BMJ Open

Life after COVID-19 the road from intensive care back to living: a prospective cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-062332
Article Type:	Original research
Date Submitted by the Author:	02-Mar-2022
Complete List of Authors:	Wiertz, Carolina; Adelante, Rehabilitation medicine; Maastricht University, Department of Rehabilitation Medicine Research School CAPHRI Hemmen, Bena; Adelante, Rehabilitation medicine; Maastricht University, Department of Rehabilitation Medicine Research School CAPHRI Sep, Simone JS; Adelante, Rehabilitation medicine; Maastricht University, Department of Rehabilitation Medicine Research School CAPHRI van Santen, Susanne; Maastricht Universitair Medisch Centrum+, Department of Intensice Care van Horn, Yvette; Adelante, Rehabilitation medicine van Kuijk, Sander; Maastricht Universitair Medisch Centrum+, Clinical Epidemiology and Medical Technology Assessment Verbunt, Jeanine; Adelante, Rehabilitation medicine; Maastricht University, Department of Rehabilitation Medicine Research School CAPHRI
Keywords:	COVID-19, REHABILITATION MEDICINE, Adult intensive & critical care < INTENSIVE & CRITICAL CARE

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Life after COVID-19 the road from intensive care back to living: a prospective cohort study

Author's names

Carolina MH Wiertz MD[1,2], Bena Hemmen MD PhD[1,2], Simone JS Sep PhD[1,2], Susanne van Santen MD[3], Yvette Y van Horn MD[1], Sander MJ van Kuijk[4], Jeanine A Verbunt MD PhD[1,2]

Affiliation of authors

[1] Adelante Zorggroep, P.O. Box 88, 6430 AB Hoensbroek, The Netherlands.

[2] Department of Rehabilitation Medicine Research School CAPHRI, Maastricht University, P.O. Box 616, 6200 MD Maastricht, The Netherlands.

[3] Department of Intensive Care Medicine, Maastricht University Medical Centre, 6202 AZ Maastricht, The Netherlands.

[4] Department of Clinical Epidemiology and Medical Technology Assessment, Maastricht University Medical Centre, 6202 AZ Maastricht, The Netherlands.

Corresponding author: Carolina Wiertz

Adelante Zorggroep

P.O. Box 88

6430 AB Hoensbroek

The Netherlands

E-mail: c.wiertz@adelante-zorggroep.nl

Life after COVID-19 the road from intensive care back to living: a prospective cohort study

Abstract

Objectives: The principal aim of the present study was to evaluate recovery of participation in post-COVID-19 patients during the first year after ICU discharge. The secondary aim was to identify the early determinants associated with recovery of participation.

Design: Prospective cohort study.

Setting: Tertiary COVID-19 post-ICU inpatient rehabilitation facility in the Netherlands, during the first epidemic wave between April and July 2020, with a one-year follow-up.

Participants: COVID-19 ICU survivors above 18 years of age needing inpatient rehabilitation.

Main outcome measures: Participation in society was periodically assessed by the 'Utrecht Scale for Evaluation of Rehabilitation-Participation (USER-P) restrictions scale'. Secondary measures of body function impairments (muscle force, pulmonary function, fatigue (MFI), breathlessness (MRC), pain (NRS)), activity limitations (6MWT, PROMIS 8b), personal factors (coping (UPCC), Anxiety and depression (HADS), post traumatic stress (GPS-PTSD-5), cognitive functioning (CLC-IC) and social factors were used. Statistical analyses: linear mixed-effects model.

Results: This study included 67 COVID-19 ICU survivors (mean age 62y, 78% male). Mean USER-P restrictions scores increased over time, with mean participation levels increasing from 62.0 (SD 23.7), 76.5 (SD 20.4) to 86.1 (SD 16.8) at one, three and 12 months respectively. After one year, 50% had not fully resumed work and restrictions were reported in physical exercise (51%), household duties (46%), and leisure activities (29%). Self-reported complaints of breathlessness and fatigue, more perceived limitations in daily life, as well as personal factors (less pro-active coping style and anxiety/depression complaints) were associated with delayed recovery of participation.

Conclusions: This study supports the view that an integral vision of health is important when looking at the long-term consequence of post-IC COVID-19. Personal factors such as having a less proactive coping style or mental impairments early on contribute to delayed recovery.

Keywords: COVID-19, Critical care, Rehabilitation medicine

Strengths and limitations of this study

- This study only included the most severely affected post-ICU COVID-19 patients referred to inpatient rehabilitation.
- This study used physical examination as well as questionnaires, which means that there was a combination of objective and subjective measurements.
- Although the sample size is small, a large number of factors were studied for their effect on the course of participation recovery.
- Twenty-three patients were not approached in time for consent to participate.
- The lockdown and the inability to perform social and outdoor activities may have affected the total USER-P score.

Word count abstract: 284

Word count main text: 2998

Number of figures and tables: 6

Introduction

In the first wave of the coronavirus disease 2019 (COVID-19) pandemic in the Netherlands about 2% of all confirmed cases needed treatment in an intensive care unit (ICU) (1,2). About three-quarters of those admitted to an ICU had acute respiratory distress syndrome (3) and many patients were recorded as having shock, acute kidney injury, thrombotic complications and/or cardiac injury (3).

Survivors of critical illness frequently experience new or worsening physical, cognitive and/or mental impairment, described as post intensive care syndrome (PICS) (4), which can have long-term effects on participation and quality of life (5–7). Immediately after ICU admission, COVID-19 patients display various physical impairments such as exertional hypoxemia, reduced overall muscle force, shoulder problems, dysphagia, and anxiety complaints (8). In the subacute phase (one to three months after ICU discharge) 90% of the post-ICU COVID patients still experience symptoms affecting at least one of the PICS domains (9,10). Due to the varying impact of severe COVID-19, patients may experience limitations in their participation in daily living, social functioning or work performance (11,12). Restrictions in participation may eventually lead to an increase in (healthcare) costs, since patients need for example more professional assistance in their ADL or return to work is delayed. Although impairments in various domains of functioning have been identified, any long-term effects on the recovery of participation are unclear. The effect that this new disease may have on participation, combined with the large number of COVID-19 ICU survivors, points to the need to study factors that could delay the recovery in participation of survivors after ICU discharge. Consequently, the present study aimed to evaluate the recovery of participation during the first year after ICU discharge in post-COVID-19 patients. The secondary aim was to identify early determinants associated with recovery of participation.

Methods

Study design and participants

This prospective cohort study was performed at Adelante Zorggroep, a rehabilitation centre in the South of the Netherlands. Patients were eligible to participate in the study if (1) referred for inpatient rehabilitation after ICU discharge for COVID-19 pneumonia/ respiratory insufficiency, (2) aged 18 or older and (3) functioning independently before their COVID-19 infection. The exclusion criterion was not speaking or reading the Dutch language fluently. All patients received inpatient multidisciplinary rehabilitation treatment including physiotherapy, occupational therapy, speech therapy and psychology according to the patient's limitations and needs. All participants provided written informed consent. Patients were transferred to the rehabilitation centre from 7 (2 academic and 5 regional) hospitals in the region. COVID-19 was confirmed with a SARS-COV-19 positive PCR test. The local medical ethics committee Zuyderland METC (METCZ20200086) approved the study.

Patient and public involvement: Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Data collection

Data was collected in the form of baseline information at admission to the rehabilitation centre and through physical examination and self-administered questionnaires after one (T1), three (T2) and twelve months (T3). Since different domains of functioning can be affected by COVID-19, measurements were chosen based on an integral vision of health and included body function impairments, activity limitations and participation restrictions as well as personal and social factors. These factors are derived as main domains in the International Classification of Functioning, Disability and Health (ICF) that supports the classification of health and health-related conditions and their effect on social participation (Figure 1) (13).

Primary outcome variable: Participation in society was assessed by the 'Utrecht Scale for Evaluation of Rehabilitation-Participation (USER-P) restriction subscale'. The restriction subscale consists of 11 items on restrictions in vocational, leisure and social activities. Items are rated from 0 'not possible' to 3 'without difficulty' and a 'not applicable' option. The total score ranges from 0 to 100, with higher scores indicating fewer restrictions in participation (14,15).

Data on age, sex, comorbidities and parameters related to critical illness severity was collected from the medical transfer letters. Comorbidities were classed into diabetes mellitus, hypertension, cardiovascular disease, lung disease and psychiatric disorders. Parameters related to severity of the critical illness were length of ICU stay, invasive mechanical ventilation (IMV) (yes/no) and duration of invasive IMV. The duration of the inpatient rehabilitation was also recorded.

Physical examination: Assessment of Muscle strength, functional exercise capacity and pulmonary function were part of a physical examination. To measure muscle strength, a handheld dynamometer (HHD) was used (16) to assess the following muscle groups: shoulder abduction, elbow flexion, wrist extension, hip flexion and knee extension, all on the patient's dominant side. HHD values were measured in Newtons and percentages of the norm compared with healthy persons of the same sex, age, and weight (17,18). For the clinical assessment of the functional exercise capacity, the 6-minute walk test (6-MWT) was used (19). To evaluate pulmonary function Quark PFT spirometry (Cosmed, Italy) was used (20). Forced expiratory volume in the first second (FEV_1), forced vital capacity (FVC) and FEV_1/FVC ratio were included in the analysis, displayed in percentage of the norm.

In addition, self-administered questionnaires were used. Breathlessness was assessed by the MRC breathlessness scale, which comprises five statements that range from 0 'no trouble with breathlessness' to 5 'I am too breathless to leave the house' (21). The Numerical Rating Scale (NRS) was used for assessing pain. Patients were asked to rate their mean and maximum pain intensities in the last seven days, ranging from 0-10, with 0 indicating 'no pain' and 10 indicating 'the worst imaginable pain' (22). The multidimensional Fatigue Inventory (MFI) is a 20-item metric for fatigue

severity. It has 5 dimensions: general fatigue, physical fatigue, mental fatigue, reduced motivation and reduced activity. Each item ranges from 1 'absence of fatigue' to 5 'severe fatigue'. A total fatigue score is calculated as the sum of the subscale scores (20–100). Higher total scores indicate higher levels of fatigue (23). The perceived limitations in daily life were assessed using the PROMIS physical function short form 8b. This survey was created for adults with chronic illnesses and it contains eight questions ranging from 1 'unable to do' to 5 'without any difficulty' (24). Calculating T-scores, where higher scores indicate better physical function (25). Anxiety and depression complaints were assessed with the Hospital Anxiety and Depression Scale (HADS). A score ≥8 on either subscale was considered to be substantial anxiety or depression symptoms (26). Post-traumatic stress complaints were assessed using the Global Psychotrauma Screen – Post Traumatic Stress Disorder (GPS-PTSD-5). The regular GPS consists of 22 items, item 1-5 can be used to generate a GPS-PTDS-5 score (range 0-5), a score ≥3 indicates PTSD (27). Cognitive functioning was assessed using the Checklist for Cognitive consequences after an ICU-admission (CLC-IC). The CLC-IC consists of 10 items; higher scores indicate more cognitive problems experienced in daily life (range 0-10). The CLC-IC is based on the CLCE-24 (28). Proactive coping skills were assessed at T3 with the Utrecht Proactive Coping Scale (UPCC), which is a 21-item self-assessment tool scored on a 4-point scale ranging from 'not competent at all' to 'competent'. The total score was the average for all item scores (range 1–4), where higher scores indicate higher levels of proactive coping (29). Premorbid social- and work situations were collected at T1.

Statistical analyses

Results are reported as mean and standard deviation (SD) or as median and interquartile range (IQR) depending on distribution. Recovery of participation levels over time was assessed with a linear mixed-effects model for repeated measures. Patient characteristics in the domains of body function, activity limitations, personal and social factors at T0 and 1 month after admission in the rehabilitation centre (T1) were added to separate models that also included time and the interaction between that covariate

and time. Next, for illustrative purposes only, linear mixed-effects model analyses were stratified according to patient characteristics that were significantly associated with the course of recovery of participation levels to visualize different patterns of change over time. A $p<0.05$ was considered as statistically significant. Statistical analyses were performed with IBM SPSS statistics 26.0 (SPSS Inc. Chicago, IL).

Results

During the first COVID-19 wave between April 2 and June 30, 2020, 103 post-ICU patients were admitted for inpatient rehabilitation. Of these, twenty-three patients were missed since this study was part of clinical practice in a very dynamic period (first COVID-19 wave) and 13 patients were excluded for reasons given in figure 2. The study sample consisted of 67 patients (78% male) with a median age of 62 (IQR 57-68) and a median length of stay of 20 (12-33) days in the ICU and 19 (11-31) days inpatient rehabilitation (Table 1). Overall, this shows an improvement in muscle strength and functional exercise capacity (6MWT), whereas fatigue complaints and perceived limitations in daily life seem to decrease in the first year after ICU discharge (Table 1).

Participation restrictions improved in the first year after ICU discharge due to a COVID-19 infection (Figure 3). Mean participation levels increased from 62.0 (6.1 95%CI), 76.5 (4.6 95%CI) to 86.1 (5.5 95%CI) at one, three and 12 months respectively. One year after ICU discharge, 50.8% of the patients still reported restrictions in physical exercise, 45.8% in performing housekeeping and 28.8% in performing leisure activities. After one year work is not applicable in 42.4% of all patients, which is comparable to the premorbid work situation, where 58% of all patients were employed. One year after ICU discharge 28.8% of all patients still reported restrictions in work/education. Taking into account the patients who were not working pre-illness, means that 50% of the pre-illness working patients had not fully resumed work after one year (Table 1).

Regarding the second aim, in the ICF domain body functions, breathlessness (MRC breathlessness), regression coefficient: 0.60 (95%CI 0.23-0.97; p-value <0.01) and fatigue (MFI), regression coefficient: 0.07 (95%CI 0.03-0.09; p-value <0.01) were the only physical variables that influenced participation recovery over time. For the ICF domain activities, the perceived limitations in daily life (PROMIS 8b) showed a different pattern in the recovery of participation restriction level, regression coefficient: -0.11 (95%CI -0.12 to -0.05; p-value <0.01). In addition, personal factors like coping style (UPCC) regression coefficient: -2.39 (95%CI -4.20 to -0.06; p-value 0.01), anxiety (HADS anxiety) regression coefficient: 0.17 (95%CI 0.02-0.31; p-value 0.03) and depression (HADS depression) regression coefficient: 0.19 (95%CI 0.07-0.31; p-value <0.01) showed different paths in resuming the level of participation over time. Other early determinants show no significant difference in the recovery of participation (Table 2).

Participation levels increased significantly between 1 and 3 months and between 3 and 12 months in patients who reported more breathlessness, more fatigue or more limitations in daily life and those with a less pro-active coping style. In contrast, patients with less breathlessness, fewer fatigue complaints, fewer restrictions in daily life and a more pro-active coping style showed no significant increase between 3 and 12 months (Figure 4). In patients with a HADS anxiety score ≥8, no differences were found in participation levels in the first 3 months, while there was a significant difference in recovery of participation levels between 3 and 12 months. While participation levels significantly improved between 1 and 3 months and between 3 and 12 months for those experiencing fewer anxiety complaints. For depressive symptoms, both groups improved significantly in participation levels between 1 to 3 months and between 3 to 12 months, although a steeper curve is seen in the recovery of participation levels at 3 to 12 months in patients with more depressive symptoms.

Table 1	T0	One month (T1)	Three months (T2)	Twelve months (T3)
Baseline characteristics				
Age, years; n=67; median (IQR)	62 (57 – 68)	-		
Sex; n=67; No (%)				
- Men	52 (77.6%)	-		
- Women	15 (22.5%)	-		
Highest level of education; n=62; No (%)				
- Lower education	42 (67.7%)	-		
- Middle education	16 (25.8%)	-		
- Higher education	4 (6.5%)	-		
Work situation; n=62; No (%)				
- Full-time job	26 (41.9%)	-		
- Parttime job	10 (16.1%)	-		
- Retired	18 (29.0%)	-		
- Not working otherwise	8 (12.9%)	-		
Comorbidities; n=67; no (%)				
- Asthma / bronchitis	6 (9.0%)	-		
- Chronic obstructive pulmonary disease	4 (6.0%)	-		
- Obstructive sleep apnoea syndrome	12 (17.9%)	-		
- Diabetes Mellitus	12 (17.9%)	-		
- Hypertension	23 (34.3%)	-		
- Cardiovascular disease	21 (31.3%)	-		
- Chronic kidney disease	5 (7.4%)	-		
- Depression	4 (6.0%)	-		
- None of the above comorbidities	25 (37.3%)	-		
Parameters related to severity critical illness				
- Duration intensive care unit, in days; n=59; median (IQR)	20 (12 – 33)	-		
- Invasive mechanical ventilation; n=67; No (%)	58 (86.6%)	-		
- Duration IMV, in days; n=55; median (IQR)	17 (9 – 24)	-		
Duration inpatient rehabilitation, days; n=67; median (IQR)				19 (11 – 31)
Coping style (UPCC); n=58; mean (SD)				3.0 (0.2)
USER-P restriction subscale [a]				
- Work/education	-	64.4%	60.6%	28.8%
- Housekeeping	-	74.6%	65.2%	45.8%
- Mobility	-	59.3%	43.9%	16.9%
- Physical exercise	-	79.7%	60.6%	50.8%
- Going out	-	45.8%	24.2%	10.2%
- Outdoor activities	-	54.2%	36.4%	16.9%
- Leisure activities	-	42.4%	28.8%	20.3%
- Partner relationship	-	28.8%	24.2%	16.9%
- Visits to family/friends	-	45.8%	31.8%	10.2%
- Visits from family/friend	-	32.2%	13.6%	8.5%
- Telephone/PC contact	-	15.3%	13.6%	11.9%
Physical examination:				
- Muscle strength				
- Mean muscle force (HHD), mean (SD)	-	75.7% (15.3)	93.5% (24.6)	101.4% (15.3)
- 6MWT; mean (SD)	-	467.8m (91.2)	518.3m (102.5)	531.0m (86.5)
- Pulmonary function; mean (SD)				
- FEV1	-	87.5% (15.8)	93.8% (19.9)	93.6% (17.7)
- FVC	-	85.9% (16.3)	92.8% (18.7)	92.2% (15.6)
- FEV1/FVC ratio	-	79.6% (9.1)	77.3% (10.6)	79.1% (11.2)
Self-administered questionnaires:				
- Breathlessness (MRC); median (IQR)	-	2.0 (1.0 – 3.0)	1.0 (1.0 – 2.0)	1.0 (1.0 – 2.0)
- Pain (NRS); median (IQR)	-	2.0 (1.0 - 3.5)	2.0 (1.5 – 5.0)	2.0 (1.0 – 3.0)
- Fatigue (MFI); mean (SD)	-	58.6 (14.0)	56.0 (15.3)	50.8 (17.6)
- perceived limitations in daily life (PROMIS 8b); mean (SD)	-	34.8 (7.4)	39.2 (6.9)	44.8 (8.0)
- Anxiety (HADS-anxiety); median (IQR)	-	3.0 (1.0 – 5.0)	3.0 (1.0 - 6.0)	2.0 (0.5 – 6.0)
Exceeded anxiety cut-off ≥8	-	7/57 (12.3%)	11/66 (16.7%)	10/59 (16.9 %)
- Depression (HADS depression); median (IQR)	-	2.0 (1.5 – 6.0)	3.0 (1.0 – 6.0)	2.0 (1.0 – 4.0)
Exceeded depression cut-off ≥8	-	10/59 (16.9%)	13/66 (19.7%)	10/59 (16.9%)
- Post-traumatic stress (GPS-PTSD-5); median (IQR)		0.0 (0.0 – 1.0)	0.0 (0.0 – 1.0)	0.0 (0.0 – 1.0)
Exceeded PTSD cut-off ≥3		5/59 (8.5%)	8/66 (12.1%)	3/59 (5.1%)
- Cognitive impairments (CLC-IC); median (IQR)		3.0 (1.0 – 6.0)	4.0 (1.0 – 7.0)	2.0 (0.0 – 7.0)

Table 1, overview of the baseline characteristics (T0) and the physical examination and self-administered questionnaires at T1, T2 and T3. Abbreviations: IMV, Invasive mechanical ventilation; UPCC, Utrecht Proactive Coping Scale; USER-P, Utrecht Scale for Evaluation of Rehabilitation-Participation; HHD, handheld dynamometer; 6MWT, 6 minute walking test; FEV1, Forced expiratory volume in the first second; FVC, Forced vital capacity; n.a., not applicable; MFI, multidimensional Fatigue Inventory; HADS, Hospital Anxiety and Depression Scale; GPS, The Global Psychotrauma Screen; CLC-IC, Checklist for Cognitive consequences after an ICU-admission. [a] Restriction items values are percentages of patients who are restricted or dissatisfied.

