified in trajectory analysis of EUROHIS-QOL-8 scores: Stable (red), Partial Recovery (green), and Marked Recovery (blue).

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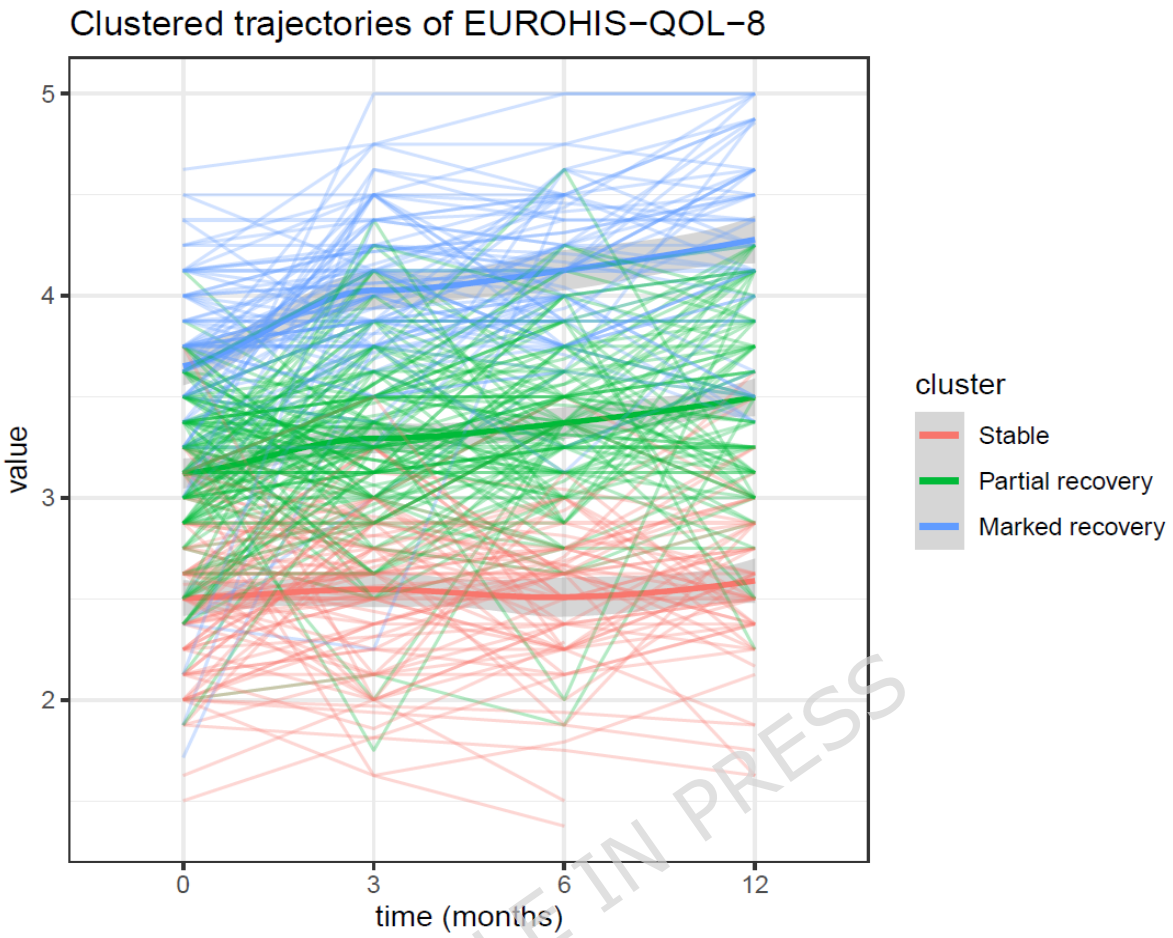

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In the Stable cluster, overall QoL measured with the EUROHIS-QOL-8 remained unchanged, ranging from 2.5 (SD 0.4) to 2.6 (SD 0.4) on the 1–5 scale over 12 months. The Partial Recovery cluster increased moderately, from 3.1 (SD 0.4) at baseline to 3.5 (SD 0.5) at 12 months. The Marked Recovery cluster exhibited the highest scores, improving from 3.7 (SD 0.5) at baseline to 4.3 (SD 0.5) at 12 months.

