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# BMJ Open

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

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3 **Life after COVID-19 the road from intensive care back to living: a prospective cohort study**  
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5

6 **Abstract**  
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9 **Objectives:** The principal aim of the present study was to evaluate recovery of participation in post-  
10 COVID-19 patients during the first year after ICU discharge. The secondary aim was to identify the early  
11 determinants associated with recovery of participation.  
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16 **Design:** Prospective cohort study.  
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19 **Setting:** Tertiary COVID-19 post-ICU inpatient rehabilitation facility in the Netherlands, during the first  
20 epidemic wave between April and July 2020, with a one-year follow-up.  
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24 **Participants:** COVID-19 ICU survivors above 18 years of age needing inpatient rehabilitation.  
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27 **Main outcome measures:** Participation in society was periodically assessed by the 'Utrecht Scale for  
28 Evaluation of Rehabilitation-Participation (USER-P) restrictions scale'. Secondary measures of body  
29 function impairments (muscle force, pulmonary function, fatigue (MFI), breathlessness (MRC), pain  
30 (NRS)), activity limitations (6MWT, PROMIS 8b), personal factors (coping (UPCC), Anxiety and  
31 depression (HADS), post traumatic stress (GPS-PTSD-5), cognitive functioning (CLC-IC) and social  
32 factors were used. Statistical analyses: linear mixed-effects model.  
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39 **Results:** This study included 67 COVID-19 ICU survivors (mean age 62y, 78% male). Mean USER-P  
40 restrictions scores increased over time, with mean participation levels increasing from 62.0 (SD 23.7),  
41 76.5 (SD 20.4) to 86.1 (SD 16.8) at one, three and 12 months respectively. After one year, 50% had not  
42 fully resumed work and restrictions were reported in physical exercise (51%), household duties (46%),  
43 and leisure activities (29%). Self-reported complaints of breathlessness and fatigue, more perceived  
44 limitations in daily life, as well as personal factors (less pro-active coping style and anxiety/depression  
45 complaints) were associated with delayed recovery of participation.  
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3 45 **Conclusions:** This study supports the view that an integral vision of health is important when looking  
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5 46 at the long-term consequence of post-IC COVID-19. Personal factors such as having a less proactive  
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7 47 coping style or mental impairments early on contribute to delayed recovery.  
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13 49 **Keywords:** COVID-19, Critical care, Rehabilitation medicine  
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19 51 **Strengths and limitations of this study**

- 20  
21 52 - This study only included the most severely affected post-ICU COVID-19 patients referred to  
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23 53 inpatient rehabilitation.  
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25 54 - This study used physical examination as well as questionnaires, which means that there was a  
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27 55 combination of objective and subjective measurements.  
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29 56 - Although the sample size is small, a large number of factors were studied for their effect on  
30  
31 57 the course of participation recovery.  
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33 58 - Twenty-three patients were not approached in time for consent to participate.  
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35 59 - The lockdown and the inability to perform social and outdoor activities may have affected the  
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37 60 total USER-P score.  
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## 66 Introduction

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

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

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## 90 **Methods**

### 91 Study design and participants

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

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

### 105 Data collection

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



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3 114 Primary outcome variable: Participation in society was assessed by the 'Utrecht Scale for Evaluation of  
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5 115 Rehabilitation-Participation (USER-P) restriction subscale'. The restriction subscale consists of 11 items  
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7 116 on restrictions in vocational, leisure and social activities. Items are rated from 0 'not possible' to 3  
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10 117 'without difficulty' and a 'not applicable' option. The total score ranges from 0 to 100, with higher  
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12 118 scores indicating fewer restrictions in participation (14,15).

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15 119 Data on age, sex, comorbidities and parameters related to critical illness severity was collected from  
16  
17 120 the medical transfer letters. Comorbidities were classed into diabetes mellitus, hypertension,  
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19 121 cardiovascular disease, lung disease and psychiatric disorders. Parameters related to severity of the  
20  
21 122 critical illness were length of ICU stay, invasive mechanical ventilation (IMV) (yes/no) and duration of  
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23 123 invasive IMV. The duration of the inpatient rehabilitation was also recorded.

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26 124 Physical examination: Assessment of Muscle strength, functional exercise capacity and pulmonary  
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28 125 function were part of a physical examination. To measure muscle strength, a handheld dynamometer  
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30 126 (HHD) was used (16) to assess the following muscle groups: shoulder abduction, elbow flexion, wrist  
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32 127 extension, hip flexion and knee extension, all on the patient's dominant side. HHD values were  
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34 128 measured in Newtons and percentages of the norm compared with healthy persons of the same sex,  
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36 129 age, and weight (17,18). For the clinical assessment of the functional exercise capacity, the 6-minute  
37  
38 130 walk test (6-MWT) was used (19). To evaluate pulmonary function Quark PFT spirometry (Cosmed,  
39  
40 131 Italy) was used (20). Forced expiratory volume in the first second (FEV<sub>1</sub>), forced vital capacity (FVC) and  
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42 132 FEV<sub>1</sub>/FVC ratio were included in the analysis, displayed in percentage of the norm.

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45 133 In addition, self-administered questionnaires were used. Breathlessness was assessed by the MRC  
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47 134 breathlessness scale, which comprises five statements that range from 0 'no trouble with  
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49 135 breathlessness' to 5 'I am too breathless to leave the house' (21). The Numerical Rating Scale (NRS)  
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51 136 was used for assessing pain. Patients were asked to rate their mean and maximum pain intensities in  
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53 137 the last seven days, ranging from 0-10, with 0 indicating 'no pain' and 10 indicating 'the worst  
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55 138 imaginable pain' (22). The multidimensional Fatigue Inventory (MFI) is a 20-item metric for fatigue  
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3 139 severity. It has 5 dimensions: general fatigue, physical fatigue, mental fatigue, reduced motivation and  
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5 140 reduced activity. Each item ranges from 1 'absence of fatigue' to 5 'severe fatigue'. A total fatigue score  
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7 141 is calculated as the sum of the subscale scores (20–100). Higher total scores indicate higher levels of  
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9 142 fatigue (23). The perceived limitations in daily life were assessed using the PROMIS physical function  
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11 143 short form 8b. This survey was created for adults with chronic illnesses and it contains eight questions  
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13 144 ranging from 1 'unable to do' to 5 'without any difficulty' (24). Calculating T-scores, where higher  
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15 145 scores indicate better physical function (25). Anxiety and depression complaints were assessed with  
16  
17 146 the Hospital Anxiety and Depression Scale (HADS). A score  $\geq 8$  on either subscale was considered to be  
18  
19 147 substantial anxiety or depression symptoms (26). Post-traumatic stress complaints were assessed  
20  
21 148 using the Global Psychotrauma Screen – Post Traumatic Stress Disorder (GPS-PTSD-5). The regular GPS  
22  
23 149 consists of 22 items, item 1-5 can be used to generate a GPS-PTDS-5 score (range 0-5), a score  $\geq 3$   
24  
25 150 indicates PTSD (27). Cognitive functioning was assessed using the Checklist for Cognitive consequences  
26  
27 151 after an ICU-admission (CLC-IC). The CLC-IC consists of 10 items; higher scores indicate more cognitive  
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29 152 problems experienced in daily life (range 0-10). The CLC-IC is based on the CLCE-24 (28). Proactive  
30  
31 153 coping skills were assessed at T3 with the Utrecht Proactive Coping Scale (UPCC), which is a 21-item  
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33 154 self-assessment tool scored on a 4-point scale ranging from 'not competent at all' to 'competent'. The  
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35 155 total score was the average for all item scores (range 1–4), where higher scores indicate higher levels  
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37 156 of proactive coping (29). Premorbid social- and work situations were collected at T1.  
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#### 47 Statistical analyses