Table 2	Estimate (95% CI)	p-value
Baseline characteristics		
Age	-0.03 (-0.08 – 0.02)	0.29
Sex	0.72 (-0.32 – 1.76)	0.17
Number of comorbidities	0.04 (-0.34 – 0.42)	0.83
Duration of inpatient rehabilitation	0.03 (-0.00 – 0.06)	0.07
Coping style (UPCC)	-2.39 (-4.20 – -0.06)	0.01*
ICU-stay specific parameters		
Length of ICU stay	0.02 (-0.01 – 0.06)	0.21
Duration of invasive mechanical ventilation	0.02 (-0.02 – 0.05)	0.37
Physical examination		
Muscle strength		
- Mean muscle force (HHD)	-0.02 (-0.06 – 0.01)	0.18
6MWT	-0.00 (-0.01 – 0.01)	0.65
Pulmonary function		
- FEV1	-0.02 (-0.06 – 0.01)	0.16
- FVC	-0.03 (-0.06 – 0.00)	0.07
- FEV1/FVC ratio	0.04 (-0.02 – 0.09)	0.24
Self-administered questionnaires		
Breathlessness (MRC)	0.60 (0.23 – 0.97)	< 0.01*
Pain (NRS)	-0.03 (-0.28 – 0.23)	0.84
Fatigue (MFI)	0.07 (0.03 – 0.09)	< 0.01*
Perceived limitations in daily life (PROMIS 8b)	-0.11 (-0.12 – -0.05)	< 0.01*
Anxiety (HADS-anxiety)	0.17 (0.02 – 0.31)	0.03*
Depression (HADS depression)	0.19 (0.07 – 0.31)	< 0.01*
Post-traumatic stress (GPS-PTSD-5)	0.24 (-0.21 – 0.70)	0.30
Cognitive impairments (CLC-IC)	0.09 (-0.07 – 0.24)	0.27

Table 2; linear mixed model for covariates at T0 or T1, as an interaction between covariate and time (1, 3, and 12 months), for the recovery of participation levels. * $p < 0.05$.
Abbreviations: UPCC, Utrecht Proactive Coping Scale; HHD, handheld dynamometer; 6MWT, 6 minute walking test; FEV1, Forced expiratory volume in the first second; FVC, Forced vital capacity; MFI, multidimensional Fatigue Inventory; HADS, Hospital Anxiety and Depression Scale; GPS, The Global Psychotrauma Screen; CLC-IC, Checklist for Cognitive consequences after an ICU-admission.

Discussion

In this prospective cohort study, recovery of participation during the first year after ICU discharge in COVID-19 ICU survivors who needed inpatient rehabilitation was evaluated and the association between early levels of body function impairments, activity limitations and personal and social factors on recovery were estimated. It is seen that in the first year after ICU discharge patients were able to improve their level of participation. Nevertheless, after one year, there are still important limitations in participation in daily life, mainly in resuming work, physical exercise, housekeeping and leisure activities. As early determinants for a delay in the resumption of a patient's habitual level of participation levels over the first year, higher levels of self-experienced breathlessness and fatigue

complaints, more perceived limitations in daily life as well as personal factors (having a less pro-active coping style, anxiety complaints or depression complaints) were found.

Heesakker et al. reported that in patients who survived one year following ICU treatment for COVID-19, physical, mental, or cognitive symptoms were often reported (30). This corresponds with the findings of the current study, whereas various physical, mental and cognitive impairments were seen one year after ICU admission. However, to our knowledge, this is the first study to report differences in the resumption of participation levels in post-ICU COVID-19 patients. Findings on current participation restriction levels one year after ICU discharge are in line with previous studies that assessed changes in recovery after a stroke or other diagnoses groups (31–33).

Moreover, these results showed that higher scores of self-experienced breathlessness, fatigue and more perceived limitations in daily life in the early phase of rehabilitation were associated with a delayed recovery of participation levels over the first year. Furthermore, patients with a less active coping style, those that were more anxious or reported to perceive more depressive complaints had a delayed recovery of their level of participation over the first year. For all these determinants, participation levels also appeared to be lower in the early phase of rehabilitation. These findings indicate that patients with a higher level of anxiety and those with a higher level of depression had a significantly slower improvement in participation levels during the first months, followed by a more progressive recovery, especially in the last months. In addition, patients with more breathlessness complaints or more fatigue complaints or more perceived limitations in daily life in the early phase of rehabilitation and patients with a less pro-active coping style showed a more progressive recovery of participation levels especially in the last months.

Complaints of fatigue or breathlessness may be due to underlying medical problems or to the contribution of personal factors. A previous study showed significant recovery of respiratory function and physical performance in the first year after ICU discharge due to COVID-19. Nevertheless, patients still experience breathlessness and fatigue complaints after one year (34). Another remarkable finding in current study was that early determinants related to the severity of the COVID-19 infection period

itself (such as ICU stay-specific parameters and physical parameters as age, sex, muscle strength, functional exercise capacity and pulmonary function) did not individually explain progress in recovery of participation over time. Contrary to expectations, this may indicate that non-physical factors such as coping style, subjectively experienced physical impairments (including fatigue and breathlessness) and mental impairments (such as anxiety and depressive symptoms) seem more important to determine progress in recovering the level of participation. Previous literature on post-ICU patients also indicated that critical care recovery has largely focused on post-ICU impairments experienced by patients. Whereas the positive aspects of recovery within the rehabilitation phase, including coping style and resilience seems to be ignored, while these factors are important for optimal recovery (35,36).

Implications for clinical practice and further research

This study underlines the importance of looking at the long-term consequence of (COVID-19) ICU survivors with an integral vision of health. Early detection of a less proactive coping style or mental impairments seems important and should therefore be included in screening during early multidisciplinary rehabilitation. Further research is needed to examine the appropriate (early) treatment to target changes in coping style or improve resilience. In addition, it can be speculated that our findings in ICU survivors can be also extrapolated to other ICU survivors or patients with post-COVID-19 syndrome, that had an initial mild infection Moreover, further research may focus on coping style and mental impairments on the recovery of participation restrictions over time in these patients.

Strengths and limitations

A strength of the present study is that it only included the most severely affected post-ICU COVID-19 patients referred to inpatient rehabilitation. In addition, this study used physical examination as well as questionnaires, which means that there was a combination of objective and subjective measurements. It is notable that even in the most severely affected COVID-19 patients delayed

recovery of participation is associated with self-experienced physical impairments, mental impairments and coping style.

Nevertheless, some limitations of the current study need to be considered. First, although the sample size is small, a large number of factors were studied for their effect on the course of participation recovery. Because this is the first exploratory study on the recovery of participation and its association with early factors, it was important to look at factors within different domains. Second, due to the high workload on the ward, 23 patients were not approached in time for consent to participate. In our opinion, this is unlikely to have led to selection bias, but this cannot be excluded. Finally, the lockdown and the inability to perform social and outdoor activities may have affected the total USER-P score as this scale allows the rating of 'not applicable'. Since the study- and lockdown period were similar for all patients, we expect no difference in the study patients. Although it may have affected the recovery course of participation recovery for the entire patient group, it is not expected to have affected the predictors.

Conclusion

For patients admitted to an ICU for COVID19, the level of participation improves in the first year after ICU discharge. However, at one year after discharge, many patients still experience limitations regarding participation in daily life, mainly in resuming work, physical exercise, housekeeping and leisure activities. Progress of recovery in participation in the first year after discharge was associated with early determinants in coping style, subjectively experienced physical impairments (breathlessness and fatigue) and mental impairments (anxiety and depression), but not with medical variables. This study supports the need for an integral perspective on health to facilitate the identification of factors that delay the recovery trajectory for participation in the first year after ICU discharge. Personal factors such as a less proactive coping style and more anxiety- or depression complaints seem relevant to this. Rehabilitation care needs to anticipate on these topics, starting in the early rehabilitation phase of post-ICU COVID-19 care.

Acknowledgements: We would like to thank all physiotherapist and students for their valuable contribution for collecting all data. We also thank all participants.

Author contributors: CW, JV, BH and SJSS were responsible for the study design. The statistical analysis plan was designed by CW, SJSS and SvK. Statistical analysis was done by CW, with control of SJSS and SvK. Practical implication was done by CW, SvS and YH. The first draft of the paper was written by CW and all co-authors reviewed and approved it for submission. CW and JV are the guarantors. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Funding: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests: All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/disclosure-of-interest/ and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the past three years; no other relationships or activities that could appear to have influenced the submitted work

Patient consent for publication: Not required.

Dissemination to participants and related patient and public communities: The study results will be disseminated to the public through our media channels or national and international conferences.

Ethical approval: The local medical ethics committee Zuyderland METC (METCZ20200086) approved the study.

Data availability statement: To guarantee the confidentiality of personal and health information, only the authors have had access to the data during the study. Data is available (anonymised), but the corresponding author must be contacted to request these data. Data will be kept for 15 years

ORCID ID: Carolina Wiertz https://orcid.org/0000-0002-7703-2508

References

1. RIVM. Actuele informatie over het nieuwe coronavirus (COVID-19) [Internet]. 22-05-2020. Available from: https://www.rivm.nl/coronavirus-covid-19/actueel

2. NICE. COVID-19 infecties op de IC's [Internet]. Nationale Intensive Care Evaluatie. [cited 2020 Jul 2]. Available from: https://www.stichting-nice.nl/COVID_rapport.pdf

3. Tan E, Song J, Deane AM, Plummer MP. Global Impact of Coronavirus Disease 2019 Infection Requiring Admission to the ICU: A Systematic Review and Meta-analysis. Chest. 2021;

4. Needham DM, Davidson J, Cohen H, Hopkins RO, Weinert C, Wunsch H, et al. Improving long-term outcomes after discharge from intensive care unit: Report from a stakeholders' conference. Crit Care Med. 2012 Feb;40(2):502–9.

5. Dowdy DW, Eid MP, Sedrakyan A, Mendez-Tellez PA, Pronovost PJ, Herridge MS, et al. Quality of life in adult survivors of critical illness: A systematic review of the literature. Vol. 31, Intensive Care Medicine. Springer Verlag; 2005. p. 611–20.

6. Desai S V., Law TJ, Needham DM. Long-term complications of critical care. Critical Care Medicine. 2011.

7. Ohtake PJ, Lee AC, Scott JC, Hinman RS, Ali NA, Hinkson CR, et al. Physical impairments associated with post-intensive care syndrome: Systematic review based on the world health organization's international classification of functioning, disability and health framework. Physical Therapy. 2018.

8. Wiertz CMH, Vints WAJ, Maas GJCM, Rasquin SMC, van Horn YY, Dremmen MPM, et al. COVID-19: patient characteristics in the first phase of post-intensive care rehabilitation. Arch Rehabil Res Clin Transl. 2021;

9. Martillo MA, Dangayach NS, Tabacof L, Spielman LA, Dams-O'Connor K, Chan CC, et al. Postintensive Care Syndrome in Survivors of Critical Illness Related to Coronavirus Disease

2019: Cohort Study from a New York City Critical Care Recovery Clinic∗. Crit Care Med. 2021;

10. Rousseau AF, Minguet P, Colson C, Kellens I, Chaabane S, Delanaye P, et al. Post-intensive care syndrome after a critical COVID-19: cohort study from a Belgian follow-up clinic. Ann Intensive Care. 2021;

11. Leite VF, Rampim DB, Jorge VC, de Lima M do CC, Cezarino LG, da Rocha CN, et al. Persistent Symptoms and Disability After COVID-19 Hospitalization: Data From a Comprehensive Telerehabilitation Program. Arch Phys Med Rehabil. 2021;

12. Veenendaal N van, van der Meulen IC, Onrust M, Paans W, Dieperink W, van der Voort PHJ. Six-month outcomes in covid-19 icu patients and their family members: A prospective cohort study. Healthc. 2021;

13. (WHO) WHO. The international Classification of Functioning, Disability and Health - ICF [Internet]. 2001. Available from: https://www.who.int/classifications/international-classification-of-functioning-disability-and-health

14. Post MWM, Van Der Zee CH, Hennink J, Schafrat CG, Visser-Meily JMA, Van Berlekom SB. Validity of the utrecht scale for evaluation of rehabilitation- participation. Disabil Rehabil. 2012;

15. Van Der Zee CH, Visser-Meily JMA, Lindeman E, Kappelle LJ, Post MWM. Participation in the chronic phase of stroke. Top Stroke Rehabil. 2013;

16. Vanpee G, Segers J, Van Mechelen H, Wouters P, Van Den Berghe G, Hermans G, et al. The interobserver agreement of handheld dynamometry for muscle strength assessment in critically ill patients. Crit Care Med. 2011;

17. Andrews AW, Thomas MW, Bohannon RW. Normative values for isometric muscle force measurements obtained with hand-held dynamometers. Phys Ther. 1996;76(3):248–59.

18. Bohannon RW. Reference values for extremity muscle strength obtained by hand-held dynamometry from adults aged 20 to 79 years. Arch Phys Med Rehabil. 1997;78(1):26–32.

19. Chan KS, Pfoh ER, Denehy L, Elliott D, Holland AE, Dinglas VD, et al. Construct validity and minimal important diff erence of 6-minute walk distance in survivors of acute respiratory failure. Chest. 2015;

20. Graham BL, Steenbruggen I, Barjaktarevic IZ, Cooper BG, Hall GL, Hallstrand TS, et al. Standardization of spirometry 2019 update an official American Thoracic Society and European Respiratory Society technical statement. American Journal of Respiratory and Critical Care Medicine. 2019.

21. Stenton C. The MRC breathlessness scale. Occup Med (Lond). 2008;

22. Williamson A, Hoggart B. Pain: A review of three commonly used pain rating scales. Journal of Clinical Nursing. 2005.

23. Smets EMA, Garssen B, Bonke B, De Haes JCJM. The multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. J Psychosom Res. 1995;

24. Feng D, Laurel F, Castille D, McCormick AKHG, Held S. Reliability, construct validity, and measurement invariance of the PROMIS Physical Function 8b—Adult Short Form v2.0. Qual Life Res. 2020;

25. HealthMeasures Scoring Service powered by Assessment CenterSM [Internet]. [cited 2021 Feb 20]. Available from: https://www.assessmentcenter.net/ac_scoringservice

26. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale: An updated literature review. J Psychosom Res. 2002;

27. Olff M, Bakker A. Global Psychotrauma Screen (GPS); User guide september 2021 [Internet]. 2016 [cited 2022 Feb 2]. Available from: https://nl.global-psychotrauma.net/gps

28. van Heugten C, Rasquin S, Winkens I, Beusmans G, Verhey F. Checklist for cognitive and emotional consequences following stroke (CLCE-24): Development, usability and quality of the self-report version. Clin Neurol Neurosurg. 2007;

29. Bode C, Thoolen B, Ridder D. Het meten van proactieve copingvaardigheden: Psychometrische eigenschappen van de Utrechtse Proactieve Coping Competentie lijst (UPCC). Psychol en Gezondh. 2008;

30. Heesakkers H, van der Hoeven JG, Corsten S, Janssen I, Ewalds E, Simons KS, et al. Clinical Outcomes Among Patients With 1-Year Survival Following Intensive Care Unit Treatment for COVID-19. JAMA. 2022;(January).

31. Van Mierlo ML, Van Heugten CM, Post MWM, Hajós TRS, Kappelle LJ, Visser-Meily JMA. Quality of life during the first two years post stroke: The Restore4Stroke cohort study. Cerebrovasc Dis. 2016;

32. de Graaf JA, van Mierlo ML, Post MWM, Achterberg WP, Kappelle LJ, Visser-Meily JMA. Long-term restrictions in participation in stroke survivors under and over 70 years of age. Disabil Rehabil. 2018;

33. Mol TI, van Bennekom CA, Schepers VP, ter Hoeve N, Kruitwagen-van Reenen ET, Visser-Meily JM, et al. Differences in Societal Participation Across Diagnostic Groups: Secondary Analyses of 8 Studies Using the Utrecht Scale for Evaluation of Rehabilitation-Participation. Arch Phys Med Rehabil. 2021;

34. Gamberini L, Mazzoli CA, Prediletto I, Sintonen H, Scaramuzzo G, Allegri D, et al. Health-related quality of life profiles, trajectories, persistent symptoms and pulmonary function one year after ICU discharge in invasively ventilated COVID-19 patients, a prospective follow-up study. Respir Med. 2021;

35. Maley JH, Brewster I, Mayoral I, Siruckova R, Adams S, McGraw KA, et al. Resilience in

survivors of critical illness in the context of the survivors' experience and recovery. Ann Am Thorac Soc. 2016;

36. Haines KJ, Hibbert E, Leggett N, Boehm LM, Hall T, Bakhru RN, et al. Transitions of Care After Critical Illness-Challenges to Recovery and Adaptive Problem Solving. Crit Care Med. 2021;

Figure Legend:

- Figure 1: ICF model and measurement instruments used.
- Figure 2: Subject recruitment flowchart.
- Figure 3: The recovery of participation levels (USER-P restriction subscale) in the first year after ICU discharge in post-COVID-19 patients.
- Figure 4: The influence of early levels of body function impairments, activity limitations and personal factors on the recovery of participation levels (USER-P restriction subscale).