Marked recovery during follow-up associated with being employed (Table 1). Patients in the Stable cluster had more comorbidities, such as asthma, musculoskeletal pain in the back or neck, anxiety, and sleep apnea, and were more often administered anti-depressant medication (Table 1). Previous hospitalization or intensive care unit (ICU) admission was not associated with recovery trajectories or QoL outcomes (Table 1).

In the recovering clusters, the most prominent improvement was seen between baseline and 3 months. Variance was observed within all the clusters, particularly during the first months of follow-up. This cluster also demonstrated a ceiling effect at approximately 4.5 points.

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When comparing the three QoL measures across recovery trajectory clusters, statistically significant differences between trajectory clusters were observed across all outcome measures throughout the follow-up period. Patients in the Stable cluster reported persistently low general QoL (VAS ranging from 3.9 at baseline to 4.5 at 12 months on a 0–10 scale) and HRQoL (15D approximately 0.7 throughout follow-up, scale 0–1) (Table 2).

Table 2. EUROHIS-QOL-8 and SSD-12 questionnaire replies at baseline and during follow-up. All the items were significantly associated with the trajectory clusters (p<.001). Patients in the Stable cluster reported persistently low general QoL (VAS and EUROHIS-QOL-8) and HRQoL (15D). They also had consistently elevated levels of distressing symptom-related perceptions (SSD-12). In contrast, patients in the Marked Recovery cluster reported good general QoL and HRQoL, and low SSD-12. The Partial Recovery cluster rated consistently between these two groups.

Questionnaire replies	**Total**	**Trajectory clusters**		
		Stable cluster	**Partial recovery cluster**	**Marked recovery cluster**
EUROHIS-QOL-8 Mean (SD): Baseline	3.1 (0.6)	2.5 (0.4)	3.1 (0.4)	3.7 (0.5)
Month 3	3.3 (0.7)	2.6 (0.4)	3.3 (0.5)	4.1 (0.4)
Month 6	3.4 (0.7)	2.5 (0.4)	3.4 (0.4)	4.1 (0.4)
Month 12	3.5 (0.8)	2.6 (0.4)	3.5 (0.5)	4.3 (0.5)
VAS 0-10 QoL Mean (SD): Baseline	5.0 (2.1)	3.9 (2.0)	5.0 (2.0)	6.2 (1.7)
Month 3	5.8 (2.1)	4.3 (1.7)	5.7 (1.9)	7.4 (1.6)
Month 6	6.0 (2.0)	4.3 (1.7)	6.0 (1.7)	7.7 (1.2)
Month 12	6.4 (2.1)	4.5 (1.7)	6.4 (1.6)	8.2 (1.4)
QoL-15D Mean (SD): Baseline	0.8 (0.1)	0.7 (0.1)	0.8 (0.1)	0.8 (0.1)
Month 3	0.8 (0.1)	0.7 (0.1)	0.8 (0.1)	0.9 (0.1)
Month 6	0.8 (0.1)	0.7 (0.1)	0.8 (0.1)	0.9 (0.1)
Month 12	0.8 (0.1)	0.7 (0.1)	0.8 (0.1)	0.9 (0.1)
SSD-12 Mean (SD): Baseline	23.3 (8.4)	26.5 (8.0)	23.5 (7.9)	19.9 (8.3)
Month 3	20.0 (9.1)	25.1 (8.1)	21.4 (7.9)	13.4 (7.8)
Month 6	18.3 (9.7)	26.4 (7.6)	19.1 (8.1)	10.2 (7.2)
Month 12	17.9 (10.9)	26.1 (8.3)	18.2 (9.9)	9.9 (8.4)

EUROHIS-8 = EUROHIS-QOL 8-item index, QoL-15D = quality of life, 15-dimensional questionnaire, SD = standard deviation, SSD-12 = somatic symptom disorder questionnaire (12 questions), VAS = visual analogue scale.