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50 159 Results are reported as mean and standard deviation (SD) or as median and interquartile range (IQR)  
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52 160 depending on distribution. Recovery of participation levels over time was assessed with a linear mixed-  
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54 161 effects model for repeated measures. Patient characteristics in the domains of body function, activity  
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56 162 limitations, personal and social factors at T0 and 1 month after admission in the rehabilitation centre  
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58 163 (T1) were added to separate models that also included time and the interaction between that covariate  
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3 164 and time. Next, for illustrative purposes only, linear mixed-effects model analyses were stratified  
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5 165 according to patient characteristics that were significantly associated with the course of recovery of  
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7 166 participation levels to visualize different patterns of change over time. A  $p < 0.05$  was considered as  
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10 167 statistically significant. Statistical analyses were performed with IBM SPSS statistics 26.0 (SPSS Inc.  
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12 168 Chicago, IL).

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## 170 **Results**

171 During the first COVID-19 wave between April 2 and June 30, 2020, 103 post-ICU patients were  
172 admitted for inpatient rehabilitation. Of these, twenty-three patients were missed since this study was  
173 part of clinical practice in a very dynamic period (first COVID-19 wave) and 13 patients were excluded  
174 for reasons given in figure 2. The study sample consisted of 67 patients (78% male) with a median age  
175 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  
176 rehabilitation (Table 1). Overall, this shows an improvement in muscle strength and functional exercise  
177 capacity (6MWT), whereas fatigue complaints and perceived limitations in daily life seem to decrease  
178 in the first year after ICU discharge (Table 1).

179 Participation restrictions improved in the first year after ICU discharge due to a COVID-19 infection  
180 (Figure 3). Mean participation levels increased from 62.0 (6.1 95%CI), 76.5 (4.6 95%CI) to 86.1 (5.5  
181 95%CI) at one, three and 12 months respectively. One year after ICU discharge, 50.8% of the patients  
182 still reported restrictions in physical exercise, 45.8% in performing housekeeping and 28.8% in  
183 performing leisure activities. After one year work is not applicable in 42.4% of all patients, which is  
184 comparable to the premorbid work situation, where 58% of all patients were employed. One year after  
185 ICU discharge 28.8% of all patients still reported restrictions in work/education. Taking into account  
186 the patients who were not working pre-illness, means that 50% of the pre-illness working patients had  
187 not fully resumed work after one year (Table 1).

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3 188 Regarding the second aim, in the ICF domain body functions, breathlessness (MRC breathlessness),  
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5 189 regression coefficient: 0.60 (95%CI 0.23-0.97; p-value <0.01) and fatigue (MFI), regression coefficient:  
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7 190 0.07 (95%CI 0.03-0.09; p-value <0.01) were the only physical variables that influenced participation  
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10 191 recovery over time. For the ICF domain activities, the perceived limitations in daily life (PROMIS 8b)  
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12 192 showed a different pattern in the recovery of participation restriction level, regression coefficient: -  
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14 193 0.11 (95%CI -0.12 to -0.05; p-value <0.01). In addition, personal factors like coping style (UPCC)  
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16 194 regression coefficient: -2.39 (95%CI -4.20 to -0.06; p-value 0.01), anxiety (HADS anxiety) regression  
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18 195 coefficient: 0.17 (95%CI 0.02-0.31; p-value 0.03) and depression (HADS depression) regression  
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20 196 coefficient: 0.19 (95%CI 0.07-0.31; p-value <0.01) showed different paths in resuming the level of  
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22 197 participation over time. Other early determinants show no significant difference in the recovery of  
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24 198 participation (Table 2).

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28 199 Participation levels increased significantly between 1 and 3 months and between 3 and 12 months in  
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30 200 patients who reported more breathlessness, more fatigue or more limitations in daily life and those  
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32 201 with a less pro-active coping style. In contrast, patients with less breathlessness, fewer fatigue  
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34 202 complaints, fewer restrictions in daily life and a more pro-active coping style showed no significant  
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36 203 increase between 3 and 12 months (Figure 4). In patients with a HADS anxiety score  $\geq 8$ , no differences  
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38 204 were found in participation levels in the first 3 months, while there was a significant difference in  
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40 205 recovery of participation levels between 3 and 12 months. While participation levels significantly  
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42 206 improved between 1 and 3 months and between 3 and 12 months for those experiencing fewer anxiety  
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44 207 complaints. For depressive symptoms, both groups improved significantly in participation levels  
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46 208 between 1 to 3 months and between 3 to 12 months, although a steeper curve is seen in the recovery  
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48 209 of participation levels at 3 to 12 months in patients with more depressive symptoms.

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Table 1	T0	One month (T1)	Three months (T2)	Twelve months (T3)
<b>Baseline characteristics</b>				
Age, years; n=67; median (IQR)	62 (57 – 68)	-		
Sex; n=67; No (%)				
- Men	52 (77.6%)	-		
- Women	15 (22.5%)	-		
<b>Highest level of education; n=62; No (%)</b>				
- Lower education	42 (67.7%)	-		
- Middle education	16 (25.8%)	-		
- Higher education	4 (6.5%)	-		
<b>Work situation; n=62; No (%)</b>				
- Full-time job	26 (41.9%)	-		
- Parttime job	10 (16.1%)	-		
- Retired	18 (29.0%)	-		
- Not working otherwise	8 (12.9%)	-		
<b>Comorbidities; n=67; no (%)</b>				
- 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%)	-		
<b>Parameters related to severity critical illness</b>				
- 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)	-		
<b>Duration inpatient rehabilitation, days; n=67; median (IQR)</b>				19 (11 – 31)
<b>Coping style (UPCC); n=58; mean (SD)</b>				3.0 (0.2)
<b>USER-P restriction subscale <sup>a</sup></b>				
- 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%
<b>Physical examination:</b>				
- 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)
<b>Self-administered questionnaires:</b>				
- 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. <sup>a</sup> Restriction items values are percentages of patients who are restricted or dissatisfied.