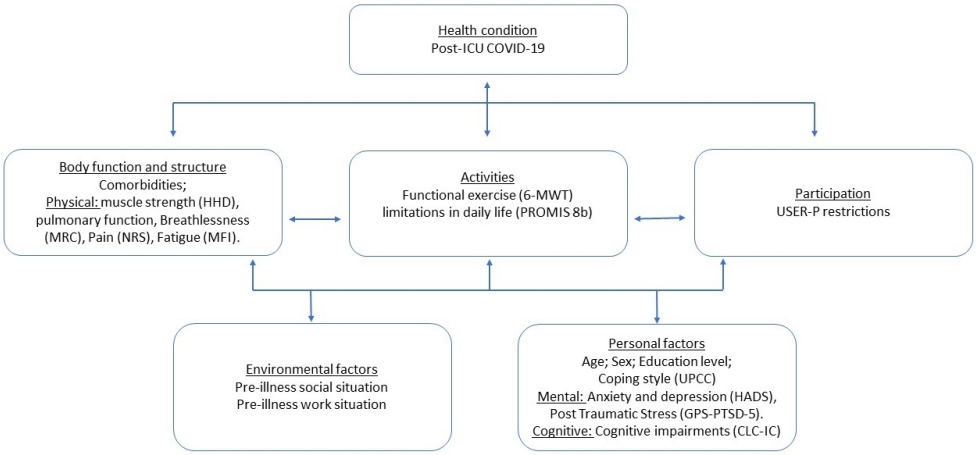

Figure 1. ICF model and measurement instruments used.
Abbreviations: PICS, post intensive care syndrome; USER-P, Utrecht Scale for Evaluation of Rehabilitation-Participation; HHD, handheld dynamometer; MFI, multidimensional Fatigue Inventory; HADS, Hospital Anxiety and Depression Scale; GPS, The Global Psychotrauma Screen; CLC-IC, Checklist for Cognitive consequences after an ICU-admission; 6-MWT, 6-minute walk test; UPCC, Utrecht Proactive Coping Scale ICF, International Classification of Functioning, Disability and Health

338x164mm (96 x 96 DPI)

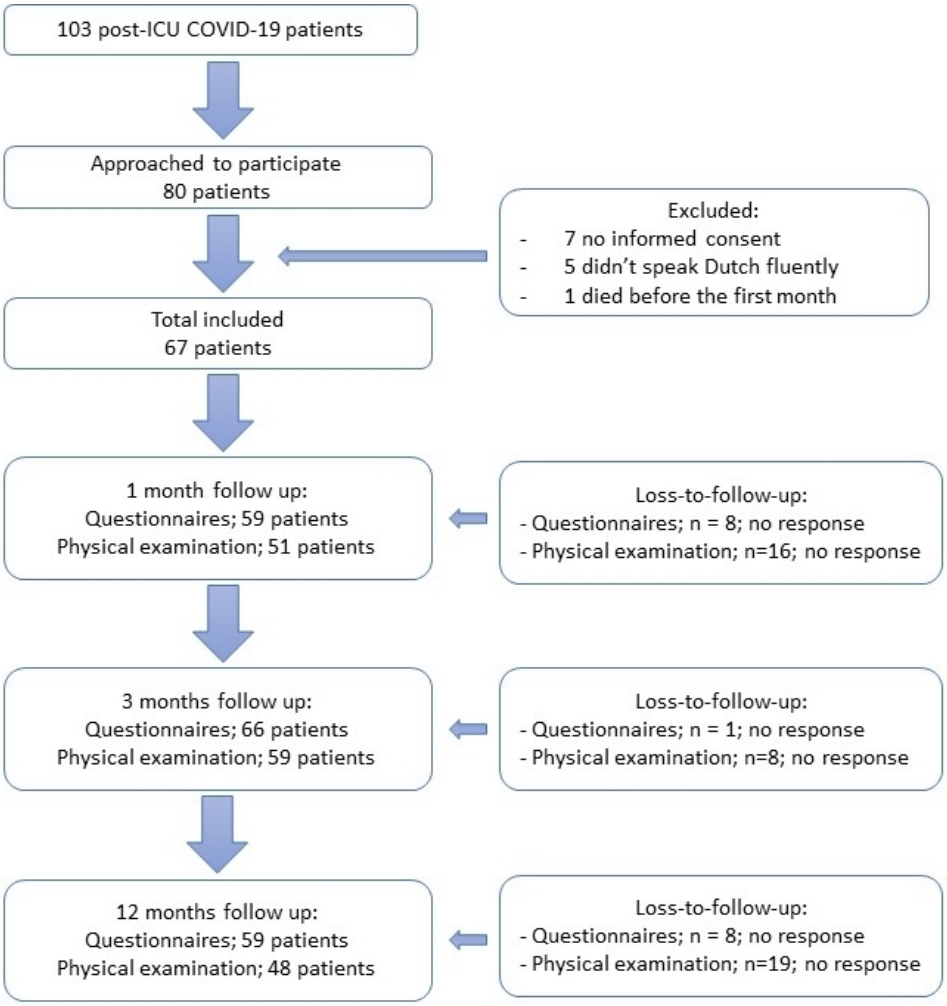

Figure 2; Subject recruitment flowchart.

179x181mm (96 x 96 DPI)

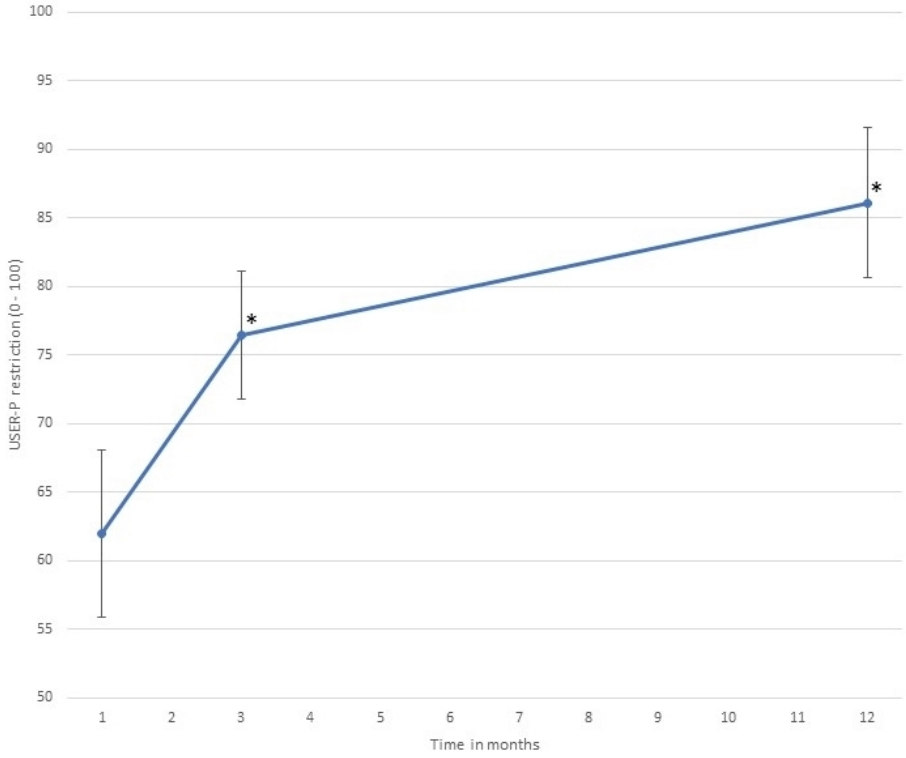

Figure 3; The recovery of participation levels (USER-P restriction subscale) in the first year after ICU discharge in post-COVID-19 patients. Results are expressed as mean with corresponding 95% confidence interval. * $p < 0.01$ (compared to previous measurement moment)

202x164mm (96 x 96 DPI)

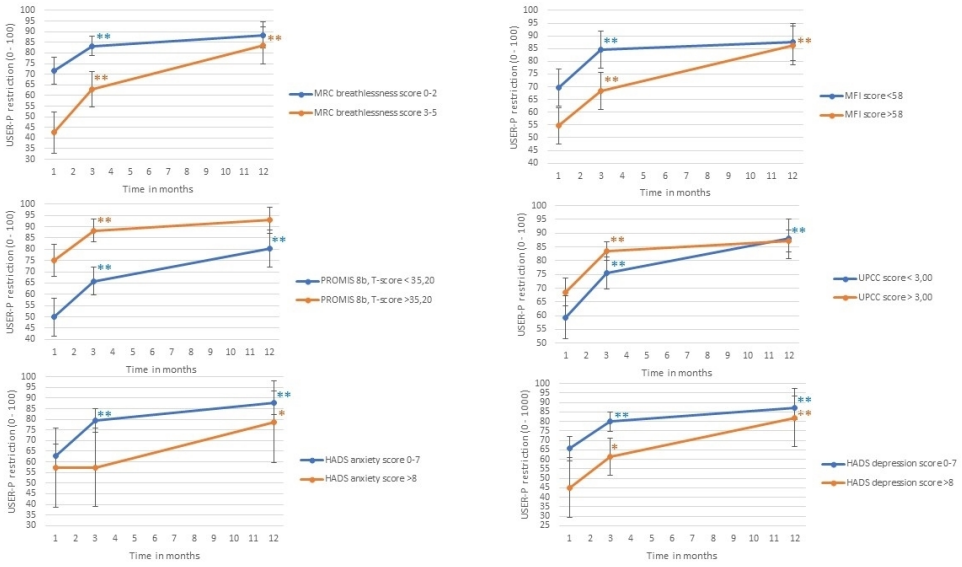

Figure 4; The influence of early levels of body function impairments, activity limitations and personal factors on the recovery of participation levels (USER-P restriction subscale). For illustrative purposes, subgroups have been created based on cut-off value (HADS) or the median if no specific cut-off value is known (MRC, MFI, PROMIS 8b, UPCC). Results are expressed as means with corresponding 95% confidence interval. * $p < 0.05$ and ** $p < 0.01$ (compared to previous measurement moment).

314x176mm (96 x 96 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8 Fig2

		(b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	Report numbers of outcome events or summary measures over time	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	8-9
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-9
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Life after COVID-19 the road from intensive care back to living: a prospective cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-062332.R1
Article Type:	Original research
Date Submitted by the Author:	16-Jul-2022
Complete List of Authors:	Wiertz, Carolina; Adelante, Rehabilitation medicine; Maastricht University, Department of Rehabilitation Medicine Research School CAPHRI Hemmen, Bena; Adelante, Rehabilitation medicine; Maastricht University, Department of Rehabilitation Medicine Research School CAPHRI Sep, Simone JS; Adelante, Rehabilitation medicine; Maastricht University, Department of Rehabilitation Medicine Research School CAPHRI van Santen, Susanne; Maastricht Universitair Medisch Centrum+, Department of Intensice Care van Horn, Yvette; Adelante, Rehabilitation medicine van Kuijk, Sander; Maastricht Universitair Medisch Centrum+, Clinical Epidemiology and Medical Technology Assessment Verbunt, Jeanine; Adelante, Rehabilitation medicine; Maastricht University, Department of Rehabilitation Medicine Research School CAPHRI
Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Intensive care
Keywords:	COVID-19, REHABILITATION MEDICINE, Adult intensive & critical care < INTENSIVE & CRITICAL CARE

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Life after COVID-19 the road from intensive care back to living: a prospective cohort study

Author's names

Carolina MH Wiertz MD[1,2], Bena Hemmen MD PhD[1,2], Simone JS Sep PhD[1,2], Susanne van Santen MD[3], Yvette Y van Horn MD[1], Sander MJ van Kuijk[4], Jeanine A Verbunt MD PhD[1,2]

Affiliation of authors

[1] Adelante Zorggroep, P.O. Box 88, 6430 AB Hoensbroek, The Netherlands.

[2] Department of Rehabilitation Medicine Research School CAPHRI, Maastricht University, P.O. Box 616, 6200 MD Maastricht, The Netherlands.

[3] Department of Intensive Care Medicine, Maastricht University Medical Centre, 6202 AZ Maastricht, The Netherlands.

[4] Department of Clinical Epidemiology and Medical Technology Assessment, Maastricht University Medical Centre, 6202 AZ Maastricht, The Netherlands.

Corresponding author: Carolina Wiertz

Adelante Zorggroep

P.O. Box 88

6430 AB Hoensbroek

The Netherlands

E-mail: c.wiertz@adelante-zorggroep.nl

Life after COVID-19 the road from intensive care back to living: a prospective cohort study

Abstract

Objectives: The aim of the study was to evaluate recovery of participation in post-COVID-19 patients during the first year after ICU discharge. The secondary aim was to identify the early determinants associated with recovery of participation.

Design: Prospective cohort study.

Setting: COVID-19 post-ICU inpatient rehabilitation in the Netherlands, during the first epidemic wave between April - July 2020, with one-year follow-up.

Participants: COVID-19 ICU survivors ≥18 years of age needing inpatient rehabilitation.

Main outcome measures: Participation in society was assessed by the 'Utrecht Scale for Evaluation of Rehabilitation-Participation (USER-P) restrictions scale'. Secondary measures of body function impairments (muscle force, pulmonary function, fatigue (MFI), breathlessness (MRC), pain (NRS)), activity limitations (6MWT, PROMIS 8b), personal factors (coping (UPCC), Anxiety and depression (HADS), post traumatic stress (GPS-PTSD-5), cognitive functioning (CLC-IC)) and social factors were used. Statistical analyses: linear mixed-effects model, with recovery of participation levels as dependent variable. Patient characteristics in domains of body function, activity limitations, personal and social factors were added as independent variables

Results: This study included 67 COVID-19 ICU survivors (mean age 62y, 78% male). Mean USER-P restrictions scores increased over time; mean participation levels increasing from 62.0, 76.5 to 86.1 at one, three and 12 months respectively. After one year, 50% had not fully resumed work and restrictions were reported in physical exercise (51%), household duties (46%), and leisure activities (29%). Self-reported complaints of breathlessness and fatigue, more perceived limitations in daily life, as well as personal factors (less pro-active coping style and anxiety/depression complaints) were associated with delayed recovery of participation (all p-value < 0.05).

Conclusions: This study supports the view that an integral vision of health is important when looking at the long-term consequence of post-IC COVID-19. Personal factors such as having a less proactive coping style or mental impairments early on contribute to delayed recovery.

Keywords: COVID-19, Critical care, Rehabilitation medicine

Strengths and limitations of this study

- This study only included the most severely affected post-ICU COVID-19 patients referred to inpatient rehabilitation.
- This study used physical examination as well as questionnaires, which means that there was a combination of objective and subjective measurements.
- Although the sample size is small, a large number of factors were studied for their effect on the course of participation recovery.
- Twenty-three patients were not approached in time for consent to participate.
- The lockdown and the inability to perform social and outdoor activities may have affected the total USER-P score.

Word count abstract: 300

Word count main text: 3370

Number of figures and tables: 6

Introduction

In the first wave of the coronavirus disease 2019 (COVID-19) pandemic in the Netherlands about 2% of all confirmed cases needed treatment in an intensive care unit (ICU) (1,2). About three-quarters of those admitted to ICU had acute respiratory distress syndrome (3) and many patients were recorded as having shock, acute kidney injury, thrombotic complications and/or cardiac injury (3).

Survivors of critical illness frequently experience new or worsening physical, cognitive and/or mental impairment, described as post intensive care syndrome (PICS) (4), which can have long-term effects on participation and quality of life (5–7). Immediately after ICU admission, COVID-19 patients display various physical impairments such as exertional hypoxemia, reduced overall muscle force, shoulder problems, dysphagia, and anxiety complaints (8). In the subacute phase (one to three months after ICU discharge) 90% of the post-ICU COVID patients still experience symptoms affecting at least one of the PICS domains (9,10). Due to the varying impact of severe COVID-19, patients may experience limitations in their participation in daily living, social functioning or work performance (11,12). Restrictions in participation may eventually lead to an increase in (healthcare) costs, since patients need for example more professional assistance in their ADL or return to work is delayed. Although impairments in various domains of functioning have been identified, any long-term effects on the recovery of participation are unclear. The effect that this new disease may have on participation, combined with the large number of COVID-19 ICU survivors, points to the need to study factors that could delay the recovery in participation of survivors after ICU discharge. Consequently, the present study aimed to evaluate the recovery of participation during the first year after ICU discharge in post-COVID-19 patients. The secondary aim was to identify early determinants associated with recovery of participation.

Methods

Study design and participants

This prospective cohort study was performed at Adelante Zorggroep, a rehabilitation centre in the South of the Netherlands. Patients with an indication for inpatient multidisciplinary rehabilitation were transferred to the rehabilitation centre. The indication was determined in the hospital by a consultant in rehabilitation medicine, based on their clinical judgement of the severity of physical, mental and/or cognitive impairments (13,14). All patients (aged 18 or older) referred for inpatient rehabilitation after ICU discharge for COVID-19 were eligible to participate in the study. The exclusion criterion was not speaking or reading the Dutch language fluently. All patients received inpatient multidisciplinary rehabilitation treatment including physiotherapy, occupational therapy, speechtherapy and psychology personalized to patient's limitations and needs according to the Dutch guideline for post-COVID ICU rehabilitation (13,15). All participants provided written informed consent. Patients were transferred to the rehabilitation centre from 7 (2 academic and 5 regional) hospitals in the region. COVID-19 was confirmed with a SARS-COV-19 positive PCR test. The local medical ethics committee Zuyderland METC (METCZ20200086) approved the study.

Patient and public involvement: Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Data collection

Data was collected in the form of baseline information at admission to the rehabilitation centre (T0), through physical examination and self-administered questionnaires after one (T1), three (T2) and twelve months (T3). Since different domains of functioning can be affected by COVID-19, measurements were chosen based on an integral vision of health and included body function impairments, activity limitations and participation restrictions as well as personal and social factors. These factors are derived as main domains in the International Classification of Functioning, Disability

and Health (ICF) that supports the classification of health and health-related conditions and their effect on social participation (Figure 1) (14).

Primary outcome variable: Participation in society was assessed by the 'Utrecht Scale for Evaluation of Rehabilitation-Participation (USER-P) restriction subscale'. This subscale consists of 11 items on restrictions in vocational, leisure and social activities. Items are rated from 0 'not possible' to 3 'without difficulty' and a 'not applicable' option. The total score ranges from 0 to 100, higher scores indicating fewer restrictions in participation (16,17).