They also had persistently elevated levels of distressing symptom-related perceptions, with mean SSD-12 scores remaining around 26 (out of 48). In

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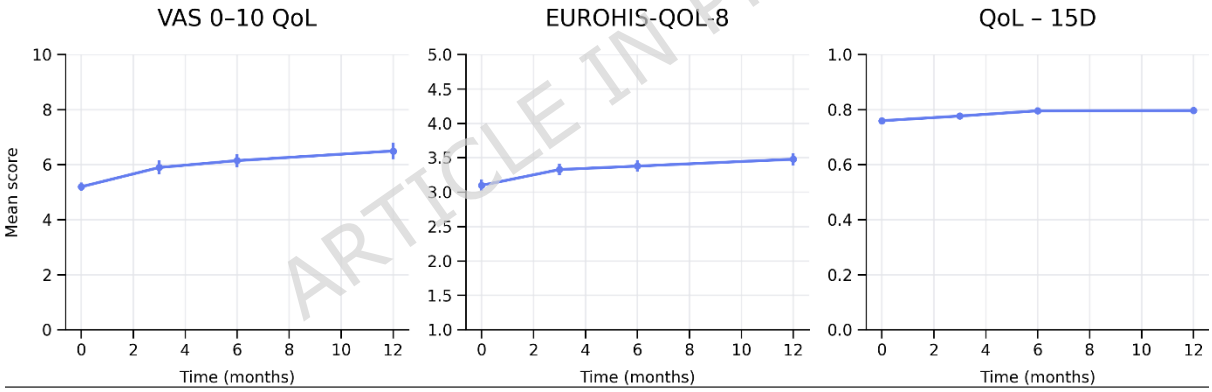
contrast, patients in the Marked Recovery cluster reported consistently higher general QoL (VAS ranging from 7.4 to 8.2) and HRQoL (15D approximately 0.9), along with lower SSD-12 scores (10–13) across follow-up. The Partial Recovery cluster showed values consistently between these two groups.

3.2. Primary outcome measure: QoL by VAS

In the total cohort, based on LMM estimates adjusted for age (the only covariate retained based on the attrition analysis), patient-reported mean QoL on a 0-10 VAS scale improved from 5.2 (confidence interval (CI) 5.0-5.4, standard error (SE) 0.10) at baseline to 5.9 (CI 5.6-6.1, SE 0.13) at 3 months and further to 6.5 (CI 6.2-6.8, SE 0.14) at 12 months (Figure 3). Improvement was seen throughout the follow-up period, although the period of most improvement was between baseline and 3 months.

Figure 3. Temporal development of quality of life (QoL) and health-related QoL measured by self-reported QoL on a 0-10 Visual Analogue Scale (VAS) scale, the European Health Interview Survey QoL 8-item Index (EUROHIS-QOL-8), and the 15-dimensional HRQoL measure (QOL-15D). The scores are marginal means with standard error from linear mixed models.



3.3. Secondary outcome measures: QoL by EUROHIS-QOL-8 and HRQoL by 15D

QoL assessed by the EUROHIS-QOL-8 showed similar trends to the VAS, with the greatest improvement between baseline and 3 months, increasing from 3.1 (CI 3.0-3.2, SE 0.03) at baseline to 3.3 (CI 3.2-3.4, SE 0.04) at 3 months and further to 3.5 (CI 3.4-3.6, SE 0.04) at 12 months (Figure 3).

The mean HRQoL measured by 15D increased from 0.76 (CI 0.75-0.77) at baseline to 0.78 at 3 months, 0.80 at 6 months, and remained stable at 0.80 (CI 0.78-0.81, SE 0.007) at 12 months (Figure 3). The greatest improvement occurred between baseline and 6 months, after which values plateaued.