Table 2	Estimate (95% CI)	p-value
<b>Baseline characteristics</b>		
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*
<b>ICU-stay specific parameters</b>		
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
<b>Physical examination</b>		
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
<b>Self-administered questionnaires</b>		
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

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3 233 complaints, more perceived limitations in daily life as well as personal factors (having a less pro-active  
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5 234 coping style, anxiety complaints or depression complaints) were found.  
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7 235 Heesakker et al. reported that in patients who survived one year following ICU treatment for COVID-  
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9 236 19, physical, mental, or cognitive symptoms were often reported (30). This corresponds with the  
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11 237 findings of the current study, whereas various physical, mental and cognitive impairments were seen  
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13 238 one year after ICU admission. However, to our knowledge, this is the first study to report differences  
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15 239 in the resumption of participation levels in post-ICU COVID-19 patients. Findings on current  
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17 240 participation restriction levels one year after ICU discharge are in line with previous studies that  
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19 241 assessed changes in recovery after a stroke or other diagnoses groups (31–33).  
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23 242 Moreover, these results showed that higher scores of self-experienced breathlessness, fatigue and  
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25 243 more perceived limitations in daily life in the early phase of rehabilitation were associated with a  
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27 244 delayed recovery of participation levels over the first year. Furthermore, patients with a less active  
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29 245 coping style, those that were more anxious or reported to perceive more depressive complaints had a  
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31 246 delayed recovery of their level of participation over the first year. For all these determinants,  
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33 247 participation levels also appeared to be lower in the early phase of rehabilitation. These findings  
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35 248 indicate that patients with a higher level of anxiety and those with a higher level of depression had a  
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37 249 significantly slower improvement in participation levels during the first months, followed by a more  
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39 250 progressive recovery, especially in the last months. In addition, patients with more breathlessness  
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41 251 complaints or more fatigue complaints or more perceived limitations in daily life in the early phase of  
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43 252 rehabilitation and patients with a less pro-active coping style showed a more progressive recovery of  
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45 253 participation levels especially in the last months.  
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49 254 Complaints of fatigue or breathlessness may be due to underlying medical problems or to the  
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51 255 contribution of personal factors. A previous study showed significant recovery of respiratory function  
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53 256 and physical performance in the first year after ICU discharge due to COVID-19. Nevertheless, patients  
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55 257 still experience breathlessness and fatigue complaints after one year (34). Another remarkable finding  
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57 258 in current study was that early determinants related to the severity of the COVID-19 infection period  
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3 259 itself (such as ICU stay-specific parameters and physical parameters as age, sex, muscle strength,  
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5 260 functional exercise capacity and pulmonary function) did not individually explain progress in recovery  
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7 261 of participation over time. Contrary to expectations, this may indicate that non-physical factors such  
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9 262 as coping style, subjectively experienced physical impairments (including fatigue and breathlessness)  
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11 263 and mental impairments (such as anxiety and depressive symptoms) seem more important to  
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13 264 determine progress in recovering the level of participation. Previous literature on post-ICU patients  
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15 265 also indicated that critical care recovery has largely focused on post-ICU impairments experienced by  
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17 266 patients. Whereas the positive aspects of recovery within the rehabilitation phase, including coping  
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19 267 style and resilience seems to be ignored, while these factors are important for optimal recovery  
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21 268 (35,36).  
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#### 28 270 Implications for clinical practice and further research

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30 271 This study underlines the importance of looking at the long-term consequence of (COVID-19) ICU  
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32 272 survivors with an integral vision of health. Early detection of a less proactive coping style or mental  
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34 273 impairments seems important and should therefore be included in screening during early  
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36 274 multidisciplinary rehabilitation. Further research is needed to examine the appropriate (early)  
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38 275 treatment to target changes in coping style or improve resilience. In addition, it can be speculated that  
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40 276 our findings in ICU survivors can be also extrapolated to other ICU survivors or patients with post-  
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42 277 COVID-19 syndrome, that had an initial mild infection Moreover, further research may focus on coping  
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44 278 style and mental impairments on the recovery of participation restrictions over time in these patients.  
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#### 50 280 Strengths and limitations

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52 281 A strength of the present study is that it only included the most severely affected post-ICU COVID-19  
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54 282 patients referred to inpatient rehabilitation. In addition, this study used physical examination as well  
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56 283 as questionnaires, which means that there was a combination of objective and subjective  
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58 284 measurements. It is notable that even in the most severely affected COVID-19 patients delayed  
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3 285 recovery of participation is associated with self-experienced physical impairments, mental  
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5 286 impairments and coping style.  
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7 287 Nevertheless, some limitations of the current study need to be considered. First, although the sample  
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9 288 size is small, a large number of factors were studied for their effect on the course of participation  
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11 289 recovery. Because this is the first exploratory study on the recovery of participation and its association  
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13 290 with early factors, it was important to look at factors within different domains. Second, due to the high  
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15 291 workload on the ward, 23 patients were not approached in time for consent to participate. In our  
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17 292 opinion, this is unlikely to have led to selection bias, but this cannot be excluded. Finally, the lockdown  
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19 293 and the inability to perform social and outdoor activities may have affected the total USER-P score as  
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21 294 this scale allows the rating of 'not applicable'. Since the study- and lockdown period were similar for  
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23 295 all patients, we expect no difference in the study patients. Although it may have affected the recovery  
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25 296 course of participation recovery for the entire patient group, it is not expected to have affected the  
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27 297 predictors.  
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### 34 299 Conclusion

36 300 For patients admitted to an ICU for COVID19, the level of participation improves in the first year after  
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38 301 ICU discharge. However, at one year after discharge, many patients still experience limitations  
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40 302 regarding participation in daily life, mainly in resuming work, physical exercise, housekeeping and  
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42 303 leisure activities. Progress of recovery in participation in the first year after discharge was associated  
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44 304 with early determinants in coping style, subjectively experienced physical impairments (breathlessness  
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46 305 and fatigue) and mental impairments (anxiety and depression), but not with medical variables. This  
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48 306 study supports the need for an integral perspective on health to facilitate the identification of factors  
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50 307 that delay the recovery trajectory for participation in the first year after ICU discharge. Personal factors  
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52 308 such as a less proactive coping style and more anxiety- or depression complaints seem relevant to this.  
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54 309 Rehabilitation care needs to anticipate on these topics, starting in the early rehabilitation phase of  
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56 310 post-ICU COVID-19 care.  
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4  
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6  
7

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9  
10 314 plan was designed by CW, SJSS and SvK. Statistical analysis was done by CW, with control of SJSS and  
11  
12 315 SvK. Practical implication was done by CW, SvS and YH. The first draft of the paper was written by CW  
13  
14 316 and all co-authors reviewed and approved it for submission. CW and JV are the guarantors. The  
15  
16 317 corresponding author attests that all listed authors meet authorship criteria and that no others  
17  
18 318 meeting the criteria have been omitted.  
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30  
31 323 submitted work; no financial relationships with any organisations that might have an interest in the  
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33 324 submitted work in the past three years; no other relationships or activities that could appear to have  
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35 325 influenced the submitted work  
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39 326 Patient consent for publication: Not required.  
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42 327 Dissemination to participants and related patient and public communities: The study results will be  
43  
44 328 disseminated to the public through our media channels or national and international conferences.  
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47 329 Ethical approval: The local medical ethics committee Zuyderland METC (METCZ20200086) approved  
48  
49 330 the study.  
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52 331 Data availability statement: To guarantee the confidentiality of personal and health information, only  
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54 332 the authors have had access to the data during the study. Data is available (anonymised), but the  
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56 333 corresponding author must be contacted to request these data. Data will be kept for 15 years  
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16 441 **Figure Legend:**

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18 442 - Figure 1: ICF model and measurement instruments used.  
19 443 - Figure 2: Subject recruitment flowchart.  
20 444 - Figure 3: The recovery of participation levels (USER-P restriction subscale) in the first year  
21 445 after ICU discharge in post-COVID-19 patients.  
22 446 - Figure 4: The influence of early levels of body function impairments, activity limitations and  
23 447 personal factors on the recovery of participation levels (USER-P restriction subscale).