Data on age, sex, comorbidities and parameters related to critical illness were collected from the medical transfer letters (T0). Comorbidities were classed into diabetes mellitus, hypertension, cardiovascular disease, lung disease and psychiatric disorders. Parameters related to severity of the critical illness were length of ICU stay, invasive mechanical ventilation (IMV) (yes/no) and duration of invasive IMV. The duration of the inpatient rehabilitation was recorded.

Physical examination: Assessment of muscle strength, functional exercise capacity and pulmonary function were part of physical examination. To measure muscle strength, a handheld dynamometer (HHD) was used (18) to assess the following muscle groups: shoulder abduction, elbow flexion, wrist extension, hip flexion and knee extension, all on patient's dominant side. HHD values were measured in Newtons and percentages of the norm compared with healthy persons of the same sex, age, and weight (19,20). Severe muscle weakness was defined as <80% of the norm score. For the clinical assessment of the functional exercise capacity, the 6-minute walk test (6-MWT) was used, displayed in meters and percentage of the norm (21,22). To evaluate pulmonary function Quark PFT spirometry (Cosmed, Italy) was used (23). Forced expiratory volume in the first second (FEV_1), forced vital capacity (FVC) and FEV_1/FVC ratio were included in the analysis, displayed in percentage of the norm.

In addition, self-administered questionnaires were used. Breathlessness was assessed by the MRC breathlessness scale, which comprises five statements that range from 0 'no trouble with breathlessness' to 5 'I am too breathless to leave the house' (24). The Numerical Rating Scale (NRS)

was used for assessing pain. Patients were asked to rate their mean pain intensities in the last seven days, ranging from 0-10, with 0 indicating 'no pain' and 10 indicating 'the worst imaginable pain' (25). The multidimensional Fatigue Inventory (MFI) is a 20-item metric for fatigue severity. It has 5 dimensions: general fatigue, physical fatigue, mental fatigue, reduced motivation and reduced activity. Each item ranges from 1 'absence of fatigue' to 5 'severe fatigue'. A total score is calculated as the sum of the subscale scores (20–100). Higher scores indicate higher levels of fatigue (26). The perceived limitations in daily life were assessed using the PROMIS physical function shortform 8b. This survey contains eight questions ranging from 1 'unable to do' to 5 'without any difficulty' (27). A web-based scoring service was used to calculate T-scores (maximum score 60.1 and mean 50.0, corresponding to the mean in the general population of the USA), whereas a higher scores indicates better physical function (28). Anxiety and depression complaints were assessed with the Hospital Anxiety and Depression Scale (HADS). A score ≥8 on either subscale was considered to be substantial anxiety or depression symptoms (29). Post-traumatic stress was assessed using the Global Psychotrauma Screen – Post Traumatic Stress Disorder (GPS-PTSD-5). The regular GPS consists of 22 items, item 1-5 can be used to generate a GPS-PTDS-5 score (range 0-5), score ≥3 indicates PTSD (30). Cognitive functioning was assessed using the Checklist for Cognitive consequences after ICU-admission (CLC-IC). The CLC-IC consists of 10 items; higher scores indicate more cognitive problems experienced in daily life (range 0-10). The CLC-IC is based on the CLCE-24 (31). Proactive coping skills were assessed at T3 with the Utrecht Proactive Coping Scale (UPCC), which is a 21-item questionnaire scored on a 4-point scale ranging from 'not competent at all' to 'competent'. The total score was the average for all item scores (range 1–4), where higher scores indicate higher levels of proactive coping (32). Premorbid social- and work situations were collected at T1.

Statistical analyses

Results are reported as mean and standard deviation (SD) or median and interquartile range (IQR) depending on distribution. Recovery of participation levels over time were assessed with linear mixed-

effects model for repeated measures. Patient characteristics in the domains body function, activity limitations, personal and social factors at T0 and and 1 month after admission in the rehabilitation centre (T1) were added to separate models that also included time and the interaction between that covariate and time. Next, for illustrative purposes only, linear mixed-effects model analyses were stratified according to patient characteristics that were significantly associated with the course of recovery of participation levels to visualize different patterns of change over time. A $p<0.05$ was considered as statistically significant. Statistical analyses were performed with IBM SPSS statistics 26.0 (SPSS Inc. Chicago, IL).

Results

During the first COVID-19 wave between April 2 and June 30, 2020, 103 post-ICU patients were admitted for inpatient rehabilitation. Of these, twenty-three patients were missed since this study was part of clinical practice in a very dynamic period and 13 patients were excluded excluded for reasons given in figure 2. The study sample consisted of 67 patients (78% male) with a median age of 62 (IQR 57-68) and a median length of stay of 20 (12-33) days in the ICU and 19 (11-31) days inpatient rehabilitation (Table 1). Overall, an improvement in muscle strength and functional exercise capacity (6MWT) was found, whereas fatigue complaints and perceived limitations in daily life seem to decrease in the first year after ICU discharge (Table 1).

Participation restrictions improved in the first year after ICU discharge due to a COVID-19 infection (Figure 3). Mean participation levels increased from 62.0 (95%CI 55.9-68.1), 76.5 (95%CI 71.9-81.1) to 86.1 (95%CI 80.6-91.6) at one, three and 12 months respectively. One year after ICU discharge, 50.8% of the patients still reported restrictions in physical exercise, 45.8% in performing housekeeping and 28.8% in performing leisure activities. After one year work is not applicable in 42.4% of all patients, which is comparable to the premorbid work situation, where 58% of all patients were employed. One year after ICU discharge 28.8% of all patients still reported restrictions in work/education. Taking into

192 account the patients who were not working pre-illness, means that 50% of the pre-illness working

193 patients had not fully resumed work after one year (Table 1).

Table 1	T0	One month (T1)	Three months (T2)	Twelve months (T3)
Baseline characteristics				
Age, years; n=67; median (IQR)	62 (57 – 68)	-		
Sex; n=67; No (%)				
- Men	52 (77.6%)	-		
- Women	15 (22.5%)	-		
Highest level of education; n=62; No (%)				
- Lower education	42 (67.7%)	-		
- Higher education	20 (32.3%)	-		
Work situation; n=62; No (%)		-		
- Full-time job	26 (41.9%)			
- Parttime job	10 (16.1%)	-		
- Retired	18 (29.0%)	-		
- Not working otherwise	8 (12.9%)	-		
Comorbidities; n=67; no (%)		-		
- Asthma / bronchitis	6 (9.0%)			
- Chronic obstructive pulmonary disease	4 (6.0%)	-		
- Obstructive sleep apnoea syndrome	12 (17.9%)	-		
- Diabetes Mellitus	12 (17.9%)	-		
- Hypertension	23 (34.3%)	-		
- Cardiovascular disease	21 (31.3%)	-		
- Chronic kidney disease	5 (7.4%)	-		
- Depression	4 (6.0%)	-		
- None of the above comorbidities	25 (37.3%)	-		
Parameters related to severity critical illness		-		
- Duration intensive care unit, in days; n=59; median (IQR)	20 (12 – 33)			
- Invasive mechanical ventilation; n=67; No (%)	58 (86.6%)	-		
- Duration IMV, in days; n=55; median (IQR)	17 (9 – 24)	-		
- Presence of ICU-acquired weakness, n=61; No (%)	45 (73.8%)	-		
Duration inpatient rehabilitation, days; n=67; median (IQR)	19 (11 – 31)			
Coping style (UPCC); n=58; mean (SD)	3.0 (0.2)			
USER-P restriction subscale [a]				
- Work/education	-	64.4%	60.6%	28.8%
- Housekeeping	-	74.6%	65.2%	45.8%
- Mobility	-	59.3%	43.9%	16.9%
- Physical exercise	-	79.7%	60.6%	50.8%
- Going out	-	45.8%	24.2%	10.2%
- Outdoor activities	-	54.2%	36.4%	16.9%
- Leisure activities	-	42.4%	28.8%	20.3%
- Partner relationship	-	28.8%	24.2%	16.9%
- Visits to family/friends	-	45.8%	31.8%	10.2%
- Visits from family/friend	-	32.2%	13.6%	8.5%
- Telephone/PC contact	-	15.3%	13.6%	11.9%
Physical examination:				
- Muscle strength				
- Mean muscle force (HHD), mean (SD)	-	75.7% (15.3)	93.5% (24.6)	101.4% (15.3)
- 6MWT; mean (SD)	-	467.8m (91.2)	518.3m (102.5)	531.0m (86.5)
- **percentage of predicted**		69.5% (13.7)	76.9% (13.7)	79.2% (10.4)
- Pulmonary function; mean (SD)	-			
- FEV1	-	87.5% (15.8)	93.8% (19.9)	93.6% (17.7)
- FVC	-	85.9% (16.3)	92.8% (18.7)	92.2% (15.6)
- FEV1/FVC ratio		79.6% (9.1)	77.3% (10.6)	79.1% (11.2)
Self-administered questionnaires:				
- Breathlessness (MRC); median (IQR)	-	2.0 (1.0 – 3.0)	1.0 (1.0 – 2.0)	1.0 (1.0 – 2.0)
- Pain (NRS); median (IQR)	-	2.0 (1.0 - 3.5)	2.0 (1.5 – 5.0)	2.0 (1.0 – 3.0)
- Fatigue (MFI); mean (SD)	-	58.6 (14.0)	56.0 (15.3)	50.8 (17.6)
- perceived limitations in daily life (PROMIS 8b); mean (SD)	-	34.8 (7.4)	39.2 (6.9)	44.8 (8.0)
- Anxiety (HADS-anxiety); median (IQR)	-	3.0 (1.0 – 5.0)	3.0 (1.0 - 6.0)	2.0 (0.5 – 6.0)
Exceeded anxiety cut-off ≥8	-	7/57 (12.3%)	11/66 (16.7%)	10/59 (16.9 %)
- Depression (HADS depression); median (IQR)	-	2.0 (1.5 – 6.0)	3.0 (1.0 – 6.0)	2.0 (1.0 – 4.0)
Exceeded depression cut-off ≥8	-	10/59 (16.9%)	13/66 (19.7%)	10/59 (16.9%)
- Post-traumatic stress (GPS-PTSD-5); median (IQR)		0.0 (0.0 – 1.0)	0.0 (0.0 – 1.0)	0.0 (0.0 – 1.0)
Exceeded PTSD cut-off ≥3		5/59 (8.5%)	8/66 (12.1%)	3/59 (5.1%)
- Cognitive impairments (CLC-IC); median (IQR)		3.0 (1.0 – 6.0)	4.0 (1.0 – 7.0)	2.0 (0.0 – 7.0)

Table 1, overview of the baseline characteristics (T0) and the physical examination and self-administered questionnaires at T1, T2 and T3.Low educational level was determined as 'primary and secondary education and post-secondary school'. High educational level was determined as 'bachelor's degree, master's degree or doctorate or equivalent'. Abbreviations: IMV, Invasive mechanical ventilation; UPCC, Utrecht Proactive Coping Scale; USER-P, Utrecht Scale for Evaluation of Rehabilitation-Participation; HHD, handheld dynamometer; 6MWT, 6 minute walking test; FEV1, Forced expiratory volume in the first second; FVC, Forced vital capacity; n.a., not applicable; MFI, multidimensional Fatigue Inventory; HADS, Hospital Anxiety and Depression Scale; GPS, The Global Psychotrauma Screen; CLC-IC, Checklist for Cognitive consequences after an ICU-admission. [a] Restriction items values are percentages of patients who are restricted or dissatisfied.

Regarding the second aim, in the ICF domain body functions, breathlessness (MRC breathlessness), regression coefficient: 0.60 (95%CI 0.23-0.97; p-value <0.01) and fatigue (MFI), regression coefficient: 0.07 (95%CI 0.03-0.09; p-value <0.01) were the only physical variables that influenced participation recovery over time. For the ICF domain activities, perceived limitations in daily life (PROMIS 8b) showed a different pattern in the recovery of participation restriction levels, regression coefficient: -0.11 (95%CI -0.12 to -0.05; p-value <0.01). In addition, personal factors like coping style (UPCC) regression coefficient: -2.39 (95%CI -4.20 to -0.06; p-value 0.01), anxiety (HADS anxiety) regression coefficient: 0.17 (95%CI 0.02-0.31; p-value 0.03) and depression (HADS depression) regression coefficient: 0.19 (95%CI 0.07-0.31; p-value <0.01) showed different paths in resuming the level of participation over time. Other early determinants show no significant difference in the recovery of participation (Table 2).

Table 2	Estimate (95% CI)	p-value
Baseline characteristics		
Age	-0.03 (-0.08 – 0.02)	0.29
Sex	0.72 (-0.32 – 1.76)	0.17
Number of comorbidities	0.04 (-0.34 – 0.42)	0.83
Duration of inpatient rehabilitation	0.03 (-0.00 – 0.06)	0.07
Coping style (UPCC)	-2.39 (-4.20 – -0.06)	0.01*
ICU-stay specific parameters		
Length of ICU stay	0.02 (-0.01 – 0.06)	0.21
Duration of invasive mechanical ventilation	0.02 (-0.02 – 0.05)	0.37
ICU-acquired weakness	-0.23 (-1.31 – 0.85)	0.67
Physical examination		
Muscle strength		
- Mean muscle force (HHD)	-0.02 (-0.06 – 0.01)	0.18
6MWT	-0.00 (-0.01 – 0.01)	0.65
Pulmonary function		
- FEV1	-0.02 (-0.06 – 0.01)	0.16
- FVC	-0.03 (-0.06 – 0.00)	0.07
- FEV1/FVC ratio	0.04 (-0.02 – 0.09)	0.24
Self-administered questionnaires		
Breathlessness (MRC)	0.60 (0.23 – 0.97)	< 0.01*
Pain (NRS)	-0.03 (-0.28 – 0.23)	0.84
Fatigue (MFI)	0.07 (0.03 – 0.09)	< 0.01*
Perceived limitations in daily life (PROMIS 8b)	-0.11 (-0.12 – -0.05)	< 0.01*
Anxiety (HADS-anxiety)	0.17 (0.02 – 0.31)	0.03*
Depression (HADS depression)	0.19 (0.07 – 0.31)	< 0.01*
Post-traumatic stress (GPS-PTSD-5)	0.24 (-0.21 – 0.70)	0.30
Cognitive impairments (CLC-IC)	0.09 (-0.07 – 0.24)	0.27

Table 2; linear mixed model for covariates at T0 or T1, as an interaction between covariate and time (1, 3, and 12 months), for the recovery of participation levels. * $p < 0.05$. Abbreviations: UPCC, Utrecht Proactive Coping Scale; HHD, handheld dynamometer; 6MWT, 6 minute walking test; FEV1, Forced expiratory volume in the first second; FVC, Forced vital capacity; MFI, multidimensional Fatigue Inventory; HADS, Hospital Anxiety and Depression Scale; GPS, The Global Psychotrauma Screen; CLC-IC, Checklist for Cognitive consequences after an ICU-admission.

Participation levels increased significantly between 1 and 3 months and between 3 and 12 months in patients who reported more breathlessness, more fatigue or more limitations in daily life and those with a passive coping style. In contrast, patients with less breathlessness, fewer fatigue complaints, fewer restrictions in daily life and a pro-active coping style showed no significant increase between 3 and 12 months (Figure 4). For patients with HADS anxiety score ≥8, no differences were found in participation levels in the first 3 months, while there was significant difference in recovery of participation levels between 3 and 12 months. However, for patients with fewer anxiety complanits (HADS anxiety score ≤8) participation levels significantly improved between 1 and 3 months and

between 3 and 12 months. For depressive symptoms, both groups improved significantly in participation levels between 1 to 3 months and between 3 to 12 months, although a steeper curve is seen in recovery of participation levels at 3 to 12 months in patients with more depressive symptoms.

Discussion

In this prospective cohort study, recovery of participation during the first year after ICU discharge in COVID-19 ICU survivors who needed inpatient rehabilitation was evaluated and the association between early levels of body function impairments, activity limitations and personal and social factors on recovery were estimated. It is seen that in the first year after ICU discharge patients were able to improve their participation levels. Nevertheless, after one year, there are still important limitations in daily life, mainly in resuming work, physical exercise, housekeeping and leisure activities. As early determinants for a delay in the resumption of patient's habitual level of participation levels over the first year, higher levels of self-experienced breathlessness and fatigue complaints, more perceived limitations in daily life as well as personal factors (having a passive coping style, anxiety complaints or depression complaints) were found.

In previous Dutch studies focusing on overall post-ICU COVID-19 survivors, an average age of 61-63 was found, 69-72% men, with a median length of stay of 18-20 days in the ICU (33,34). These demographic data seem to correspond with findings of current study, taking into account that in the first COVID-19 wave, 83% of all post-ICU COVID-19 patients were transferred to a rehabilitation centre (34). Heesakker et al. reported that in patients who survived one year following ICU treatment for COVID-19, physical, mental, or cognitive symptoms were often reported (33). This corresponds with the findings of the current study, whereas various physical, mental and cognitive impairments were seen one year after ICU admission. However, to our knowledge, this is the first study to report differences in the resumption of participation levels in post-ICU COVID-19 patients. Mean participation levels increased to 86.1 one year after ICU discharge. As a reference, in other non-COVID patients (i.e.

stroke, acquired brain injury, progressive neurologic diseases, spinal cord injury and acute coronary syndrome), participation levels between 70.6-83.5 have been observed (35–37). In all non-COVID patient groups, patients mainly reported restrictions in work/education, housekeeping, physical exercise and performing leisure activities, which is in accordance with restrictions in participation reported in current study (36,37).

Moreover, these results showed that higher scores of self-experienced breathlessness or fatigue and more perceived limitations in daily life in the early phase of rehabilitation were associated with a delayed recovery of participation levels over the first year. Furthermore, patients with a less active coping style, those that were more anxious or reported to perceive more depressive complaints had a delayed recovery of their level of participation over the first year. For all these determinants, participation levels also appeared to be lower in the early phase of rehabilitation. These findings indicate that patients with a higher level of anxiety and those with a higher level of depression had a significantly slower improvement in participation levels during the first months, followed by a more progressive recovery, especially in the last months. In addition, patients with more breathlessness complaints, more fatigue complaints or more perceived limitations in daily life in the early phase of rehabilitation and patients with a passive coping style showed a more progressive recovery of participation levels especially in the last months.