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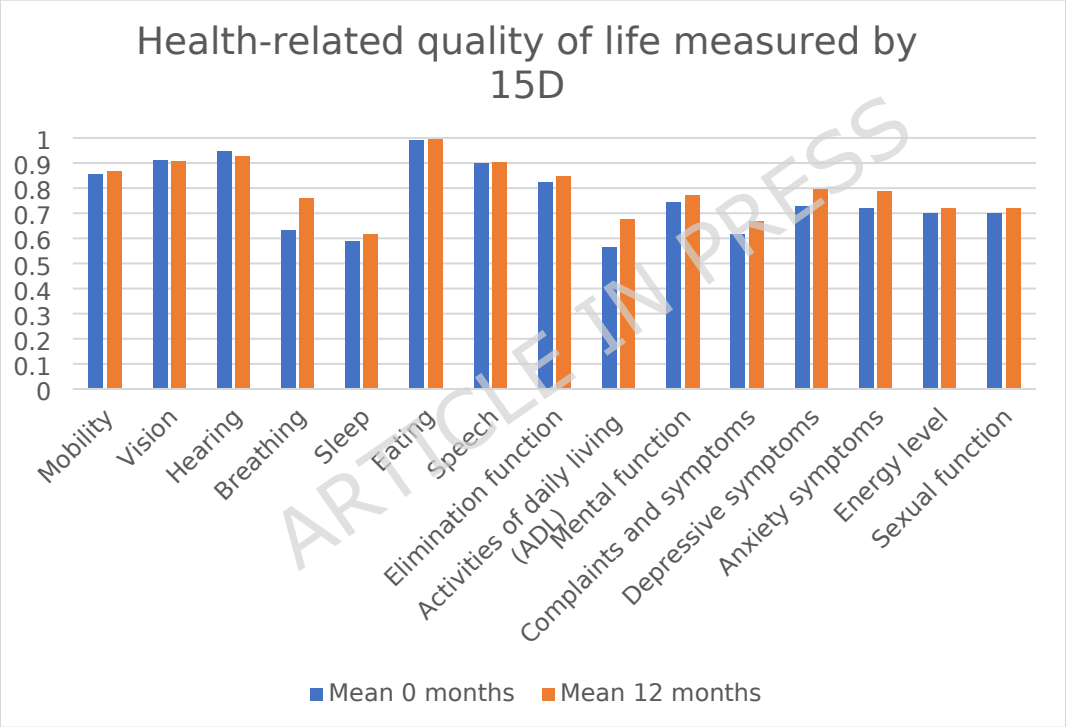
At baseline, the most affected dimensions were breathing (0.63), sleep (0.59), activities of daily living (ADL) (0.57), and complaints and symptoms (0.61) (Figure 4). Of these, breathing and ADL improved most by 12 months (0.76 and 0.67 respectively), while sleep problems remained largely unchanged (0.62). Additionally, depressive and anxious symptoms improved from baseline to 12 months.

Figure 4. The different dimensions of health-related quality of life measured by 15-dimensional HRQoL measure (15D) at baseline and at 12 months. The scores are marginal means with standard error from linear mixed models. At baseline, the most affected dimensions were breathing (0.63), sleep (0.59), activities of daily living (ADL) (0.57), and complaints and symptoms (0.61). Of these, breathing and ADL improved most by 12 months (0.76 and 0.67 respectively), while sleep problems remained largely unchanged (0.62).



3.4. Characteristics of patients lost to follow-up

To assess potential attrition bias, we compared non-responders, partial responders, and full responders. Detailed descriptive characteristics of these groups are presented in Supplementary Table S1. Younger age was associated with lower follow-up participation and was therefore included as a covariate in the final models. Full responders were on average slightly older (48.5 years; SD 10.9) than partial responders (44.7 years; SD 10.3) and non-responders (41.1 years; SD 11.9) ($p<0.001$). No significant differences were

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observed regarding sociodemographics, hospitalization, comorbidities, or baseline or follow-up QoL and HRQoL.

Table S1. Characteristics of participants according to questionnaire reply category (None – only baseline information, Partial – 1 or 2 follow-ups, Full – 3 follow-ups). Green line indicates statistically significant difference between groups ($p < 0.05$).