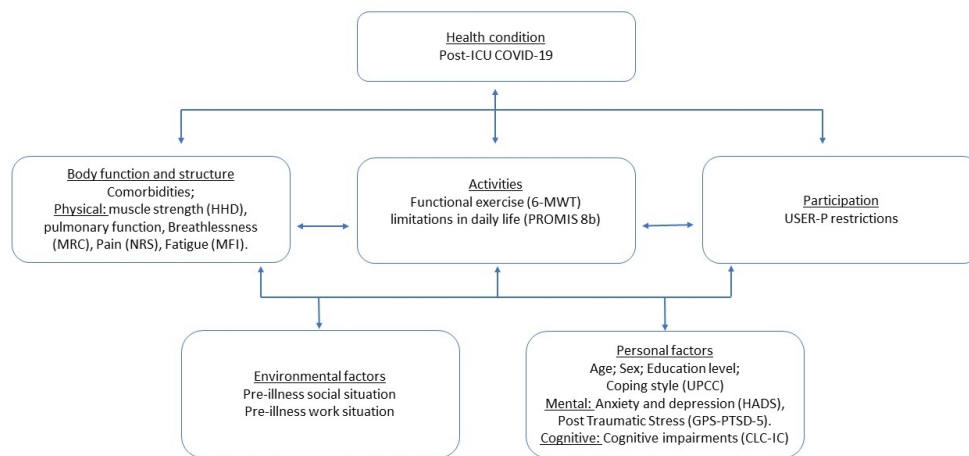


Figure 1. ICF model and measurement instruments used.

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

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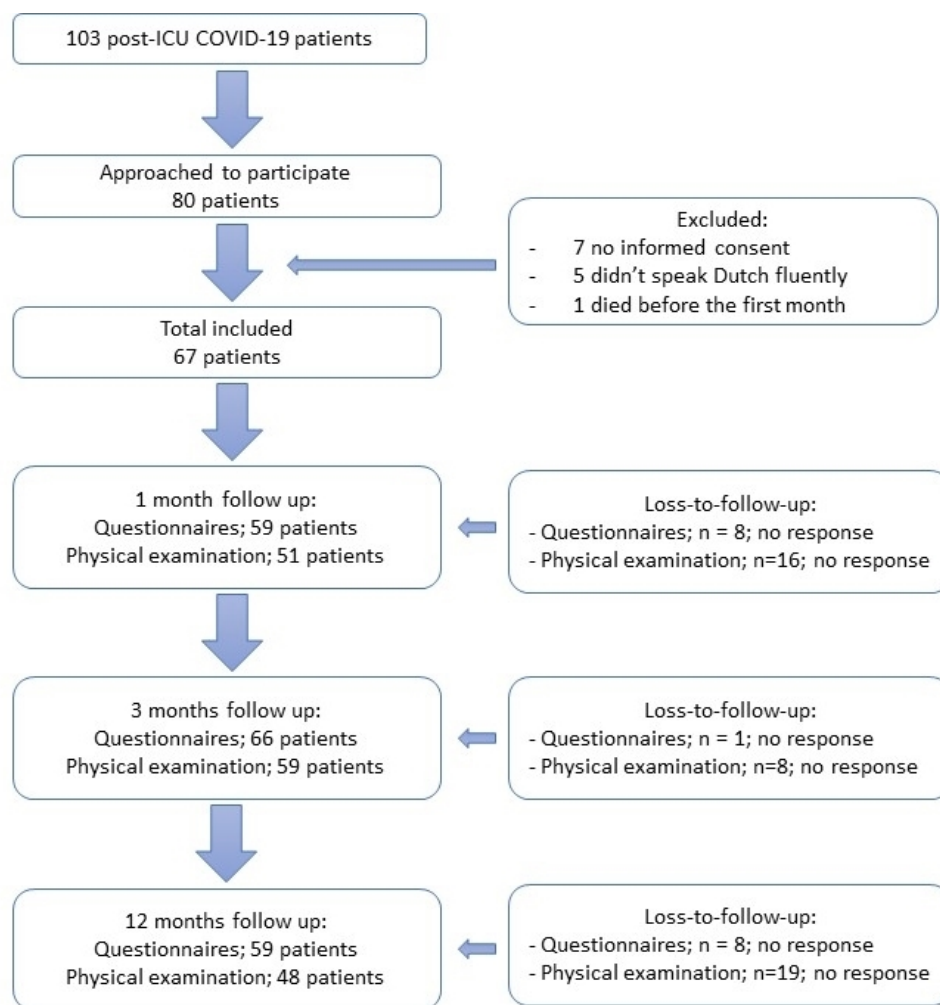


Figure 2; Subject recruitment flowchart.

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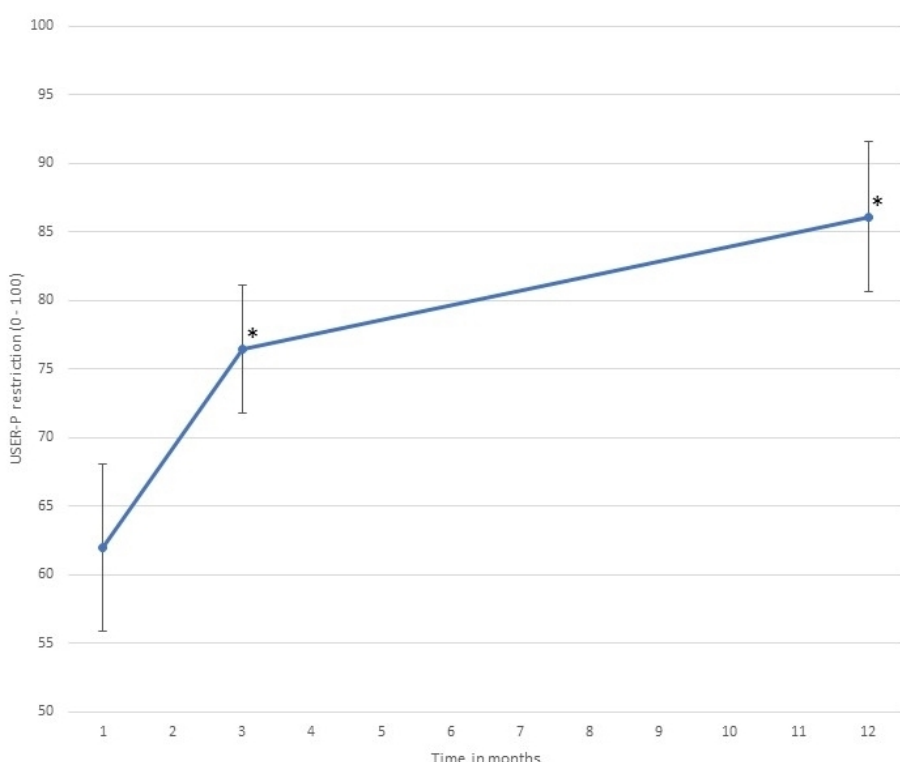


Figure 3; The recovery of participation levels (USER-P restriction subscale) in the first year after ICU discharge in post-COVID-19 patients. Results are expressed as mean with corresponding 95% confidence interval. \* p < 0.01 (compared to previous measurement moment)

202x164mm (96 x 96 DPI)