Complaints of fatigue or breathlessness may be due to underlying medical problems or to the contribution of personal factors. Previous study's showed significant recovery of respiratory function and physical performance in the first year after ICU discharge due to COVID-19. Nevertheless, patients still experience breathlessness and fatigue complaints after one year (38,39). Another finding in current study was that early determinants related to the severity of the COVID-19 infection period itself (such as ICU stay-specific parameters and physical parameters as age, sex, muscle strength, functional exercise capacity and pulmonary function) did not individually explain progress in recovery of participation over time. Contrary to expectations, this may indicate that non-physical factors such as coping style, subjectively experienced physical impairments (including fatigue and breathlessness)

and mental health issues (such as anxiety and depressive symptoms) seem more important to determine progress in recovering the level of participation. Previous literature on post-ICU patients indicated that critical care recovery has focused on post-ICU impairments experienced by patients. Whereas the positive aspects of recovery within the rehabilitation phase, including coping style and resilience seems to be ignored (40,41). Resilience refers to the ability to face the challenges and difficulties of life in a positive and adaptive manner, as well as the capacity to recover from an adverse event (42). Higher levels of resilience have been linked to improved mental and physical health (43). It is possible to improve the level of resilience. Which implies that resilience can be used to improve (emotional) well-being, with the possible consequence of improving participation levels.

Implications for clinical practice and further research

This study underlines the importance of looking at long-term consequence of COVID-19 ICU survivors with an integral vision of health. Whether identical variables can be used to identify a delay in recovery in patients who had a milder infection is currently still unclear. In this study, conclusions can be made for a selected group (with ICU admission) of patients. Extrapolation to other populations needs to be done with caution. Early detection of a passive coping style or mental impairments seems important and should therefore be included in screening during early multidisciplinary rehabilitation. Further research is needed to study the effect of early screening of a patients' level of coping/ resilience during the first months after ICU discharge. As a consequence, an early intervention to increase resilience/strengthen coping on indication could be promising to further strengthen social participation, but needs to be further studied.

Strengths and limitations

A strength of the study is that it only included the most severely affected post-ICU COVID-19 patients referred to inpatient rehabilitation. In addition, this study used physical examination as well as questionnaires, which means there was a combination of objective and subjective measurements. It is

notable that even in the most severely affected COVID-19 patients delayed recovery of participation is associated with self-experienced physical impairments, mental impairments and coping style.

Nevertheless, some limitations of the current study need to be considered. First, sample size is limited and a number of factors were studied for their effect on the course of participation recovery. The limited sample size contributed to relatively wide confidence intervals. The risk of type II error should therefore be considered while interpreting the data. A post-hoc power calculation revealed however that the study had 90% power to detect an effect size of 0.2 for changes in participation levels over time (alpha = 0.05, mean correlation between repeated measures = 0.53). Still, p-values of the multiple tests of association should be interpreted cautiously, because we cannot exclude erroneous interpretations of statistical significant findings (i.e. type I error). However, since our results support a certain pattern, we believe that the main conclusions of this study are solid. Second, number of variables available to describe the acute illness severity were limited. Further research is needed to investigate this in a larger cohort (all ICU patients, not just rehabilitation patients) to confirm this finding. Third, due to high workload on the ward, 23 patients were not approached in time for consent to participate. In our opinion, this is unlikely to have led to selection bias, but this cannot be excluded. Finally, the lockdown and the inability to perform social and outdoor activities may have affected the total USER-P score as this scale allows the rating of 'not applicable'. Since the study- and lockdown period were similar for all patients, we expect no difference in the study patients. Although it may have affected the recovery course of participation recovery for the entire patient group, it is not expected to have affected the predictors.

Conclusion

For patients admitted to an ICU for COVID-19, participation levels improves in the first year after ICU discharge. However, at one year after discharge, many patients still experience limitations in daily life, mainly in resuming work, physical exercise, housekeeping and leisure activities. Our results indicate that progress of recovery in participation in the first year after discharge is associated with early

determinants in coping style, subjectively experienced physical impairments (breathlessness and fatigue) and mental impairments (anxiety and depression) rather than medical variables. This study supports the need for an integral perspective on health to facilitate the identification of factors that delay the recovery trajectory for participation in the first year after ICU discharge. Personal factors such as a passive coping style and more anxiety- or depression complaints seem relevant to this. Rehabilitation care needs to anticipate on these topics, starting in the early rehabilitation phase of post-ICU COVID-19 care.

Acknowledgements: We would like to thank all physiotherapist and students for their valuable contribution for collecting all data. We also thank all participants.

Author contributors: CW, JV, BH and SJSS were responsible for the study design. The statistical analysis plan was designed by CW, SJSS and SvK. Statistical analysis was done by CW, with control of SJSS and SvK. Practical implication was done by CW, SvS and YH. The first draft of the paper was written by CW and all co-authors reviewed and approved it for submission. CW and JV are the guarantors. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Funding: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests: All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/disclosure-of-interest/ and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the past three years; no other relationships or activities that could appear to have influenced the submitted work

Patient consent for publication: Not required.

Dissemination to participants and related patient and public communities: The study results will be disseminated to the public through our media channels or national and international conferences.

Ethical approval: The local medical ethics committee Zuyderland METC (METCZ20200086) approved the study.

Data availability statement: To guarantee the confidentiality of personal and health information, only the authors have had access to the data during the study. Data is available (anonymised), but the corresponding author must be contacted to request these data. Data will be kept for 15 years

ORCID ID: Carolina Wiertz https://orcid.org/0000-0002-7703-2508

References

1. RIVM. Actuele informatie over het nieuwe coronavirus (COVID-19) [Internet]. 22-05-2020. Available from: https://www.rivm.nl/coronavirus-covid-19/actueel

2. NICE. COVID-19 infecties op de IC's [Internet]. Nationale Intensive Care Evaluatie. [cited 2020 Jul 2]. Available from: https://www.stichting-nice.nl/COVID_rapport.pdf

3. Tan E, Song J, Deane AM, Plummer MP. Global Impact of Coronavirus Disease 2019 Infection Requiring Admission to the ICU: A Systematic Review and Meta-analysis. Chest. 2021;

4. Needham DM, Davidson J, Cohen H, Hopkins RO, Weinert C, Wunsch H, et al. Improving long-term outcomes after discharge from intensive care unit: Report from a stakeholders' conference. Crit Care Med. 2012 Feb;40(2):502–9.

5. Dowdy DW, Eid MP, Sedrakyan A, Mendez-Tellez PA, Pronovost PJ, Herridge MS, et al. Quality of life in adult survivors of critical illness: A systematic review of the literature. Vol. 31, Intensive Care Medicine. Springer Verlag; 2005. p. 611–20.

6. Desai S V., Law TJ, Needham DM. Long-term complications of critical care. Critical Care Medicine. 2011.

7. Ohtake PJ, Lee AC, Scott JC, Hinman RS, Ali NA, Hinkson CR, et al. Physical impairments associated with post-intensive care syndrome: Systematic review based on the world health organization's international classification of functioning, disability and health framework. Physical Therapy. 2018.

8. Wiertz CMH, Vints WAJ, Maas GJCM, Rasquin SMC, van Horn YY, Dremmen MPM, et al. COVID-19: patient characteristics in the first phase of post-intensive care rehabilitation. Arch Rehabil Res Clin Transl. 2021;

9. Martillo MA, Dangayach NS, Tabacof L, Spielman LA, Dams-O'Connor K, Chan CC, et al. Postintensive Care Syndrome in Survivors of Critical Illness Related to Coronavirus Disease

2019: Cohort Study from a New York City Critical Care Recovery Clinic∗. Crit Care Med. 2021;

10. Rousseau AF, Minguet P, Colson C, Kellens I, Chaabane S, Delanaye P, et al. Post-intensive care syndrome after a critical COVID-19: cohort study from a Belgian follow-up clinic. Ann Intensive Care. 2021;

11. Leite VF, Rampim DB, Jorge VC, de Lima M do CC, Cezarino LG, da Rocha CN, et al. Persistent Symptoms and Disability After COVID-19 Hospitalization: Data From a Comprehensive Telerehabilitation Program. Arch Phys Med Rehabil. 2021;

12. Veenendaal N van, van der Meulen IC, Onrust M, Paans W, Dieperink W, van der Voort PHJ. Six-month outcomes in covid-19 icu patients and their family members: A prospective cohort study. Healthc. 2021;

13. FMS. COVID-19 [Internet]. 2022. Available from: https://richtlijnendatabase.nl/richtlijn/covid-19/startpagina_-_covid-19.html

14. (WHO) WHO. The international Classification of Functioning, Disability and Health - ICF [Internet]. 2001. Available from: https://www.who.int/classifications/international-classification-of-functioning-disability-and-health

15. de Graaf J, Brouwers M, Post M. Behandelprogramma COVID-19 post-IC in de Medisch Specialistische Revalidatie (De Hoogstraat). Utrecht, The Netherlands; 2020.

16. Post MWM, Van Der Zee CH, Hennink J, Schafrat CG, Visser-Meily JMA, Van Berlekom SB. Validity of the utrecht scale for evaluation of rehabilitation- participation. Disabil Rehabil. 2012;

17. Van Der Zee CH, Visser-Meily JMA, Lindeman E, Kappelle LJ, Post MWM. Participation in the chronic phase of stroke. Top Stroke Rehabil. 2013;

18. Vanpee G, Segers J, Van Mechelen H, Wouters P, Van Den Berghe G, Hermans G, et al. The

interobserver agreement of handheld dynamometry for muscle strength assessment in critically ill patients. Crit Care Med. 2011;

19. Andrews AW, Thomas MW, Bohannon RW. Normative values for isometric muscle force measurements obtained with hand-held dynamometers. Phys Ther. 1996;76(3):248–59.

20. Bohannon RW. Reference values for extremity muscle strength obtained by hand-held dynamometry from adults aged 20 to 79 years. Arch Phys Med Rehabil. 1997;78(1):26–32.

21. Chan KS, Pfoh ER, Denehy L, Elliott D, Holland AE, Dinglas VD, et al. Construct validity and minimal important diff erence of 6-minute walk distance in survivors of acute respiratory failure. Chest. 2015;

22. Troosters T, Gosselink R, Decramer M. Six minute walking distance in healthy elderly subjects. Eur Respir J. 1999;

23. Graham BL, Steenbruggen I, Barjaktarevic IZ, Cooper BG, Hall GL, Hallstrand TS, et al. Standardization of spirometry 2019 update an official American Thoracic Society and European Respiratory Society technical statement. American Journal of Respiratory and Critical Care Medicine. 2019.

24. Stenton C. The MRC breathlessness scale. Occup Med (Lond). 2008;

25. Williamson A, Hoggart B. Pain: A review of three commonly used pain rating scales. Journal of Clinical Nursing. 2005.

26. Smets EMA, Garssen B, Bonke B, De Haes JCJM. The multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. J Psychosom Res. 1995;

27. Feng D, Laurel F, Castille D, McCormick AKHG, Held S. Reliability, construct validity, and measurement invariance of the PROMIS Physical Function 8b—Adult Short Form v2.0. Qual Life Res. 2020;

28. HealthMeasures Scoring Service powered by Assessment CenterSM [Internet]. [cited 2021 Feb 20]. Available from: https://www.assessmentcenter.net/ac_scoringservice

29. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale: An updated literature review. J Psychosom Res. 2002;

30. Olff M, Bakker A. Global Psychotrauma Screen (GPS); User guide september 2021 [Internet]. 2016 [cited 2022 Feb 2]. Available from: https://nl.global-psychotrauma.net/gps

31. van Heugten C, Rasquin S, Winkens I, Beusmans G, Verhey F. Checklist for cognitive and emotional consequences following stroke (CLCE-24): Development, usability and quality of the self-report version. Clin Neurol Neurosurg. 2007;

32. Bode C, Thoolen B, Ridder D. Het meten van proactieve copingvaardigheden: Psychometrische eigenschappen van de Utrechtse Proactieve Coping Competentie lijst (UPCC). Psychol en Gezondh. 2008;

33. Heesakkers H, van der Hoeven JG, Corsten S, Janssen I, Ewalds E, Simons KS, et al. Clinical Outcomes Among Patients With 1-Year Survival Following Intensive Care Unit Treatment for COVID-19. JAMA. 2022;(January).

34. van Gassel RJJ, Bels JLM, Raafs A, van Bussel BCT, van de Poll MCG, Simons SO, et al. High prevalence of pulmonary sequelae at 3 months after hospital discharge in mechanically ventilated survivors of COVID-19. American Journal of Respiratory and Critical Care Medicine. 2021.

35. Van Mierlo ML, Van Heugten CM, Post MWM, Hajós TRS, Kappelle LJ, Visser-Meily JMA. Quality of life during the first two years post stroke: The Restore4Stroke cohort study. Cerebrovasc Dis. 2016;

36. de Graaf JA, van Mierlo ML, Post MWM, Achterberg WP, Kappelle LJ, Visser-Meily JMA. Long-term restrictions in participation in stroke survivors under and over 70 years of age. Disabil

Rehabil. 2018;

37. Mol TI, van Bennekom CA, Schepers VP, ter Hoeve N, Kruitwagen-van Reenen ET, Visser-Meily JM, et al. Differences in Societal Participation Across Diagnostic Groups: Secondary Analyses of 8 Studies Using the Utrecht Scale for Evaluation of Rehabilitation-Participation. Arch Phys Med Rehabil. 2021;

38. Gamberini L, Mazzoli CA, Prediletto I, Sintonen H, Scaramuzzo G, Allegri D, et al. Health-related quality of life profiles, trajectories, persistent symptoms and pulmonary function one year after ICU discharge in invasively ventilated COVID-19 patients, a prospective follow-up study. Respir Med. 2021;

39. Bels JLM, van Gassel RJJ, Timmerman L, Hemmen B, van de Poll MCG, Peters NHGM, et al. One year respiratory and functional outcomes of mechanically ventilated COVID-19 survivors: A prospective cohort study. Am J Respir Crit Care Med. 2022;Online ahead of print.

40. Maley JH, Brewster I, Mayoral I, Siruckova R, Adams S, McGraw KA, et al. Resilience in survivors of critical illness in the context of the survivors' experience and recovery. Ann Am Thorac Soc. 2016;

41. Haines KJ, Hibbert E, Leggett N, Boehm LM, Hall T, Bakhru RN, et al. Transitions of Care After Critical Illness-Challenges to Recovery and Adaptive Problem Solving. Crit Care Med. 2021;

42. Steinhardt M, Dolbier C. Evaluation of a resilience intervention to enhance coping strategies and protective factors and decrease symptomatology. J Am Coll Heal. 2008;

43. Schure MB, Odden M, Goins RT. The association of resilience with mental and physical health among older american indians: The native elder care study. Am Indian Alaska Nativ Ment Heal Res. 2013;

Figure Legend:

- Figure 1: ICF model and measurement instruments used.
- Figure 2: Subject recruitment flowchart.
- Figure 3: The recovery of participation levels (USER-P restriction subscale) in the first year after ICU discharge in post-COVID-19 patients.
- Figure 4: The influence of early levels of body function impairments, activity limitations and personal factors on the recovery of participation levels (USER-P restriction subscale).

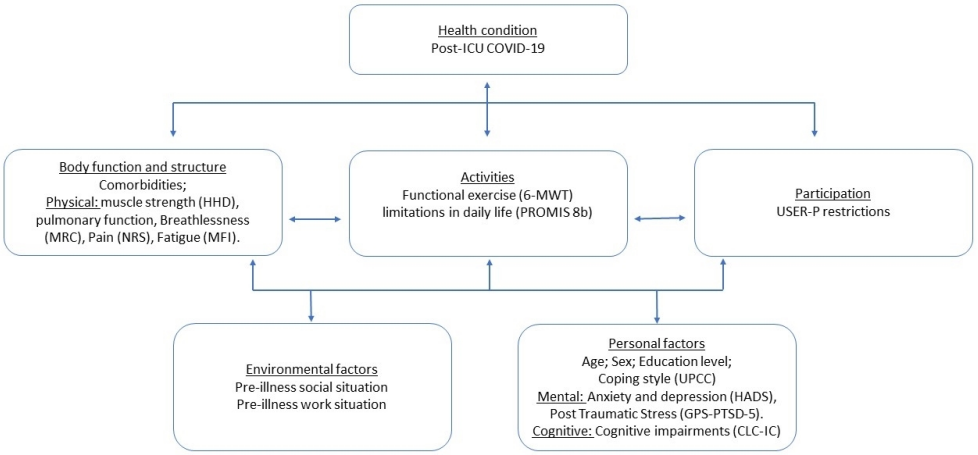

Figure 1. ICF model and measurement instruments used.
Abbreviations: PICS, post intensive care syndrome; USER-P, Utrecht Scale for Evaluation of Rehabilitation-Participation; HHD, handheld dynamometer; MFI, multidimensional Fatigue Inventory; HADS, Hospital Anxiety and Depression Scale; GPS, The Global Psychotrauma Screen; CLC-IC, Checklist for Cognitive consequences after an ICU-admission; 6-MWT, 6-minute walk test; UPCC, Utrecht Proactive Coping Scale ICF, International Classification of Functioning, Disability and Health

338x164mm (96 x 96 DPI)

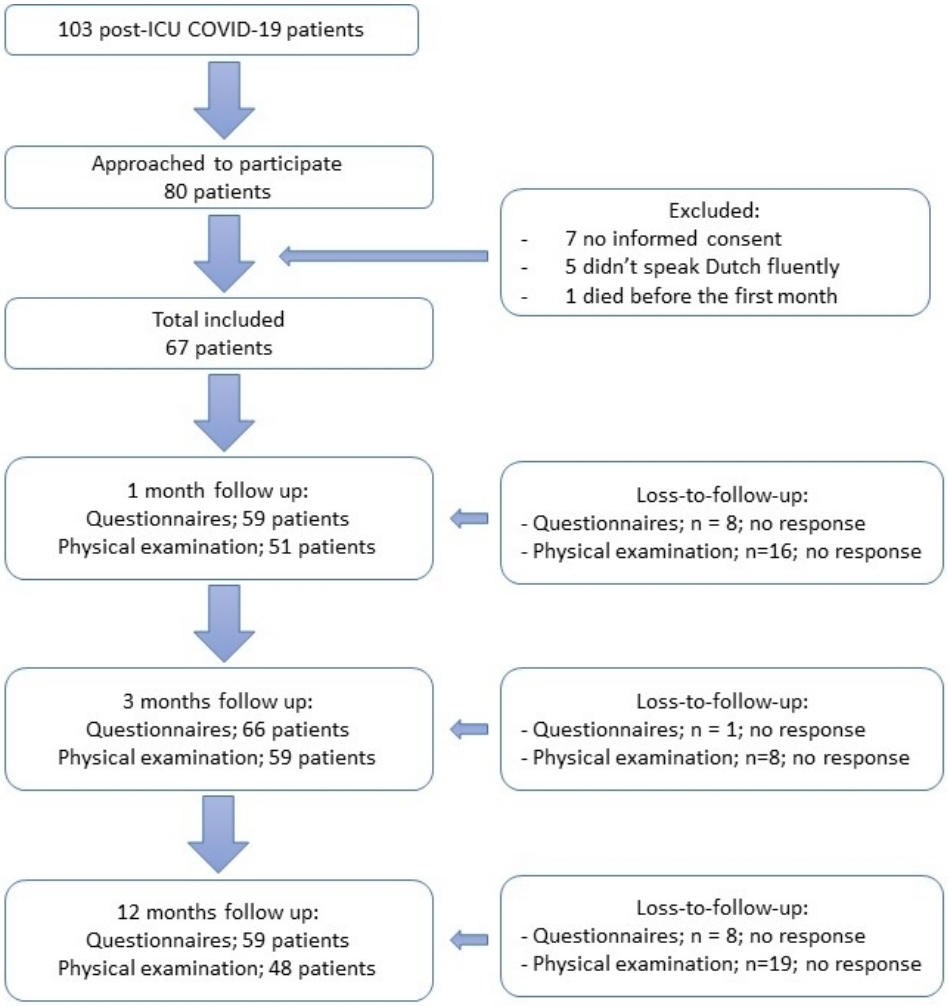

Figure 2; Subject recruitment flowchart.