	Total	**Replies**			**p-value**
		None	**Partial**	**Full**	
Total, n (% of total)	442 (100.0)	129 (29.2)	183 (41.4)	130 (29.4)	NA
Patient characteristics					
Female, n (%)	312 (70.6)	94 (72.9)	128 (69.9)	90 (69.2)	0.80
Age (years), mean (SD)	44.8 (11.3)	41.1 (11.9)	44.7 (10.3)	48.5 (10.9)	< .001
BMI (kg/m2), mean (SD)	27.4 (5.8)	26.9 (5.7)	27.3 (5.6)	28.0 (6.3)	0.41
Living alone, n (%)	118 (26.7)	37 (28.7)	49(26.8)	32 (24.6)	0.77
Tertiary education, n (%)	249 (58.3)	64 (52.5)	105(59.0)	80 (63.0)	0.24
Employed, n (%)	298 (68.5)	81 (64.3)	128(71.5)	89 (68.5)	0.42
Monthly doses of alcohol, mean (SD)	7.1 (9.5)	7.3 (8.4)	7.1 (9.9)	7.0 (10.0)	0.88
Smoking, n (%)	30 (7.0)	13 (10.7)	15(8.5)	2 (1.6)	0.006
PCC-variables					
Symptom duration (months), mean (SD)	10.8 (7.2)	12 (7.2)	9.6 (6.0)	10.8 (8.4)	0.17
Hospitalization during acute COVID-19, n (%)	37 (8.5)	15 (11.9)	11(6.0)	11 (8.6)	0.19
Intensive care during acute COVID-19, n (%)	18 (4.1)	7 (5.6)	4(2.2)	7 (5.5)	0.28
Comorbidities					
Number of comorbidities, mean (SD)	1.1 (1.4)	1.0 (1.3)	1.1 (1.3)	1.2 (1.5)	0.58
At least one comorbidity, n (%)	230 (53.6)	63 (51.2)	94(52.8)	73 (57.0)	0.62
Antidepressant medication, n (%)	50 (11.5)	15 (11.9)	18(9.9)	17 (13.3)	0.65
Asthma, n (%)	67 (15.6)	11 (8.9)	26(14.6)	30 (23.4)	0.007
Musculoskeletal pain, n (%)	36 (8.4)	8 (6.5)	17(9.6)	11 (8.6)	0.65
Anxiety disorder, n (%)	38 (8.9)	18 (14.6)	11(6.2)	9 (7.0)	0.03
Sleep apnea, n (%)	33 (7.7)	6 (4.9)	16(9.0)	11 (8.6)	0.40
Hypertension, n (%)	36 (8.4)	9 (7.3)	13(7.3)	14 (10.9)	0.46
Migraine, n (%)	28 (6.5)	8 (6.5)	12(6.7)	8 (6.2)	> .99
Depression, n (%)	28 (6.5)	11 (8.9)	9(5.1)	8 (6.2)	0.42
Hypothyroidism, n (%)	20 (4.7)	4 (3.3)	12(6.7)	4 (3.1)	0.26
Long term insomnia, n (%)	16 (3.7)	5 (4.1)	7(3.9)	4 (3.1)	0.90
Diabetes, n (%)	14 (3.3)	3 (2.4)	5(2.8)	6 (4.7)	0.61
Irritable bowel syndrome (IBS), n (%)	10 (2.3)	2 (1.6)	5(2.8)	3 (2.3)	0.92
Questionnaire replies					

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Baseline VAS 0-10 QoL, mean (SD)	5.1 (2.1)	5.3 (2.1)	5.2 (2.1)	4.9 (2.0)	0.45
Baseline EUROHIS-8, mean (SD)	3.1 (0.6)	3.1 (0.6)	3.1 (0.6)	3.1 (0.6)	0.67
Baseline QOL-15D, mean (SD)	0.8 (0.1)	0.8 (0.1)	0.8 (0.1)	0.8 (0.1)	0.19
Baseline SSD-12, mean (SD)	23.7 (8.9)	24.4 (10.1)	23.7 (8.8)	22.8 (7.7)	0.36

BMI = body mass index, EUROHIS-8 = EUROHIS-QOL 8-item index, PCC=post-covid condition, SD = standard deviation, VAS = visual analogue scale, SSD-12 = somatic symptom disorder questionnaire, 12 questions, QOL-15D = health-related quality of life, 15-dimensional questionnaire.