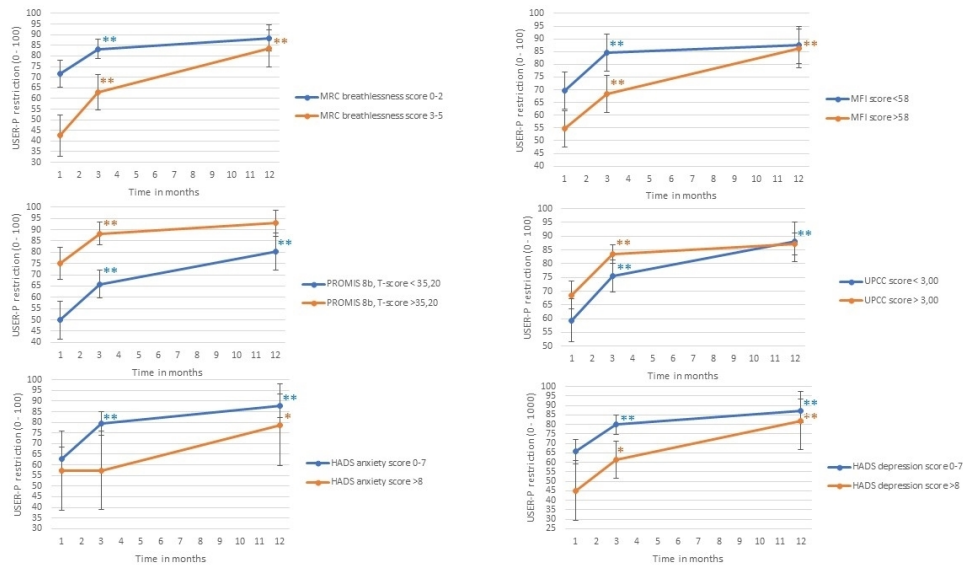


Figure 4; The influence of early levels of body function impairments, activity limitations and personal factors on the recovery of participation levels (USER-P restriction subscale). For illustrative purposes, subgroups have been created based on cut-off value (HADS) or the median if no specific cut-off 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
<b>Title and abstract</b>	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
<b>Introduction</b>			
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
<b>Methods</b>			
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  (b) For matched studies, give matching criteria and number of exposed and unexposed	5
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  (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	7
<b>Results</b>			
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
<b>Discussion</b>			
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
<b>Other information</b>			
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

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3 **Life after COVID-19 the road from intensive care back to living: a prospective cohort study**  
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3 **Life after COVID-19 the road from intensive care back to living: a prospective cohort study**  
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5

6 **Abstract**  
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9 **Objectives:** The aim of the study was to evaluate recovery of participation in post-COVID-19 patients  
10 during the first year after ICU discharge. The secondary aim was to identify the early determinants  
11 associated with recovery of participation.  
12  
13  
14

15  
16 **Design:** Prospective cohort study.  
17  
18

19 **Setting:** COVID-19 post-ICU inpatient rehabilitation in the Netherlands, during the first epidemic wave  
20 between April - July 2020, with one-year follow-up.  
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22  
23

24 **Participants:** COVID-19 ICU survivors  $\geq 18$  years of age needing inpatient rehabilitation.  
25  
26

27 **Main outcome measures:** Participation in society was assessed by the 'Utrecht Scale for Evaluation of  
28 Rehabilitation-Participation (USER-P) restrictions scale'. Secondary measures of body function  
29 impairments (muscle force, pulmonary function, fatigue (MFI), breathlessness (MRC), pain (NRS)),  
30 activity limitations (6MWT, PROMIS 8b), personal factors (coping (UPCC), Anxiety and depression  
31 (HADS), post traumatic stress (GPS-PTSD-5), cognitive functioning (CLC-IC)) and social factors were  
32 used. Statistical analyses: linear mixed-effects model, with recovery of participation levels as  
33 dependent variable. Patient characteristics in domains of body function, activity limitations, personal  
34 and social factors were added as independent variables  
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45 **Results:** This study included 67 COVID-19 ICU survivors (mean age 62y, 78% male). Mean USER-P  
46 restrictions scores increased over time; mean participation levels increasing from 62.0, 76.5 to 86.1 at  
47 one, three and 12 months respectively. After one year, 50% had not fully resumed work and  
48 restrictions were reported in physical exercise (51%), household duties (46%), and leisure activities  
49 (29%). Self-reported complaints of breathlessness and fatigue, more perceived limitations in daily life,  
50 as well as personal factors (less pro-active coping style and anxiety/depression complaints) were  
51 associated with delayed recovery of participation (all p-value < 0.05).  
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3 47 **Conclusions:** This study supports the view that an integral vision of health is important when looking  
4  
5 48 at the long-term consequence of post-IC COVID-19. Personal factors such as having a less proactive  
6  
7 49 coping style or mental impairments early on contribute to delayed recovery.  
8  
9

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11 50

12  
13 51 **Keywords:** COVID-19, Critical care, Rehabilitation medicine  
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17 52

18  
19 53 **Strengths and limitations of this study**

- 20  
21 54 - This study only included the most severely affected post-ICU COVID-19 patients referred to  
22  
23 55 inpatient rehabilitation.  
24  
25  
26 56 - This study used physical examination as well as questionnaires, which means that there was a  
27  
28 57 combination of objective and subjective measurements.  
29  
30 58 - Although the sample size is small, a large number of factors were studied for their effect on  
31  
32 59 the course of participation recovery.  
33  
34  
35 60 - Twenty-three patients were not approached in time for consent to participate.  
36  
37 61 - The lockdown and the inability to perform social and outdoor activities may have affected the  
38  
39 62 total USER-P score.  
40

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44 64 Word count abstract: 300  
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47 65 Word count main text: 3370  
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50 66 Number of figures and tables: 6  
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## 68 Introduction

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

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

90

91

## 92 **Methods**

### 93 Study design and participants

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

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

109

### 110 Data collection

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

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2  
3 117 and Health (ICF) that supports the classification of health and health-related conditions and their effect  
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5 118 on social participation (Figure 1) (14).

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7  
8 119 Primary outcome variable: Participation in society was assessed by the 'Utrecht Scale for Evaluation of  
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10 120 Rehabilitation-Participation (USER-P) restriction subscale'. This subscale consists of 11 items on  
11  
12 121 restrictions in vocational, leisure and social activities. Items are rated from 0 'not possible' to 3 'without  
13  
14 122 difficulty' and a 'not applicable' option. The total score ranges from 0 to 100, higher scores indicating  
15  
16 123 fewer restrictions in participation (16,17).

17  
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19  
20 124 Data on age, sex, comorbidities and parameters related to critical illness were collected from the  
21  
22 125 medical transfer letters (T0). Comorbidities were classed into diabetes mellitus, hypertension,  
23  
24 126 cardiovascular disease, lung disease and psychiatric disorders. Parameters related to severity of the  
25  
26 127 critical illness were length of ICU stay, invasive mechanical ventilation (IMV) (yes/no) and duration of  
27  
28 128 invasive IMV. The duration of the inpatient rehabilitation was recorded.