179x181mm (96 x 96 DPI)

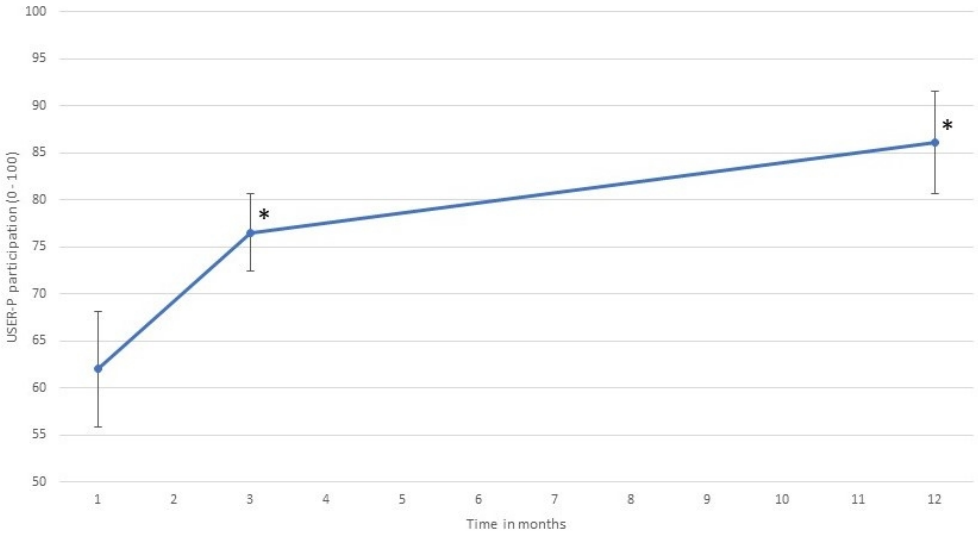

Figure 3; The recovery of participation levels (USER-P restriction subscale) in the first year after ICU discharge in post-COVID-19 patients. Results are expressed as mean with corresponding 95% confidence interval. * $p < 0.01$ (compared to previous measurement moment)

222x129mm (96 x 96 DPI)

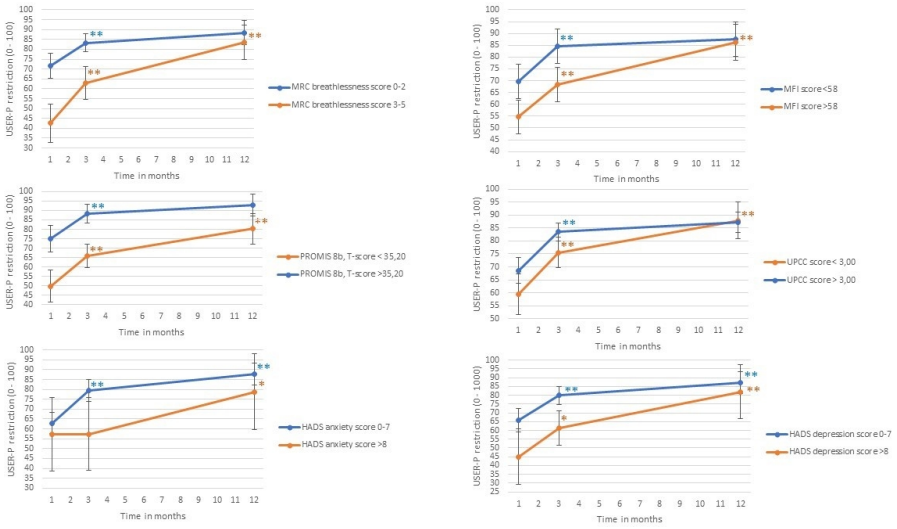

Figure 4; The influence of early levels of body function impairments, activity limitations and personal factors on the recovery of participation levels (USER-P restriction subscale). For illustrative purposes, subgroups have been created based on cut-off value (HADS) or the median if no specific cut-off value is known (MRC, MFI, PROMIS 8b, UPCC). Results are expressed as means with corresponding 95% confidence interval. * $p < 0.05$ and ** $p < 0.01$ (compared to previous measurement moment).

338x177mm (96 x 96 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8 Fig2

		(b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	Report numbers of outcome events or summary measures over time	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	8-11
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Life after COVID-19 the road from intensive care back to living: a prospective cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-062332.R2
Article Type:	Original research
Date Submitted by the Author:	02-Sep-2022
Complete List of Authors:	Wiertz, Carolina; Adelante, Rehabilitation medicine; Maastricht University, Department of Rehabilitation Medicine Research School CAPHRI Hemmen, Bena; Adelante, Rehabilitation medicine; Maastricht University, Department of Rehabilitation Medicine Research School CAPHRI Sep, Simone JS; Adelante, Rehabilitation medicine; Maastricht University, Department of Rehabilitation Medicine Research School CAPHRI van Santen, Susanne; Maastricht Universitair Medisch Centrum+, Department of Intensice Care van Horn, Yvette; Adelante, Rehabilitation medicine van Kuijk, Sander; Maastricht Universitair Medisch Centrum+, Clinical Epidemiology and Medical Technology Assessment Verbunt, Jeanine; Adelante, Rehabilitation medicine; Maastricht University, Department of Rehabilitation Medicine Research School CAPHRI
Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Intensive care
Keywords:	COVID-19, REHABILITATION MEDICINE, Adult intensive & critical care < INTENSIVE & CRITICAL CARE

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Life after COVID-19 the road from intensive care back to living: a prospective cohort study

Author's names

Carolina MH Wiertz MD[1,2], Bena Hemmen MD PhD[1,2], Simone JS Sep PhD[1,2], Susanne van Santen MD[3], Yvette Y van Horn MD[1], Sander MJ van Kuijk[4], Jeanine A Verbunt MD PhD[1,2]

Affiliation of authors

[1] Adelante Zorggroep, P.O. Box 88, 6430 AB Hoensbroek, The Netherlands.

[2] Department of Rehabilitation Medicine Research School CAPHRI, Maastricht University, P.O. Box 616, 6200 MD Maastricht, The Netherlands.

[3] Department of Intensive Care Medicine, Maastricht University Medical Centre, 6202 AZ Maastricht, The Netherlands.

[4] Department of Clinical Epidemiology and Medical Technology Assessment, Maastricht University Medical Centre, 6202 AZ Maastricht, The Netherlands.

Corresponding author: Carolina Wiertz

Adelante Zorggroep

P.O. Box 88

6430 AB Hoensbroek

The Netherlands

E-mail: c.wiertz@adelante-zorggroep.nl

Life after COVID-19 the road from intensive care back to living: a prospective cohort study

Abstract

Objectives: The aim of the study was to evaluate recovery of participation in post-COVID-19 patients during the first year after ICU discharge. The secondary aim was to identify the early determinants associated with recovery of participation.

Design: Prospective cohort study.

Setting: COVID-19 post-ICU inpatient rehabilitation in the Netherlands, during the first epidemic wave between April - July 2020, with one-year follow-up.

Participants: COVID-19 ICU survivors ≥18 years of age needing inpatient rehabilitation.

Main outcome measures: Participation in society was assessed by the 'Utrecht Scale for Evaluation of Rehabilitation-Participation (USER-P) restrictions scale'. Secondary measures of body function impairments (muscle force, pulmonary function, fatigue (MFI), breathlessness (MRC), pain (NRS)), activity limitations (6MWT, PROMIS 8b), personal factors (coping (UPCC), Anxiety and depression (HADS), post traumatic stress (GPS-PTSD-5), cognitive functioning (CLC-IC)) and social factors were used. Statistical analyses: linear mixed-effects model, with recovery of participation levels as dependent variable. Patient characteristics in domains of body function, activity limitations, personal and social factors were added as independent variables

Results: This study included 67 COVID-19 ICU survivors (mean age 62y, 78% male). Mean USER-P restrictions scores increased over time; mean participation levels increasing from 62.0, 76.5 to 86.1 at one, three and 12 months respectively. After one year, 50% had not fully resumed work and restrictions were reported in physical exercise (51%), household duties (46%), and leisure activities (29%). Self-reported complaints of breathlessness and fatigue, more perceived limitations in daily life, as well as personal factors (less pro-active coping style and anxiety/depression complaints) were associated with delayed recovery of participation (all p-value < 0.05).

Conclusions: This study supports the view that an integral vision of health is important when looking at the long-term consequence of post-IC COVID-19. Personal factors such as having a less proactive coping style or mental impairments early on contribute to delayed recovery.

Keywords: COVID-19, Critical care, Rehabilitation medicine

Strengths and limitations of this study

- This study only included the most severely affected post-ICU COVID-19 patients referred to inpatient rehabilitation.
- This study used physical examination as well as questionnaires, which means that there was a combination of objective and subjective measurements.
- Although the sample size is small, a large number of factors were studied for their effect on the course of participation recovery.
- Twenty-three patients were not approached in time for consent to participate.
- The lockdown and the inability to perform social and outdoor activities may have affected the total USER-P score.

Word count abstract: 300

Word count main text: 3370

Number of figures and tables: 6

Introduction

In the first wave of the coronavirus disease 2019 (COVID-19) pandemic in the Netherlands about 2% of all confirmed cases needed treatment in an intensive care unit (ICU) (1,2). About three-quarters of those admitted to ICU had acute respiratory distress syndrome (3) and many patients were recorded as having shock, acute kidney injury, thrombotic complications and/or cardiac injury (3).

Survivors of critical illness frequently experience new or worsening physical, cognitive and/or mental impairment, described as post intensive care syndrome (PICS) (4), which can have long-term effects on participation and quality of life (5–7). Immediately after ICU admission, COVID-19 patients display various physical impairments such as exertional hypoxemia, reduced overall muscle force, shoulder problems, dysphagia, and anxiety complaints (8). In the subacute phase (one to three months after ICU discharge) 90% of the post-ICU COVID patients still experience symptoms affecting at least one of the PICS domains (9,10). Due to the varying impact of severe COVID-19, patients may experience limitations in their participation in daily living, social functioning or work performance (11,12). Restrictions in participation may eventually lead to an increase in (healthcare) costs, since patients need for example more professional assistance in their ADL or return to work is delayed. Although impairments in various domains of functioning have been identified, any long-term effects on the recovery of participation are unclear. The effect that this new disease may have on participation, combined with the large number of COVID-19 ICU survivors, points to the need to study factors that could delay the recovery in participation of survivors after ICU discharge. Consequently, the aim of this study is to evaluate the recovery of participation of COVID-19 patients in the first year after ICU discharge followed by inpatient rehabilitation. The secondary aim was to identify early determinants associated with recovery of participation.

Methods

Study design and participants

This prospective cohort study was performed at Adelante Zorggroep, a rehabilitation centre in the South of the Netherlands. Patients with an indication for inpatient multidisciplinary rehabilitation were transferred to the rehabilitation centre. The indication was determined in the hospital by a consultant in rehabilitation medicine, based on their clinical judgement of the severity of physical, mental and/or cognitive impairments (13,14). All patients (aged 18 or older) referred for inpatient rehabilitation after ICU discharge for COVID-19 were eligible to participate in the study. The exclusion criterion was not speaking or reading the Dutch language fluently. All patients received inpatient multidisciplinary rehabilitation treatment including physiotherapy, occupational therapy, speechtherapy and psychology personalized to patient's limitations and needs according to the Dutch guideline for post-COVID ICU rehabilitation (13,15). All participants provided written informed consent. Patients were transferred to the rehabilitation centre from 7 (2 academic and 5 regional) hospitals in the region. COVID-19 was confirmed with a SARS-COV-19 positive PCR test. The local medical ethics committee Zuyderland METC (METCZ20200086) approved the study.

Patient and public involvement: Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Data collection

Data was collected in the form of baseline information at admission to the rehabilitation centre (T0), through physical examination and self-administered questionnaires after one (T1), three (T2) and twelve months (T3). Since different domains of functioning can be affected by COVID-19, measurements were chosen based on an integral vision of health and included body function impairments, activity limitations and participation restrictions as well as personal and social factors. These factors are derived as main domains in the International Classification of Functioning, Disability

and Health (ICF) that supports the classification of health and health-related conditions and their effect on social participation (Figure 1) (14).

Primary outcome variable: Participation in society was assessed by the 'Utrecht Scale for Evaluation of Rehabilitation-Participation (USER-P) restriction subscale'. This subscale consists of 11 items on restrictions in vocational, leisure and social activities. Items are rated from 0 'not possible' to 3 'without difficulty' and a 'not applicable' option. The total score ranges from 0 to 100, higher scores indicating fewer restrictions in participation (16,17).

Data on age, sex, comorbidities and parameters related to critical illness were collected from the medical transfer letters (T0). Comorbidities were classed into diabetes mellitus, hypertension, cardiovascular disease, lung disease and psychiatric disorders. Parameters related to severity of the critical illness were length of ICU stay, invasive mechanical ventilation (IMV) (yes/no) and duration of invasive IMV. The duration of the inpatient rehabilitation was recorded.

Physical examination: Assessment of muscle strength, functional exercise capacity and pulmonary function were part of physical examination. To measure muscle strength, a handheld dynamometer (HHD) was used (18) to assess the following muscle groups: shoulder abduction, elbow flexion, wrist extension, hip flexion and knee extension, all on patient's dominant side. HHD values were measured in Newtons and percentages of the norm compared with healthy persons of the same sex, age, and weight (19,20). Severe muscle weakness was defined as <80% of the norm score. For the clinical assessment of the functional exercise capacity, the 6-minute walk test (6-MWT) was used, displayed in meters and percentage of the norm (21,22). To evaluate pulmonary function Quark PFT spirometry (Cosmed, Italy) was used (23). Forced expiratory volume in the first second (FEV_1), forced vital capacity (FVC) and FEV_1/FVC ratio were included in the analysis, displayed in percentage of the norm.

In addition, self-administered questionnaires were used. Breathlessness was assessed by the MRC breathlessness scale, which comprises five statements that range from 0 'no trouble with breathlessness' to 5 'I am too breathless to leave the house' (24). The Numerical Rating Scale (NRS)

was used for assessing pain. Patients were asked to rate their mean pain intensities in the last seven days, ranging from 0-10, with 0 indicating 'no pain' and 10 indicating 'the worst imaginable pain' (25). The multidimensional Fatigue Inventory (MFI) is a 20-item metric for fatigue severity. It has 5 dimensions: general fatigue, physical fatigue, mental fatigue, reduced motivation and reduced activity. Each item ranges from 1 'absence of fatigue' to 5 'severe fatigue'. A total score is calculated as the sum of the subscale scores (20–100). Higher scores indicate higher levels of fatigue (26). The perceived limitations in daily life were assessed using the PROMIS physical function shortform 8b. This survey contains eight questions ranging from 1 'unable to do' to 5 'without any difficulty' (27). A web-based scoring service was used to calculate T-scores (maximum score 60.1 and mean 50.0, corresponding to the mean in the general population of the USA), whereas a higher scores indicates better physical function (28). Anxiety and depression complaints were assessed with the Hospital Anxiety and Depression Scale (HADS). A score ≥8 on either subscale was considered to be substantial anxiety or depression symptoms (29). Post-traumatic stress was assessed using the Global Psychotrauma Screen – Post Traumatic Stress Disorder (GPS-PTSD-5). The regular GPS consists of 22 items, item 1-5 can be used to generate a GPS-PTDS-5 score (range 0-5), score ≥3 indicates PTSD (30). Cognitive functioning was assessed using the Checklist for Cognitive consequences after ICU-admission (CLC-IC). The CLC-IC consists of 10 items; higher scores indicate more cognitive problems experienced in daily life (range 0-10). The CLC-IC is based on the CLCE-24 (31). Proactive coping skills were assessed at T3 with the Utrecht Proactive Coping Scale (UPCC), which is a 21-item questionnaire scored on a 4-point scale ranging from 'not competent at all' to 'competent'. The total score was the average for all item scores (range 1–4), where higher scores indicate higher levels of proactive coping (32). Premorbid social- and work situations were collected at T1.

Statistical analyses

Results are reported as mean and standard deviation (SD) or median and interquartile range (IQR) depending on distribution. Recovery of participation levels over time were assessed with linear mixed-

effects model for repeated measures. Patient characteristics in the domains body function, activity limitations, personal and social factors at T0 and and 1 month after admission in the rehabilitation centre (T1) were added to separate models that also included time and the interaction between that covariate and time. Next, for illustrative purposes only, linear mixed-effects model analyses were stratified according to patient characteristics that were significantly associated with the course of recovery of participation levels to visualize different patterns of change over time. A $p<0.05$ was considered as statistically significant. Statistical analyses were performed with IBM SPSS statistics 26.0 (SPSS Inc. Chicago, IL).

Results

During the first COVID-19 wave between April 2 and June 30, 2020, 103 post-ICU patients were admitted for inpatient rehabilitation. Of these, twenty-three patients were missed since this study was part of clinical practice in a very dynamic period and 13 patients were excluded excluded for reasons given in figure 2. The study sample consisted of 67 patients (78% male) with a median age of 62 (IQR 57-68) and a median length of stay of 20 (12-33) days in the ICU and 19 (11-31) days inpatient rehabilitation (Table 1). Overall, an improvement in muscle strength and functional exercise capacity (6MWT) was found, whereas fatigue complaints and perceived limitations in daily life seem to decrease in the first year after ICU discharge (Table 1).

Participation restrictions improved in the first year after ICU discharge due to a COVID-19 infection (Figure 3). Mean participation levels increased from 62.0 (95%CI 55.9-68.1), 76.5 (95%CI 71.9-81.1) to 86.1 (95%CI 80.6-91.6) at one, three and 12 months respectively. One year after ICU discharge, 50.8% of the patients still reported restrictions in physical exercise, 45.8% in performing housekeeping and 28.8% in performing leisure activities. After one year work is not applicable in 42.4% of all patients, which is comparable to the premorbid work situation, where 58% of all patients were employed. One year after ICU discharge 28.8% of all patients still reported restrictions in work/education. Taking into

192 account the patients who were not working pre-illness, means that 50% of the pre-illness working

193 patients had not fully resumed work after one year (Table 1).