4. Discussion

In this prospective cohort of patients with PCC treated at a specialized clinic, both general QoL and HRQoL improved during the one-year follow-up. Overall, 73.8% of patients belonged to recovering trajectories. Mean self-rated QoL increased from 5.2 to 6.5 on a 0–10 scale, with most improvement occurring during the first three months. Similarly, HRQoL, measured by the 15D instrument, increased significantly from 0.76 to 0.80, reflecting recovery across multiple domains. Despite these positive changes, overall levels remained lower than those typically reported in general population samples[53,55], indicating an ongoing burden even after one year.

To capture the multifaceted impact of PCC, we used both general QoL and HRQoL instruments. HRQoL measures, such as the 15D, focus on health-specific domains including physical functioning, psychological well-being, and symptom-related limitations [10,11,59], whereas general QoL assessments extend beyond health to encompass overall life satisfaction and social participation [15,60,61]. Using both perspectives allowed us to address PCC's wider consequences for daily life, enabling comparisons with previous studies that relied on either construct alone [4,15,32,62]. Our findings are broadly consistent with these studies in showing reduced QoL in PCC, but further highlight the heterogeneity of recovery trajectories and the close alignment between general QoL, HRQoL, and symptom-related distress.

Trajectory analyses also demonstrated that both higher baseline QoL and HRQoL and lower SSD-12 scores were among the strongest predictors of favorable recovery, highlighting the prognostic value of patients' symptom perceptions as well as their initial subjective health status alongside demographic and clinical variables. These patterns underscore the heterogeneity of recovery in PCC and provide the foundation for discussing prognosis and implications for care. These findings are consistent with previous studies indicating that baseline health status and symptom burden are key determinants of recovery and long-term QoL in PCC and further

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support the role of symptom-related distress and psychological factors in shaping recovery trajectories [18,39,41,42].

The observed heterogeneity may also reflect underlying differences in the clinical presentation and overall impact of PCC. In the present study, we did not operationalize PCC severity as a single measure or symptom-based score, as our focus was on patient-reported QoL and HRQoL. Future studies integrating symptom-based severity measures with longitudinal QoL trajectories may help further elucidate these relationships.

A VAS scale was selected as the primary outcome measure due to its simplicity and applicability in fatigued patients, which is particularly relevant in PCC, where fatigue is one of the most commonly reported and burdensome symptoms [63]. While multifaceted tools like EUROHIS-QOL-8 provided broader insights into different aspects of QoL, the VAS proved to be a quick and reliable method for capturing overall well-being consistently over time. Previous studies have demonstrated the reliability and construct validity of single-item global QoL scales using a 0–10 VAS format [52,53], supporting their use as pragmatic indicators of general QoL. The parallel patterns observed in VAS and EUROHIS-QOL-8 scores further support the VAS as an effective and responsive tool for monitoring QoL in PCC populations.

Recovery shown by EUROHIS-QOL-8 progression, revealed three main trajectories. EUROHIS-QOL-8 was chosen for trajectory analysis because of its validation and availability of established population reference values, which facilitate interpretation of findings in a broader context. Patients in the Marked Recovery cluster were more often employed and reported better baseline QoL than those in the other two clusters. The Stable cluster was characterized by comorbidities such as asthma, musculoskeletal pain, anxiety, and sleep apnea. These findings are consistent with previous studies indicating that better baseline functional status and socioeconomic factors such as employment are associated with more favorable recovery, while multimorbidity and pre-existing physical and mental health conditions are linked to poorer outcomes in PCC and other chronic conditions, reflecting the complex interplay between physical, psychological, and social determinants of recovery [15,16].

Additionally, patients in the Stable cluster were more often administered antidepressant medication. This finding aligns with broader evidence of increased antidepressant use during the COVID-19 pandemic [64] and may reflect both underlying mental health needs and the use of these

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medications for managing PSS [65,66]. After COVID-19, anxiety, depression and PSS like fatigue have been common, with evidence indicating they are influenced by psychological distress, somatic comorbidities, social factors (e.g., perceived stigma or lack of support), and cognitive, affective, and behavioral responses to illness [39].