29  
30  
31  
32 129 Physical examination: Assessment of muscle strength, functional exercise capacity and pulmonary  
33  
34 130 function were part of physical examination. To measure muscle strength, a handheld dynamometer  
35  
36 131 (HHD) was used (18) to assess the following muscle groups: shoulder abduction, elbow flexion, wrist  
37  
38 132 extension, hip flexion and knee extension, all on patient's dominant side. HHD values were measured  
39  
40 133 in Newtons and percentages of the norm compared with healthy persons of the same sex, age, and  
41  
42 134 weight (19,20). Severe muscle weakness was defined as <80% of the norm score. For the clinical  
43  
44 135 assessment of the functional exercise capacity, the 6-minute walk test (6-MWT) was used, displayed  
45  
46 136 in meters and percentage of the norm (21,22). To evaluate pulmonary function Quark PFT spirometry  
47  
48 137 (Cosmed, Italy) was used (23). Forced expiratory volume in the first second ( $FEV_1$ ), forced vital capacity  
49  
50 138 (FVC) and  $FEV_1/FVC$  ratio were included in the analysis, displayed in percentage of the norm.

51  
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54  
55 139 In addition, self-administered questionnaires were used. Breathlessness was assessed by the MRC  
56  
57 140 breathlessness scale, which comprises five statements that range from 0 'no trouble with  
58  
59 141 breathlessness' to 5 'I am too breathless to leave the house' (24). The Numerical Rating Scale (NRS)

1  
2  
3 142 was used for assessing pain. Patients were asked to rate their mean pain intensities in the last seven  
4  
5 143 days, ranging from 0-10, with 0 indicating 'no pain' and 10 indicating 'the worst imaginable pain' (25).  
6  
7 144 The multidimensional Fatigue Inventory (MFI) is a 20-item metric for fatigue severity. It has 5  
8  
9 145 dimensions: general fatigue, physical fatigue, mental fatigue, reduced motivation and reduced activity.  
10  
11 146 Each item ranges from 1 'absence of fatigue' to 5 'severe fatigue'. A total score is calculated as the sum  
12  
13 147 of the subscale scores (20–100). Higher scores indicate higher levels of fatigue (26). The perceived  
14  
15 148 limitations in daily life were assessed using the PROMIS physical function shortform 8b. This survey  
16  
17 149 contains eight questions ranging from 1 'unable to do' to 5 'without any difficulty' (27). A web-based  
18  
19 150 scoring service was used to calculate T-scores (maximum score 60.1 and mean 50.0, corresponding to  
20  
21 151 the mean in the general population of the USA), whereas a higher scores indicates better physical  
22  
23 152 function (28). Anxiety and depression complaints were assessed with the Hospital Anxiety and  
24  
25 153 Depression Scale (HADS). A score  $\geq 8$  on either subscale was considered to be substantial anxiety or  
26  
27 154 depression symptoms (29). Post-traumatic stress was assessed using the Global Psychotrauma Screen  
28  
29 155 – Post Traumatic Stress Disorder (GPS-PTSD-5). The regular GPS consists of 22 items, item 1-5 can be  
30  
31 156 used to generate a GPS-PTSD-5 score (range 0-5), score  $\geq 3$  indicates PTSD (30). Cognitive functioning  
32  
33 157 was assessed using the Checklist for Cognitive consequences after ICU-admission (CLC-IC). The CLC-IC  
34  
35 158 consists of 10 items; higher scores indicate more cognitive problems experienced in daily life (range 0-  
36  
37 159 10). The CLC-IC is based on the CLCE-24 (31). Proactive coping skills were assessed at T3 with the  
38  
39 160 Utrecht Proactive Coping Scale (UPCC), which is a 21-item questionnaire scored on a 4-point scale  
40  
41 161 ranging from 'not competent at all' to 'competent'. The total score was the average for all item scores  
42  
43 162 (range 1–4), where higher scores indicate higher levels of proactive coping (32). Premorbid social- and  
44  
45 163 work situations were collected at T1.

#### 164 Statistical analyses

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

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3 167 effects model for repeated measures. Patient characteristics in the domains body function, activity  
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5 168 limitations, personal and social factors at T0 and and 1 month after admission in the rehabilitation  
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7 169 centre (T1) were added to separate models that also included time and the interaction between that  
8  
9  
10 170 covariate and time. Next, for illustrative purposes only, linear mixed-effects model analyses were  
11  
12 171 stratified according to patient characteristics that were significantly associated with the course of  
13  
14 172 recovery of participation levels to visualize different patterns of change over time. A  $p < 0.05$  was  
15  
16 173 considered as statistically significant. Statistical analyses were performed with IBM SPSS statistics 26.0  
17  
18 174 (SPSS Inc. Chicago, IL).

175

## 176 **Results**

177 During the first COVID-19 wave between April 2 and June 30, 2020, 103 post-ICU patients were  
178 admitted for inpatient rehabilitation. Of these, twenty-three patients were missed since this study was  
179 part of clinical practice in a very dynamic period and 13 patients were excluded excluded for reasons  
180 given in figure 2. The study sample consisted of 67 patients (78% male) with a median age of 62 (IQR  
181 57-68) and a median length of stay of 20 (12-33) days in the ICU and 19 (11-31) days inpatient  
182 rehabilitation (Table 1). Overall, an improvement in muscle strength and functional exercise capacity  
183 (6MWT) was found, whereas fatigue complaints and perceived limitations in daily life seem to decrease  
184 in the first year after ICU discharge (Table 1).

185 Participation restrictions improved in the first year after ICU discharge due to a COVID-19 infection  
186 (Figure 3). Mean participation levels increased from 62.0 (95%CI 55.9-68.1), 76.5 (95%CI 71.9-81.1) to  
187 86.1 (95%CI 80.6-91.6) at one, three and 12 months respectively. One year after ICU discharge, 50.8%  
188 of the patients still reported restrictions in physical exercise, 45.8% in performing housekeeping and  
189 28.8% in performing leisure activities. After one year work is not applicable in 42.4% of all patients,  
190 which is comparable to the premorbid work situation, where 58% of all patients were employed. One  
191 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)
<b>Baseline characteristics</b>				
Age, years; n=67; median (IQR)	62 (57 – 68)	-		
<b>Sex; n=67; No (%)</b>				
- Men	52 (77.6%)	-		
- Women	15 (22.5%)	-		
<b>Highest level of education; n=62; No (%)</b>				
- Lower education	42 (67.7%)	-		
- Higher education	20 (32.3%)	-		
<b>Work situation; n=62; No (%)</b>				
- Full-time job	26 (41.9%)	-		
- Parttime job	10 (16.1%)	-		
- Retired	18 (29.0%)	-		
- Not working otherwise	8 (12.9%)	-		
<b>Comorbidities; n=67; no (%)</b>				
- 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%)	-		
<b>Parameters related to severity critical illness</b>				
- 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%)	-		
<b>Duration inpatient rehabilitation, days; n=67; median (IQR)</b>	19 (11 – 31)			
<b>Coping style (UPCC); n=58; mean (SD)</b>	3.0 (0.2)			
<b>USER-P restriction subscale <sup>a</sup></b>				
- 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%
<b>Physical examination:</b>				
- 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)
<b>Self-administered questionnaires:</b>				
- 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)

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3 194 Table 1, overview of the baseline characteristics (T0) and the physical examination and self-administered questionnaires at T1, T2 and T3. Low educational level  
4 195 was determined as 'primary and secondary education and post-secondary school'. High educational level was determined as 'bachelor's degree, master's degree  
5 196 or doctorate or equivalent'. Abbreviations: IMV, Invasive mechanical ventilation; UPCC, Utrecht Proactive Coping Scale; USER-P, Utrecht Scale for Evaluation of  
6 197 Rehabilitation-Participation; HHD, handheld dynamometer; 6MWT, 6 minute walking test; FEV1, Forced expiratory volume in the first second; FVC, Forced vital  
7 198 capacity; n.a., not applicable; MFI, multidimensional Fatigue Inventory; HADS, Hospital Anxiety and Depression Scale; GPS, The Global Psychotrauma Screen; CLC-  
8 199 IC, Checklist for Cognitive consequences after an ICU-admission. \* Restriction items values are percentages of patients who are restricted or dissatisfied.