Table 1	T0	One month (T1)	Three months (T2)	Twelve months (T3)
Baseline characteristics				
Age, years; n=67; median (IQR)	62 (57 – 68)	-		
Sex; n=67; No (%)				
- Men	52 (77.6%)	-		
- Women	15 (22.5%)	-		
Highest level of education; n=62; No (%)				
- Lower education	42 (67.7%)	-		
- Higher education	20 (32.3%)	-		
Work situation; n=62; No (%)		-		
- Full-time job	26 (41.9%)			
- Parttime job	10 (16.1%)	-		
- Retired	18 (29.0%)	-		
- Not working otherwise	8 (12.9%)	-		
Comorbidities; n=67; no (%)		-		
- Asthma / bronchitis	6 (9.0%)			
- Chronic obstructive pulmonary disease	4 (6.0%)	-		
- Obstructive sleep apnoea syndrome	12 (17.9%)	-		
- Diabetes Mellitus	12 (17.9%)	-		
- Hypertension	23 (34.3%)	-		
- Cardiovascular disease	21 (31.3%)	-		
- Chronic kidney disease	5 (7.4%)	-		
- Depression	4 (6.0%)	-		
- None of the above comorbidities	25 (37.3%)	-		
Parameters related to severity critical illness		-		
- Duration intensive care unit, in days; n=59; median (IQR)	20 (12 – 33)			
- Invasive mechanical ventilation; n=67; No (%)	58 (86.6%)	-		
- Duration IMV, in days; n=55; median (IQR)	17 (9 – 24)	-		
- Presence of ICU-acquired weakness, n=61; No (%)	45 (73.8%)	-		
Duration inpatient rehabilitation, days; n=67; median (IQR)	19 (11 – 31)			
Coping style (UPCC); n=58; mean (SD)	3.0 (0.2)			
USER-P restriction subscale [a]				
- Work/education	-	64.4%	60.6%	28.8%
- Housekeeping	-	74.6%	65.2%	45.8%
- Mobility	-	59.3%	43.9%	16.9%
- Physical exercise	-	79.7%	60.6%	50.8%
- Going out	-	45.8%	24.2%	10.2%
- Outdoor activities	-	54.2%	36.4%	16.9%
- Leisure activities	-	42.4%	28.8%	20.3%
- Partner relationship	-	28.8%	24.2%	16.9%
- Visits to family/friends	-	45.8%	31.8%	10.2%
- Visits from family/friend	-	32.2%	13.6%	8.5%
- Telephone/PC contact	-	15.3%	13.6%	11.9%
Physical examination:				
- Muscle strength				
- Mean muscle force (HHD), mean (SD)	-	75.7% (15.3)	93.5% (24.6)	101.4% (15.3)
- 6MWT; mean (SD)	-	467.8m (91.2)	518.3m (102.5)	531.0m (86.5)
- **percentage of predicted**		69.5% (13.7)	76.9% (13.7)	79.2% (10.4)
- Pulmonary function; mean (SD)	-			
- FEV1	-	87.5% (15.8)	93.8% (19.9)	93.6% (17.7)
- FVC	-	85.9% (16.3)	92.8% (18.7)	92.2% (15.6)
- FEV1/FVC ratio		79.6% (9.1)	77.3% (10.6)	79.1% (11.2)
Self-administered questionnaires:				
- Breathlessness (MRC); median (IQR)	-	2.0 (1.0 – 3.0)	1.0 (1.0 – 2.0)	1.0 (1.0 – 2.0)
- Pain (NRS); median (IQR)	-	2.0 (1.0 - 3.5)	2.0 (1.5 – 5.0)	2.0 (1.0 – 3.0)
- Fatigue (MFI); mean (SD)	-	58.6 (14.0)	56.0 (15.3)	50.8 (17.6)
- perceived limitations in daily life (PROMIS 8b); mean (SD)	-	34.8 (7.4)	39.2 (6.9)	44.8 (8.0)
- Anxiety (HADS-anxiety); median (IQR)	-	3.0 (1.0 – 5.0)	3.0 (1.0 - 6.0)	2.0 (0.5 – 6.0)
Exceeded anxiety cut-off ≥8	-	7/57 (12.3%)	11/66 (16.7%)	10/59 (16.9 %)
- Depression (HADS depression); median (IQR)	-	2.0 (1.5 – 6.0)	3.0 (1.0 – 6.0)	2.0 (1.0 – 4.0)
Exceeded depression cut-off ≥8	-	10/59 (16.9%)	13/66 (19.7%)	10/59 (16.9%)
- Post-traumatic stress (GPS-PTSD-5); median (IQR)		0.0 (0.0 – 1.0)	0.0 (0.0 – 1.0)	0.0 (0.0 – 1.0)
Exceeded PTSD cut-off ≥3		5/59 (8.5%)	8/66 (12.1%)	3/59 (5.1%)
- Cognitive impairments (CLC-IC); median (IQR)		3.0 (1.0 – 6.0)	4.0 (1.0 – 7.0)	2.0 (0.0 – 7.0)

Table 1, overview of the baseline characteristics (T0) and the physical examination and self-administered questionnaires at T1, T2 and T3.Low educational level was determined as 'primary and secondary education and post-secondary school'. High educational level was determined as 'bachelor's degree, master's degree or doctorate or equivalent'. Abbreviations: IMV, Invasive mechanical ventilation; UPCC, Utrecht Proactive Coping Scale; USER-P, Utrecht Scale for Evaluation of Rehabilitation-Participation; HHD, handheld dynamometer; 6MWT, 6 minute walking test; FEV1, Forced expiratory volume in the first second; FVC, Forced vital capacity; n.a., not applicable; MFI, multidimensional Fatigue Inventory; HADS, Hospital Anxiety and Depression Scale; GPS, The Global Psychotrauma Screen; CLC-IC, Checklist for Cognitive consequences after an ICU-admission. [a] Restriction items values are percentages of patients who are restricted or dissatisfied.

Regarding the second aim, in the ICF domain body functions, breathlessness (MRC breathlessness), regression coefficient: 0.60 (95%CI 0.23-0.97; p-value <0.01) and fatigue (MFI), regression coefficient: 0.07 (95%CI 0.03-0.09; p-value <0.01) were the only physical variables that influenced participation recovery over time. For the ICF domain activities, perceived limitations in daily life (PROMIS 8b) showed a different pattern in the recovery of participation restriction levels, regression coefficient: -0.11 (95%CI -0.12 to -0.05; p-value <0.01). In addition, personal factors like coping style (UPCC) regression coefficient: -2.39 (95%CI -4.20 to -0.06; p-value 0.01), anxiety (HADS anxiety) regression coefficient: 0.17 (95%CI 0.02-0.31; p-value 0.03) and depression (HADS depression) regression coefficient: 0.19 (95%CI 0.07-0.31; p-value <0.01) showed different paths in resuming the level of participation over time. Other early determinants show no significant difference in the recovery of participation (Table 2).

Table 2	Estimate (95% CI)	p-value
Baseline characteristics		
Age	-0.03 (-0.08 – 0.02)	0.29
Sex	0.72 (-0.32 – 1.76)	0.17
Number of comorbidities	0.04 (-0.34 – 0.42)	0.83
Duration of inpatient rehabilitation	0.03 (-0.00 – 0.06)	0.07
Coping style (UPCC)	-2.39 (-4.20 – -0.06)	0.01*
ICU-stay specific parameters		
Length of ICU stay	0.02 (-0.01 – 0.06)	0.21
Duration of invasive mechanical ventilation	0.02 (-0.02 – 0.05)	0.37
ICU-acquired weakness	-0.23 (-1.31 – 0.85)	0.67
Physical examination		
Muscle strength		
- Mean muscle force (HHD)	-0.02 (-0.06 – 0.01)	0.18
6MWT	-0.00 (-0.01 – 0.01)	0.65
Pulmonary function		
- FEV1	-0.02 (-0.06 – 0.01)	0.16
- FVC	-0.03 (-0.06 – 0.00)	0.07
- FEV1/FVC ratio	0.04 (-0.02 – 0.09)	0.24
Self-administered questionnaires		
Breathlessness (MRC)	0.60 (0.23 – 0.97)	< 0.01*
Pain (NRS)	-0.03 (-0.28 – 0.23)	0.84
Fatigue (MFI)	0.07 (0.03 – 0.09)	< 0.01*
Perceived limitations in daily life (PROMIS 8b)	-0.11 (-0.12 – -0.05)	< 0.01*
Anxiety (HADS-anxiety)	0.17 (0.02 – 0.31)	0.03*
Depression (HADS depression)	0.19 (0.07 – 0.31)	< 0.01*
Post-traumatic stress (GPS-PTSD-5)	0.24 (-0.21 – 0.70)	0.30
Cognitive impairments (CLC-IC)	0.09 (-0.07 – 0.24)	0.27

Table 2; linear mixed model for covariates at T0 or T1, as an interaction between covariate and time (1, 3, and 12 months), for the recovery of participation levels. * $p < 0.05$. Abbreviations: UPCC, Utrecht Proactive Coping Scale; HHD, handheld dynamometer; 6MWT, 6 minute walking test; FEV1, Forced expiratory volume in the first second; FVC, Forced vital capacity; MFI, multidimensional Fatigue Inventory; HADS, Hospital Anxiety and Depression Scale; GPS, The Global Psychotrauma Screen; CLC-IC, Checklist for Cognitive consequences after an ICU-admission.

Participation levels increased significantly between 1 and 3 months and between 3 and 12 months in patients who reported more breathlessness, more fatigue or more limitations in daily life and those with a passive coping style. In contrast, patients with less breathlessness, fewer fatigue complaints, fewer restrictions in daily life and a pro-active coping style showed no significant increase between 3 and 12 months (Figure 4). For patients with HADS anxiety score ≥8, no differences were found in participation levels in the first 3 months, while there was significant difference in recovery of participation levels between 3 and 12 months. However, for patients with fewer anxiety complanits (HADS anxiety score ≤8) participation levels significantly improved between 1 and 3 months and

between 3 and 12 months. For depressive symptoms, both groups improved significantly in participation levels between 1 to 3 months and between 3 to 12 months, although a steeper curve is seen in recovery of participation levels at 3 to 12 months in patients with more depressive symptoms.

Discussion

In this prospective cohort study, recovery of participation during the first year after ICU discharge in COVID-19 ICU survivors who needed inpatient rehabilitation was evaluated and the association between early levels of body function impairments, activity limitations and personal and social factors on recovery were estimated. It is seen that in the first year after ICU discharge patients were able to improve their participation levels. Nevertheless, after one year, there are still important limitations in daily life, mainly in resuming work, physical exercise, housekeeping and leisure activities. As early determinants for a delay in the resumption of patient's habitual level of participation levels over the first year, higher levels of self-experienced breathlessness and fatigue complaints, more perceived limitations in daily life as well as personal factors (having a passive coping style, anxiety complaints or depression complaints) were found.

In previous Dutch studies focusing on overall post-ICU COVID-19 survivors, an average age of 61-63 was found, 69-72% men, with a median length of stay of 18-20 days in the ICU (33,34). These demographic data seem to correspond with findings of current study, taking into account that in the first COVID-19 wave, 83% of all post-ICU COVID-19 patients were transferred to a rehabilitation centre (34). Heesakker et al. reported that in patients who survived one year following ICU treatment for COVID-19, physical, mental, or cognitive symptoms were often reported (33). This corresponds with the findings of the current study, whereas various physical, mental and cognitive impairments were seen one year after ICU admission. However, to our knowledge, this is the first study to report differences in the resumption of participation levels in post-ICU COVID-19 patients. Mean participation levels increased to 86.1 one year after ICU discharge. As a reference, in other non-COVID patients (i.e.

stroke, acquired brain injury, progressive neurologic diseases, spinal cord injury and acute coronary syndrome), participation levels between 70.6-83.5 have been observed (35–37). In all non-COVID patient groups, patients mainly reported restrictions in work/education, housekeeping, physical exercise and performing leisure activities, which is in accordance with restrictions in participation reported in current study (36,37).

Moreover, these results showed that higher scores of self-experienced breathlessness or fatigue and more perceived limitations in daily life in the early phase of rehabilitation were associated with a delayed recovery of participation levels over the first year. Furthermore, patients with a less active coping style, those that were more anxious or reported to perceive more depressive complaints had a delayed recovery of their level of participation over the first year. For all these determinants, participation levels also appeared to be lower in the early phase of rehabilitation. These findings indicate that patients with a higher level of anxiety and those with a higher level of depression had a significantly slower improvement in participation levels during the first months, followed by a more progressive recovery, especially in the last months. In addition, patients with more breathlessness complaints, more fatigue complaints or more perceived limitations in daily life in the early phase of rehabilitation and patients with a passive coping style showed a more progressive recovery of participation levels especially in the last months. Poor baseline situation may also have provided more opportunity to improve. However, with a mean participation restriction level of 86.1 one year after ICU discharge, the maximum score of 100 of the USER-P restriction subscale has not been reached.

Complaints of fatigue or breathlessness may be due to underlying medical problems or to the contribution of personal factors. Previous study's showed significant recovery of respiratory function and physical performance in the first year after ICU discharge due to COVID-19. Nevertheless, patients still experience breathlessness and fatigue complaints after one year (38,39). Another finding in current study was that early determinants related to the severity of the COVID-19 infection period itself (such as ICU stay-specific parameters and physical parameters as age, sex, muscle strength, functional exercise capacity and pulmonary function) did not individually explain progress in recovery

of participation over time. Contrary to expectations, this may indicate that non-physical factors such as coping style, subjectively experienced physical impairments (including fatigue and breathlessness) and mental health issues (such as anxiety and depressive symptoms) seem more important to determine progress in recovering the level of participation. Previous literature on post-ICU patients indicated that critical care recovery has focused on post-ICU impairments experienced by patients. Whereas the positive aspects of recovery within the rehabilitation phase, including coping style and resilience seems to be ignored (40,41). Resilience refers to the ability to face the challenges and difficulties of life in a positive and adaptive manner, as well as the capacity to recover from an adverse event (42). Higher levels of resilience have been linked to improved mental and physical health (43). It is possible to improve the level of resilience. Which implies that resilience can be used to improve (emotional) well-being, with the possible consequence of improving participation levels.

Implications for clinical practice and further research

This study underlines the importance of looking at long-term consequence of COVID-19 ICU survivors with an integral vision of health. Whether identical variables can be used to identify a delay in recovery in patients who had a milder infection is currently still unclear. In this study, conclusions can be made for a selected group (with ICU admission) of patients. Extrapolation to other populations needs to be done with caution. Early detection of a passive coping style or mental impairments seems important and should therefore be included in screening during early multidisciplinary rehabilitation. Further research is needed to study the effect of early screening of a patients' level of coping/ resilience during the first months after ICU discharge. As a consequence, an early intervention to increase resilience/strengthen coping on indication could be promising to further strengthen social participation, but needs to be further studied.

Strengths and limitations

A strength of the study is that it only included the most severely affected post-ICU COVID-19 patients referred to inpatient rehabilitation. In addition, this study used physical examination as well as questionnaires, which means there was a combination of objective and subjective measurements. It is notable that even in the most severely affected COVID-19 patients delayed recovery of participation is associated with self-experienced physical impairments, mental impairments and coping style.

Nevertheless, some limitations of the current study need to be considered. First, sample size is limited and a number of factors were studied for their effect on the course of participation recovery. The limited sample size contributed to relatively wide confidence intervals. The risk of type II error should therefore be considered while interpreting the data. A post-hoc power calculation revealed however that the study had 90% power to detect an effect size of 0.2 for changes in participation levels over time (alpha = 0.05, mean correlation between repeated measures = 0.53). Still, p-values of the multiple tests of association should be interpreted cautiously, because we cannot exclude erroneous interpretations of statistical significant findings (i.e. type I error). However, since our results support a certain pattern, we believe that the main conclusions of this study are solid. Second, number of variables available to describe the acute illness severity were limited. Patients referred for inpatient multidisciplinary rehabilitation were included in this study. Generalisation of the results to all ICU survivors needs to be performed with caution, and needs further study. Third, due to high workload on the ward, 23 patients were not approached in time for consent to participate. In our opinion, this is unlikely to have led to selection bias, but this cannot be excluded. Finally, the lockdown and the inability to perform social and outdoor activities may have affected the total USER-P score as this scale allows the rating of 'not applicable'. Since the study- and lockdown period were similar for all patients, we expect no difference in the study patients. Although it may have affected the recovery course of participation recovery for the entire patient group, it is not expected to have affected the predictors.

Conclusion

For patients admitted to an ICU for COVID-19, participation levels improves in the first year after ICU discharge. However, at one year after discharge, many patients still experience limitations in daily life, mainly in resuming work, physical exercise, housekeeping and leisure activities. Our results indicate that progress of recovery in participation in the first year after discharge is associated with early determinants in coping style, subjectively experienced physical impairments (breathlessness and fatigue) and mental impairments (anxiety and depression) rather than medical variables. This study supports the need for an integral perspective on health to facilitate the identification of factors that delay the recovery trajectory for participation in the first year after ICU discharge. Personal factors such as a passive coping style and more anxiety- or depression complaints seem relevant to this. Rehabilitation care needs to anticipate on these topics, starting in the early rehabilitation phase of post-ICU COVID-19 care.

Acknowledgements: We would like to thank all physiotherapist and students for their valuable contribution for collecting all data. We also thank all participants.

Author contributors: CW, JV, BH and SJSS were responsible for the study design. The statistical analysis plan was designed by CW, SJSS and SvK. Statistical analysis was done by CW, with control of SJSS and SvK. Practical implication was done by CW, SvS and YH. The first draft of the paper was written by CW and all co-authors reviewed and approved it for submission. CW and JV are the guarantors. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Funding: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests: All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/disclosure-of-interest/ and declare: no support from any organisation for the

submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the past three years; no other relationships or activities that could appear to have influenced the submitted work

Patient consent for publication: Not required.

Dissemination to participants and related patient and public communities: The study results will be disseminated to the public through our media channels or national and international conferences.

Ethical approval: The local medical ethics committee Zuyderland METC (METCZ20200086) approved the study.