SSD-12 scores provided further insight, showing that patients in the Stable cluster reported higher levels of symptom-related preoccupation—manifested as frequent health-related thoughts, emotional distress, and behavioral avoidance—compared to those who recovered. This finding is consistent with evidence linking dysfunctional symptom-related cognitive and emotional responses to lower QoL and functional impairment in PSS and PCC [37,38,42],and with recent longitudinal studies showing that fatigue, persistent symptoms, and perceived stress are key determinants of HRQoL trajectories in PCC [41]. It suggests that perceptual factors may maintain distress and functional limitations even as somatic recovery progresses. Addressing these perceptual factors and avoidance behavior could offer intervention opportunities, for example through cognitive-behavioral approaches and micro-choice-based interventions aimed at modifying illness beliefs, reducing symptom-related anxiety, and promoting adaptive responses to symptoms through small, incremental behavioral changes [43,67].

At 12 months, the mean EUROHIS-QOL-8 score in the Marked Recovery cluster was 4.2 on the 1-5 scale, reaching or slightly exceeding values reported for the general Finnish population (Health 2011 study, approximately 3.8-4.1 depending on age and sex[68]). In contrast, the Stable cluster remained below these reference values, reflecting a persistent burden on well-being despite medical stabilization.

Previous hospitalization or intensive care unit (ICU) admission did not significantly predict long-term QoL recovery, although the ICU treatment rate (3.6%) in our cohort was higher than global estimates (1.8%) [69,70]. Notably, ICU treatment was the sole predictor of antineuronal antibodies in a previous study conducted in the same cohort as the present study [71], suggesting systemic immune activation post-illness rather than targeted autoimmunity. There is also evidence of proinflammatory cytokines and other biological markers reflecting not only infection or inflammation, but also the cumulative stress from previous illness and life events, i.e. serving as psychobiological bridge markers [39]. These findings further support a holistic and interdisciplinary rehabilitation approach over narrowly focused biomedical interventions [72,73].

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Our findings demonstrate considerable HRQoL impairment in PCC. At baseline, the mean 15D score was 0.76, which is significantly lower than the average of approximately 0.92-0.95 among healthy Finnish adults [55,68]. It is comparable to scores reported for patients with major depression (mean 0.75) [74] and chronic pain (mean 0.71)[75,76]. The observed increase of 0.04 (from 0.76 to 0.80 over one year) is clinically meaningful, given that a change of 0.035 on the 15D scale corresponds to a markedly improved health status [56]. These results are consistent with the overlapping features seen between PCC and pain and mood disorders [77–79]. Some evidence also points to sensitization and nociplastic mechanisms as part of PCC's clinical picture, indicating similarity with both chronic pain and somatic symptom disorder [39,80].

The 15D instrument captures this multidimensional burden of PCC, revealing that although some residual impairments persisted, many domains improved over time. The most affected dimensions were breathing, sleep, ADL, and complaints and symptoms, reflecting both physiological and psychosocial impact [76]. Breathing and ADL improved by 12 months, but sleep problems remained, highlighting poor sleep as a key clinical target. Early recognition of HRQoL decline without corresponding objective findings may help identify individuals at risk for poorer recovery in PCC, particularly patients with pronounced symptom preoccupation or sleep disturbance. This could guide tailored interventions, such as cognitive-behavioral or sleep-focused rehabilitation programs.

A key strength of this study is its prospective cohort design with systematic follow-up of PROMs, providing a patient-centered view of QoL and its temporal development over one year. The linkage with hospital registry data strengthened the clinical context by including prior diagnoses and medication use. The retention rate was relatively high, with more than two-thirds of patients providing at least one follow-up measurement and nearly half completing the 12-month follow-up. To evaluate potential bias, we compared non-responders, partial responders, and full responders. They differed little apart from full responders being slightly older on average, suggesting attrition introduced minimal bias. Furthermore, the interdisciplinary approach at the clinic, involving multiple healthcare professionals, offered a holistic view of patient care and its impact on outcomes [51].

Another major strength lies in the combined use of both general QoL and HRQoL measures, and the inclusion of SSD-12 added a psychological

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dimension, revealing how illness beliefs and symptom-related thoughts relate to perceived recovery. This combination offers a more complete understanding of PCC's biopsychosocial nature.