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10 201 Regarding the second aim, in the ICF domain body functions, breathlessness (MRC breathlessness),  
11 202 regression coefficient: 0.60 (95%CI 0.23-0.97; p-value <0.01) and fatigue (MFI), regression coefficient:  
12 203 0.07 (95%CI 0.03-0.09; p-value <0.01) were the only physical variables that influenced participation  
13 204 recovery over time. For the ICF domain activities, perceived limitations in daily life (PROMIS 8b)  
14 205 showed a different pattern in the recovery of participation restriction levels, regression coefficient: -  
15 206 0.11 (95%CI -0.12 to -0.05; p-value <0.01). In addition, personal factors like coping style (UPCC)  
16 207 regression coefficient: -2.39 (95%CI -4.20 to -0.06; p-value 0.01), anxiety (HADS anxiety) regression  
17 208 coefficient: 0.17 (95%CI 0.02-0.31; p-value 0.03) and depression (HADS depression) regression  
18 209 coefficient: 0.19 (95%CI 0.07-0.31; p-value <0.01) showed different paths in resuming the level of  
19 210 participation over time. Other early determinants show no significant difference in the recovery of  
20 211 participation (Table 2).

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Table 2	Estimate (95% CI)	p-value
<b>Baseline characteristics</b>		
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*
<b>ICU-stay specific parameters</b>		
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
<b>Physical examination</b>		
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
<b>Self-administered questionnaires</b>		
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.

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

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3 229 between 3 and 12 months. For depressive symptoms, both groups improved significantly in  
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5 230 participation levels between 1 to 3 months and between 3 to 12 months, although a steeper curve is  
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7 231 seen in recovery of participation levels at 3 to 12 months in patients with more depressive symptoms.  
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12 234 **Discussion**

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15 235 In this prospective cohort study, recovery of participation during the first year after ICU discharge in  
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17 236 COVID-19 ICU survivors who needed inpatient rehabilitation was evaluated and the association  
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19 237 between early levels of body function impairments, activity limitations and personal and social factors  
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21 238 on recovery were estimated. It is seen that in the first year after ICU discharge patients were able to  
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23 239 improve their participation levels. Nevertheless, after one year, there are still important limitations in  
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25 240 daily life, mainly in resuming work, physical exercise, housekeeping and leisure activities. As early  
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27 241 determinants for a delay in the resumption of patient's habitual level of participation levels over the  
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29 242 first year, higher levels of self-experienced breathlessness and fatigue complaints, more perceived  
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31 243 limitations in daily life as well as personal factors (having a passive coping style, anxiety complaints or  
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33 244 depression complaints) were found.  
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38 245 In previous Dutch studies focusing on overall post-ICU COVID-19 survivors, an average age of 61-63  
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40 246 was found, 69-72% men, with a median length of stay of 18-20 days in the ICU (33,34). These  
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42 247 demographic data seem to correspond with findings of current study, taking into account that in the  
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44 248 first COVID-19 wave, 83% of all post-ICU COVID-19 patients were transferred to a rehabilitation centre  
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46 249 (34). Heesakker et al. reported that in patients who survived one year following ICU treatment for  
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48 250 COVID-19, physical, mental, or cognitive symptoms were often reported (33). This corresponds with  
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50 251 the findings of the current study, whereas various physical, mental and cognitive impairments were  
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52 252 seen one year after ICU admission. However, to our knowledge, this is the first study to report  
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54 253 differences in the resumption of participation levels in post-ICU COVID-19 patients. Mean participation  
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56 254 levels increased to 86.1 one year after ICU discharge. As a reference, in other non-COVID patients (i.e.  
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3 255 stroke, acquired brain injury, progressive neurologic diseases, spinal cord injury and acute coronary  
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5 256 syndrome), participation levels between 70.6-83.5 have been observed (35–37). In all non-COVID  
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7 257 patient groups, patients mainly reported restrictions in work/education, housekeeping, physical  
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10 258 exercise and performing leisure activities, which is in accordance with restrictions in participation  
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12 259 reported in current study (36,37).

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14 260 Moreover, these results showed that higher scores of self-experienced breathlessness or fatigue and  
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16 261 more perceived limitations in daily life in the early phase of rehabilitation were associated with a  
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18 262 delayed recovery of participation levels over the first year. Furthermore, patients with a less active  
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20 263 coping style, those that were more anxious or reported to perceive more depressive complaints had a  
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22 264 delayed recovery of their level of participation over the first year. For all these determinants,  
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24 265 participation levels also appeared to be lower in the early phase of rehabilitation. These findings  
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26 266 indicate that patients with a higher level of anxiety and those with a higher level of depression had a  
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28 267 significantly slower improvement in participation levels during the first months, followed by a more  
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30 268 progressive recovery, especially in the last months. In addition, patients with more breathlessness  
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32 269 complaints, more fatigue complaints or more perceived limitations in daily life in the early phase of  
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34 270 rehabilitation and patients with a passive coping style showed a more progressive recovery of  
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36 271 participation levels especially in the last months.

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39 272 Complaints of fatigue or breathlessness may be due to underlying medical problems or to the  
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41 273 contribution of personal factors. Previous study's showed significant recovery of respiratory function  
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43 274 and physical performance in the first year after ICU discharge due to COVID-19. Nevertheless, patients  
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45 275 still experience breathlessness and fatigue complaints after one year (38,39). Another finding in  
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47 276 current study was that early determinants related to the severity of the COVID-19 infection period  
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49 277 itself (such as ICU stay-specific parameters and physical parameters as age, sex, muscle strength,  
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51 278 functional exercise capacity and pulmonary function) did not individually explain progress in recovery  
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53 279 of participation over time. Contrary to expectations, this may indicate that non-physical factors such  
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55 280 as coping style, subjectively experienced physical impairments (including fatigue and breathlessness)  
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3 281 and mental health issues (such as anxiety and depressive symptoms) seem more important to  
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5 282 determine progress in recovering the level of participation. Previous literature on post-ICU patients  
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7 283 indicated that critical care recovery has focused on post-ICU impairments experienced by patients.  
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10 284 Whereas the positive aspects of recovery within the rehabilitation phase, including coping style and  
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12 285 resilience seems to be ignored (40,41). Resilience refers to the ability to face the challenges and  
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14 286 difficulties of life in a positive and adaptive manner, as well as the capacity to recover from an adverse  
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16 287 event (42). Higher levels of resilience have been linked to improved mental and physical health (43). It  
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18 288 is possible to improve the level of resilience. Which implies that resilience can be used to improve  
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21 289 (emotional) well-being, with the possible consequence of improving participation levels.  
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#### 25 291 Implications for clinical practice and further research