Data availability statement: To guarantee the confidentiality of personal and health information, only the authors have had access to the data during the study. Data is available (anonymised), but the corresponding author must be contacted to request these data. Data will be kept for 15 years

ORCID ID: Carolina Wiertz https://orcid.org/0000-0002-7703-2508

References

1. RIVM. Actuele informatie over het nieuwe coronavirus (COVID-19) [Internet]. 22-05-2020. Available from: https://www.rivm.nl/coronavirus-covid-19/actueel

2. NICE. COVID-19 infecties op de IC's [Internet]. Nationale Intensive Care Evaluatie. [cited 2020 Jul 2]. Available from: https://www.stichting-nice.nl/COVID_rapport.pdf

3. Tan E, Song J, Deane AM, Plummer MP. Global Impact of Coronavirus Disease 2019 Infection Requiring Admission to the ICU: A Systematic Review and Meta-analysis. Chest. 2021;

4. Needham DM, Davidson J, Cohen H, Hopkins RO, Weinert C, Wunsch H, et al. Improving long-term outcomes after discharge from intensive care unit: Report from a stakeholders' conference. Crit Care Med. 2012 Feb;40(2):502–9.

5. Dowdy DW, Eid MP, Sedrakyan A, Mendez-Tellez PA, Pronovost PJ, Herridge MS, et al. Quality of life in adult survivors of critical illness: A systematic review of the literature. Vol. 31, Intensive Care Medicine. Springer Verlag; 2005. p. 611–20.

6. Desai S V., Law TJ, Needham DM. Long-term complications of critical care. Critical Care Medicine. 2011.

7. Ohtake PJ, Lee AC, Scott JC, Hinman RS, Ali NA, Hinkson CR, et al. Physical impairments associated with post-intensive care syndrome: Systematic review based on the world health organization's international classification of functioning, disability and health framework. Physical Therapy. 2018.

8. Wiertz CMH, Vints WAJ, Maas GJCM, Rasquin SMC, van Horn YY, Dremmen MPM, et al. COVID-19: patient characteristics in the first phase of post-intensive care rehabilitation. Arch Rehabil Res Clin Transl. 2021;

9. Martillo MA, Dangayach NS, Tabacof L, Spielman LA, Dams-O'Connor K, Chan CC, et al. Postintensive Care Syndrome in Survivors of Critical Illness Related to Coronavirus Disease

2019: Cohort Study from a New York City Critical Care Recovery Clinic∗. Crit Care Med. 2021;

10. Rousseau AF, Minguet P, Colson C, Kellens I, Chaabane S, Delanaye P, et al. Post-intensive care syndrome after a critical COVID-19: cohort study from a Belgian follow-up clinic. Ann Intensive Care. 2021;

11. Leite VF, Rampim DB, Jorge VC, de Lima M do CC, Cezarino LG, da Rocha CN, et al. Persistent Symptoms and Disability After COVID-19 Hospitalization: Data From a Comprehensive Telerehabilitation Program. Arch Phys Med Rehabil. 2021;

12. Veenendaal N van, van der Meulen IC, Onrust M, Paans W, Dieperink W, van der Voort PHJ. Six-month outcomes in covid-19 icu patients and their family members: A prospective cohort study. Healthc. 2021;

13. FMS. COVID-19 [Internet]. 2022. Available from: https://richtlijnendatabase.nl/richtlijn/covid-19/startpagina_-_covid-19.html

14. (WHO) WHO. The international Classification of Functioning, Disability and Health - ICF [Internet]. 2001. Available from: https://www.who.int/classifications/international-classification-of-functioning-disability-and-health

15. de Graaf J, Brouwers M, Post M. Behandelprogramma COVID-19 post-IC in de Medisch Specialistische Revalidatie (De Hoogstraat). Utrecht, The Netherlands; 2020.

16. Post MWM, Van Der Zee CH, Hennink J, Schafrat CG, Visser-Meily JMA, Van Berlekom SB. Validity of the utrecht scale for evaluation of rehabilitation- participation. Disabil Rehabil. 2012;

17. Van Der Zee CH, Visser-Meily JMA, Lindeman E, Kappelle LJ, Post MWM. Participation in the chronic phase of stroke. Top Stroke Rehabil. 2013;

18. Vanpee G, Segers J, Van Mechelen H, Wouters P, Van Den Berghe G, Hermans G, et al. The

interobserver agreement of handheld dynamometry for muscle strength assessment in critically ill patients. Crit Care Med. 2011;

19. Andrews AW, Thomas MW, Bohannon RW. Normative values for isometric muscle force measurements obtained with hand-held dynamometers. Phys Ther. 1996;76(3):248–59.

20. Bohannon RW. Reference values for extremity muscle strength obtained by hand-held dynamometry from adults aged 20 to 79 years. Arch Phys Med Rehabil. 1997;78(1):26–32.

21. Chan KS, Pfoh ER, Denehy L, Elliott D, Holland AE, Dinglas VD, et al. Construct validity and minimal important diff erence of 6-minute walk distance in survivors of acute respiratory failure. Chest. 2015;

22. Troosters T, Gosselink R, Decramer M. Six minute walking distance in healthy elderly subjects. Eur Respir J. 1999;

23. Graham BL, Steenbruggen I, Barjaktarevic IZ, Cooper BG, Hall GL, Hallstrand TS, et al. Standardization of spirometry 2019 update an official American Thoracic Society and European Respiratory Society technical statement. American Journal of Respiratory and Critical Care Medicine. 2019.

24. Stenton C. The MRC breathlessness scale. Occup Med (Lond). 2008;

25. Williamson A, Hoggart B. Pain: A review of three commonly used pain rating scales. Journal of Clinical Nursing. 2005.

26. Smets EMA, Garssen B, Bonke B, De Haes JCJM. The multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. J Psychosom Res. 1995;

27. Feng D, Laurel F, Castille D, McCormick AKHG, Held S. Reliability, construct validity, and measurement invariance of the PROMIS Physical Function 8b—Adult Short Form v2.0. Qual Life Res. 2020;

28. HealthMeasures Scoring Service powered by Assessment CenterSM [Internet]. [cited 2021 Feb 20]. Available from: https://www.assessmentcenter.net/ac_scoringservice

29. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale: An updated literature review. J Psychosom Res. 2002;

30. Olff M, Bakker A. Global Psychotrauma Screen (GPS); User guide september 2021 [Internet]. 2016 [cited 2022 Feb 2]. Available from: https://nl.global-psychotrauma.net/gps

31. van Heugten C, Rasquin S, Winkens I, Beusmans G, Verhey F. Checklist for cognitive and emotional consequences following stroke (CLCE-24): Development, usability and quality of the self-report version. Clin Neurol Neurosurg. 2007;

32. Bode C, Thoolen B, Ridder D. Het meten van proactieve copingvaardigheden: Psychometrische eigenschappen van de Utrechtse Proactieve Coping Competentie lijst (UPCC). Psychol en Gezondh. 2008;

33. Heesakkers H, van der Hoeven JG, Corsten S, Janssen I, Ewalds E, Simons KS, et al. Clinical Outcomes Among Patients With 1-Year Survival Following Intensive Care Unit Treatment for COVID-19. JAMA. 2022;(January).

34. van Gassel RJJ, Bels JLM, Raafs A, van Bussel BCT, van de Poll MCG, Simons SO, et al. High prevalence of pulmonary sequelae at 3 months after hospital discharge in mechanically ventilated survivors of COVID-19. American Journal of Respiratory and Critical Care Medicine. 2021.

35. Van Mierlo ML, Van Heugten CM, Post MWM, Hajós TRS, Kappelle LJ, Visser-Meily JMA. Quality of life during the first two years post stroke: The Restore4Stroke cohort study. Cerebrovasc Dis. 2016;

36. de Graaf JA, van Mierlo ML, Post MWM, Achterberg WP, Kappelle LJ, Visser-Meily JMA. Long-term restrictions in participation in stroke survivors under and over 70 years of age. Disabil

Rehabil. 2018;

37. Mol TI, van Bennekom CA, Schepers VP, ter Hoeve N, Kruitwagen-van Reenen ET, Visser-Meily JM, et al. Differences in Societal Participation Across Diagnostic Groups: Secondary Analyses of 8 Studies Using the Utrecht Scale for Evaluation of Rehabilitation-Participation. Arch Phys Med Rehabil. 2021;

38. Gamberini L, Mazzoli CA, Prediletto I, Sintonen H, Scaramuzzo G, Allegri D, et al. Health-related quality of life profiles, trajectories, persistent symptoms and pulmonary function one year after ICU discharge in invasively ventilated COVID-19 patients, a prospective follow-up study. Respir Med. 2021;

39. Bels JLM, van Gassel RJJ, Timmerman L, Hemmen B, van de Poll MCG, Peters NHGM, et al. One year respiratory and functional outcomes of mechanically ventilated COVID-19 survivors: A prospective cohort study. Am J Respir Crit Care Med. 2022;Online ahead of print.

40. Maley JH, Brewster I, Mayoral I, Siruckova R, Adams S, McGraw KA, et al. Resilience in survivors of critical illness in the context of the survivors' experience and recovery. Ann Am Thorac Soc. 2016;

41. Haines KJ, Hibbert E, Leggett N, Boehm LM, Hall T, Bakhru RN, et al. Transitions of Care After Critical Illness-Challenges to Recovery and Adaptive Problem Solving. Crit Care Med. 2021;

42. Steinhardt M, Dolbier C. Evaluation of a resilience intervention to enhance coping strategies and protective factors and decrease symptomatology. J Am Coll Heal. 2008;

43. Schure MB, Odden M, Goins RT. The association of resilience with mental and physical health among older american indians: The native elder care study. Am Indian Alaska Nativ Ment Heal Res. 2013;

Figure Legend:

- Figure 1: ICF model and measurement instruments used.
- Figure 2: Subject recruitment flowchart.
- Figure 3: The recovery of participation levels (USER-P restriction subscale) in the first year after ICU discharge in post-COVID-19 patients.
- Figure 4: The influence of early levels of body function impairments, activity limitations and personal factors on the recovery of participation levels (USER-P restriction subscale).

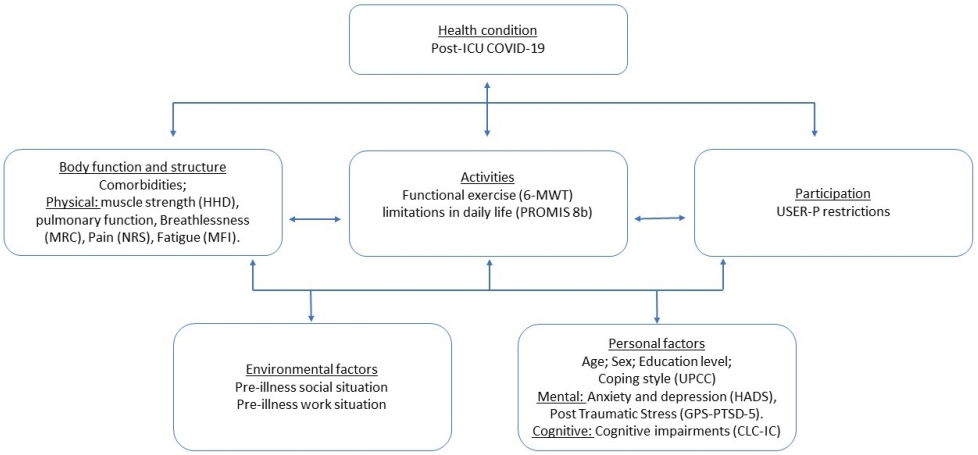

Figure 1. ICF model and measurement instruments used.
Abbreviations: PICS, post intensive care syndrome; USER-P, Utrecht Scale for Evaluation of Rehabilitation-Participation; HHD, handheld dynamometer; MFI, multidimensional Fatigue Inventory; HADS, Hospital Anxiety and Depression Scale; GPS, The Global Psychotrauma Screen; CLC-IC, Checklist for Cognitive consequences after an ICU-admission; 6-MWT, 6-minute walk test; UPCC, Utrecht Proactive Coping Scale ICF, International Classification of Functioning, Disability and Health

338x164mm (96 x 96 DPI)

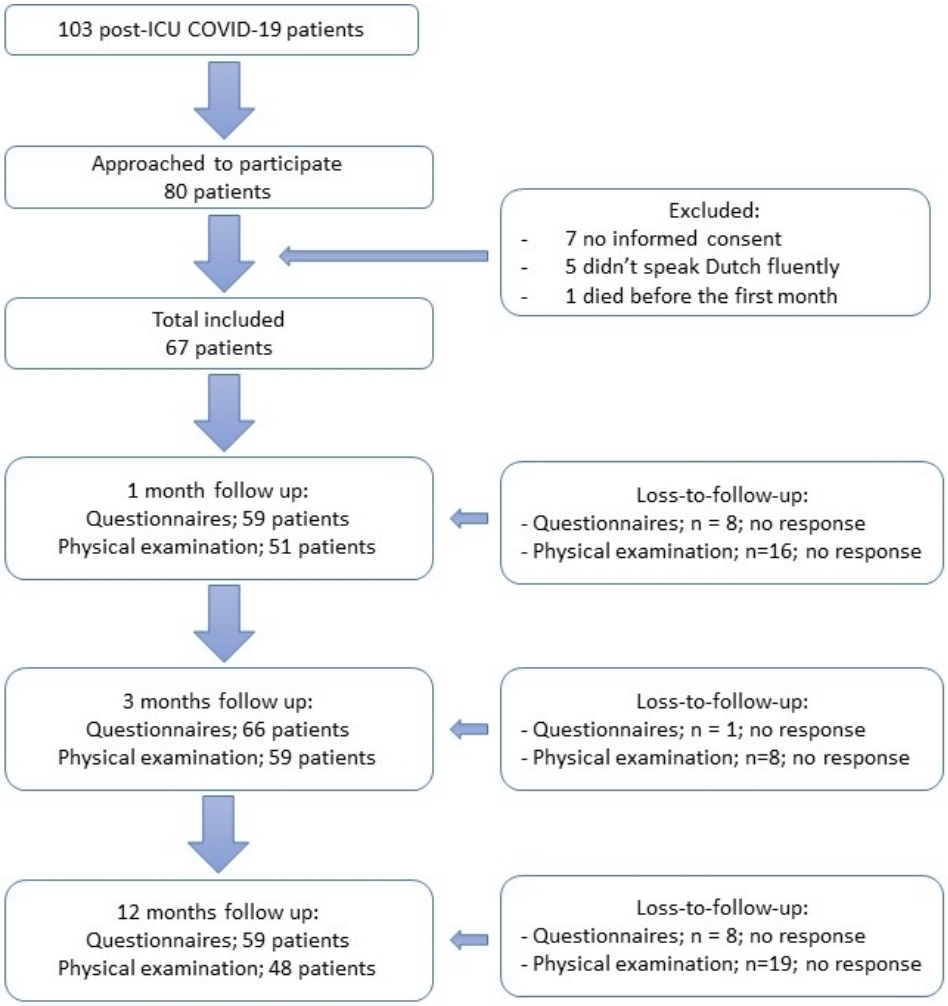

Figure 2; Subject recruitment flowchart.

179x181mm (96 x 96 DPI)

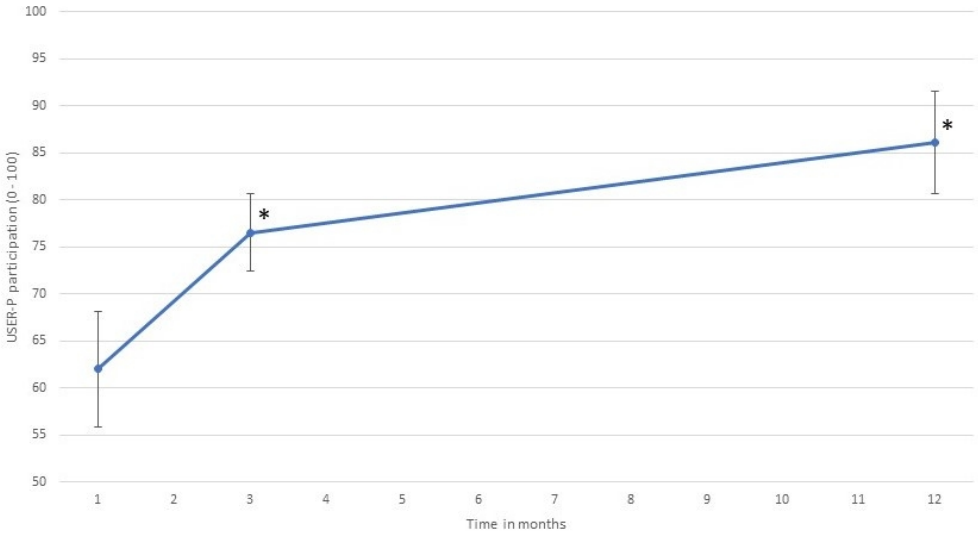

Figure 3; The recovery of participation levels (USER-P restriction subscale) in the first year after ICU discharge in post-COVID-19 patients. Results are expressed as mean with corresponding 95% confidence interval. * $p < 0.01$ (compared to previous measurement moment)

222x129mm (96 x 96 DPI)

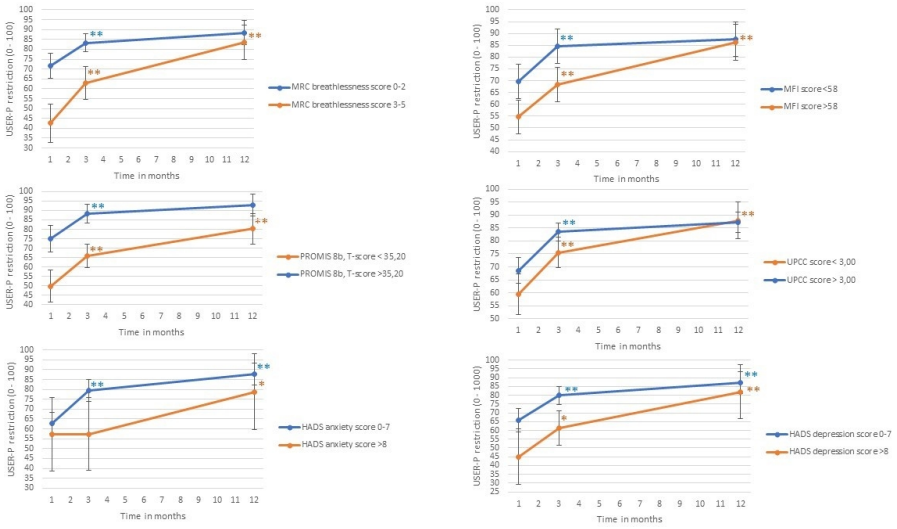

Figure 4; The influence of early levels of body function impairments, activity limitations and personal factors on the recovery of participation levels (USER-P restriction subscale). For illustrative purposes, subgroups have been created based on cut-off value (HADS) or the median if no specific cut-off value is known (MRC, MFI, PROMIS 8b, UPCC). Results are expressed as means with corresponding 95% confidence interval. * $p < 0.05$ and ** $p < 0.01$ (compared to previous measurement moment).

338x177mm (96 x 96 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8 Fig2

		(b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	Report numbers of outcome events or summary measures over time	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	8-11
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.