This study also adds new understanding to prospective PCC research. In addition to our findings that recovery in QoL and HRQoL was associated with psychological distress, somatic and mental comorbidities, employment status, and socioeconomic factors, consistent with previous work [20–23,25,36,81], we also found that recovery was strongly predicted by baseline QoL and HRQoL. This emphasizes the prognostic value of the patients' initial assessments, promoting early identification of patients at risk.

An essential consideration in our methodological approach was the ability to accommodate missing data. For this purpose, we applied trajectory clustering based on DTW distance, which allows comparison of trajectories despite incomplete observations. Longitudinal analyses were conducted using linear mixed models, which are well suited for repeated measures data and enable inclusion of participants with incomplete follow-up.

This study also has limitations. Our study was conducted in a tertiary care unit that was able to accept no more than half of all referrals. Decisions regarding referral acceptance were based on clinical judgement rather than standardized criteria. Patients whose referrals were not accepted were typically redirected to primary care with management recommendations from the hospital. This process ensured appropriate allocation of care but also meant that our study population was relatively well-defined, comprising individuals with symptoms persistent enough to require tertiary care but still suitable for timely rehabilitation. As in many tertiary care cohorts, the participants were socioeconomically more advantaged than the general population, with nearly two thirds having tertiary education compared to 43% nationally [82]. This may influence the observed recovery trajectories and modifying factors. This is important given recent evidence that socioeconomic disadvantage is strongly associated with poorer HRQoL outcomes in PCC, particularly among patients with lower education or out of work [83].

We did not systematically account for the number of SARS-CoV-2 infections or reinfections during follow-up, which may influence the course and severity of post-COVID condition. Future studies incorporating such data may help clarify its impact on recovery trajectories.

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Ethnicity was also not systematically recorded in this study. As participation required sufficient proficiency in Finnish to complete the questionnaires, the cohort likely represents primarily Finnish-born or long-term Finnish-speaking residents. While this reflected the availability of validated study instruments and practical constraints of a clinical setting, it may limit generalizability of our results to patients of non-Finnish origin.

In addition, reasons for loss to follow-up and detailed exclusion criteria were not systematically recorded, which limits the ability to fully assess potential sources of attrition.

Although the used HRQoL and QoL instruments comprehensively assessed key domains including physical, mental, and social well-being, they do not fully capture exposure to life stressors or availability of social support during follow-up, while these have been shown to influence long-term outcomes after COVID-19 [36,39,42,84]. Our SSD-12 findings also align with the relevance of psychological factors in PCC.

Future studies would benefit from incorporating such contextual factors and from including more socioeconomically diverse populations, as these may help in further explaining individual differences in recovery trajectories and guide more tailored interventions. Longer follow-up periods will also be important to determine whether the observed trajectories remain stable or evolve over time.

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5. Conclusion

In this prospective cohort of mainly non-hospitalized PCC patients seen in a specialized PCC clinic, general and health-related quality of life improved over 12 months, although recovery trajectories differed. Distressing illness-related perceptions, as well as comorbidity burden, being unemployed, and poor baseline QoL and HRQoL were associated with unfavorable prognosis. These findings support integrating psychosocial assessment into PCC care and highlight the value of promoting non-threatening illness beliefs and expectations to enhance recovery.

Data Availability Statement

The cohort dataset contains sensitive personal health information and cannot be publicly shared due to GDPR and Finnish data protection regulations. De-identified data can be made available from the corresponding author upon reasonable request and subject to a data-sharing agreement and appropriate ethical approvals.

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Declaration of generative AI and AI-assisted technologies in the writing process

The authors used ChatGPT (GPT-5, OpenAI) for spell-checking and proofreading assistance. While using this tool, they reviewed and edited the content as needed and take full responsibility for the publication.

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Additional information

No potential conflict of interest was reported by the authors.

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CRediT Authorship Statement

We thank the participants for making this research possible. HL, MSa, HRV, and JA contributed to the conceptualization and study design. HRV, SS, VVK and AS collected the data. MVa and MVe performed formal analysis. HL, MSi, and HRV drafted the manuscript, and HL, MSi, MSa, MK, KK, AM, AK and JA contributed to reviewing and editing. All authors contributed to interpretation of the data, critically revised the manuscript, and approved the final version.