27 292 This study underlines the importance of looking at long-term consequence of COVID-19 ICU survivors  
28  
29 293 with an integral vision of health. Whether identical variables can be used to identify a delay in recovery  
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31 294 in patients who had a milder infection is currently still unclear. In this study, conclusions can be made  
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33 295 for a selected group (with ICU admission) of patients. Extrapolation to other populations needs to be  
34  
35 296 done with caution. Early detection of a passive coping style or mental impairments seems important  
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37 297 and should therefore be included in screening during early multidisciplinary rehabilitation. Further  
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39 298 research is needed to study the effect of early screening of a patients' level of coping/ resilience during  
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41 299 the first months after ICU discharge. As a consequence, an early intervention to increase  
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43 300 resilience/strengthen coping on indication could be promising to further strengthen social  
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45 301 participation, but needs to be further studied.  
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#### 52 303 Strengths and limitations

54 304 A strength of the study is that it only included the most severely affected post-ICU COVID-19 patients  
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56 305 referred to inpatient rehabilitation. In addition, this study used physical examination as well as  
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58 306 questionnaires, which means there was a combination of objective and subjective measurements. It is  
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3 307 notable that even in the most severely affected COVID-19 patients delayed recovery of participation is  
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5 308 associated with self-experienced physical impairments, mental impairments and coping style.  
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7 309 Nevertheless, some limitations of the current study need to be considered. First, sample size is limited  
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9 310 and a number of factors were studied for their effect on the course of participation recovery. The  
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11 311 limited sample size contributed to relatively wide confidence intervals. The risk of type II error should  
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13 312 therefore be considered while interpreting the data. A post-hoc power calculation revealed however  
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15 313 that the study had 90% power to detect an effect size of 0.2 for changes in participation levels over  
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17 314 time ( $\alpha = 0.05$ , mean correlation between repeated measures = 0.53). Still, p-values of the multiple  
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19 315 tests of association should be interpreted cautiously, because we cannot exclude erroneous  
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21 316 interpretations of statistical significant findings (i.e. type I error). However, since our results support a  
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23 317 certain pattern, we believe that the main conclusions of this study are solid. Second, number of  
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25 318 variables available to describe the acute illness severity were limited. Further research is needed to  
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27 319 investigate this in a larger cohort (all ICU patients, not just rehabilitation patients) to confirm this  
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29 320 finding. Third, due to high workload on the ward, 23 patients were not approached in time for consent  
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31 321 to participate. In our opinion, this is unlikely to have led to selection bias, but this cannot be excluded.  
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33 322 Finally, the lockdown and the inability to perform social and outdoor activities may have affected the  
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35 323 total USER-P score as this scale allows the rating of 'not applicable'. Since the study- and lockdown  
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37 324 period were similar for all patients, we expect no difference in the study patients. Although it may have  
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39 325 affected the recovery course of participation recovery for the entire patient group, it is not expected  
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41 326 to have affected the predictors.  
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## 50 328 Conclusion

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52 329 For patients admitted to an ICU for COVID-19, participation levels improves in the first year after ICU  
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54 330 discharge. However, at one year after discharge, many patients still experience limitations in daily life,  
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56 331 mainly in resuming work, physical exercise, housekeeping and leisure activities. Our results indicate  
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58 332 that progress of recovery in participation in the first year after discharge is associated with early  
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3 333 determinants in coping style, subjectively experienced physical impairments (breathlessness and  
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5 334 fatigue) and mental impairments (anxiety and depression) rather than medical variables. This study  
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7 335 supports the need for an integral perspective on health to facilitate the identification of factors that  
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9 336 delay the recovery trajectory for participation in the first year after ICU discharge. Personal factors  
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11 337 such as a passive coping style and more anxiety- or depression complaints seem relevant to this.  
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13 338 Rehabilitation care needs to anticipate on these topics, starting in the early rehabilitation phase of  
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15 339 post-ICU COVID-19 care.  
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22  
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29  
30 345 plan was designed by CW, SJSS and SvK. Statistical analysis was done by CW, with control of SJSS and  
31  
32 346 SvK. Practical implication was done by CW, SvS and YH. The first draft of the paper was written by CW  
33  
34 347 and all co-authors reviewed and approved it for submission. CW and JV are the guarantors. The  
35  
36 348 corresponding author attests that all listed authors meet authorship criteria and that no others  
37  
38 349 meeting the criteria have been omitted.  
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53 355 submitted work in the past three years; no other relationships or activities that could appear to have  
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55 356 influenced the submitted work  
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59 357 Patient consent for publication: Not required.  
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3 358 Dissemination to participants and related patient and public communities: The study results will be  
4  
5 359 disseminated to the public through our media channels or national and international conferences.  
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8 360 Ethical approval: The local medical ethics committee Zuyderland METC (METCZ20200086) approved  
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10 361 the study.  
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13 362 Data availability statement: To guarantee the confidentiality of personal and health information, only  
14  
15 363 the authors have had access to the data during the study. Data is available (anonymised), but the  
16  
17 364 corresponding author must be contacted to request these data. Data will be kept for 15 years  
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3 490 **Figure Legend:**  
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- 5 491 - Figure 1: ICF model and measurement instruments used.  
6 492 - Figure 2: Subject recruitment flowchart.  
7 493 - Figure 3: The recovery of participation levels (USER-P restriction subscale) in the first year  
8 494 after ICU discharge in post-COVID-19 patients.  
9 495 - Figure 4: The influence of early levels of body function impairments, activity limitations and  
10 496 personal factors on the recovery of participation levels (USER-P restriction subscale).  
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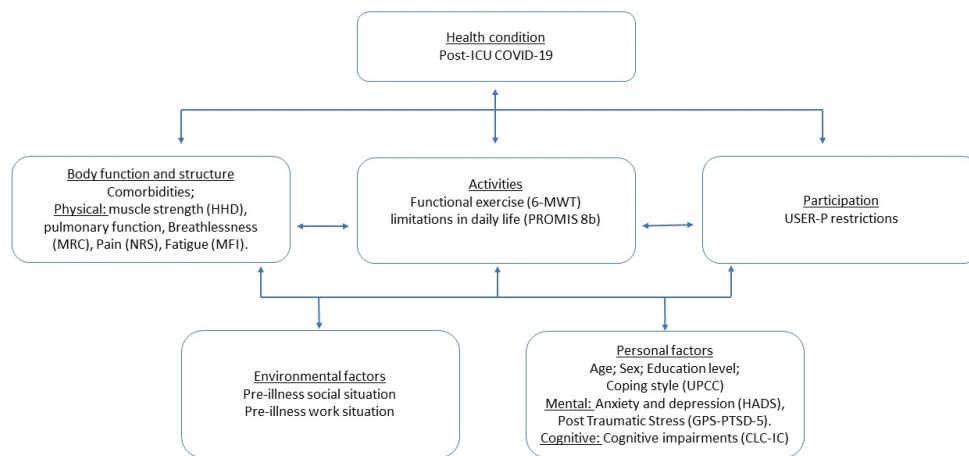


Figure 1. ICF model and measurement instruments used.

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

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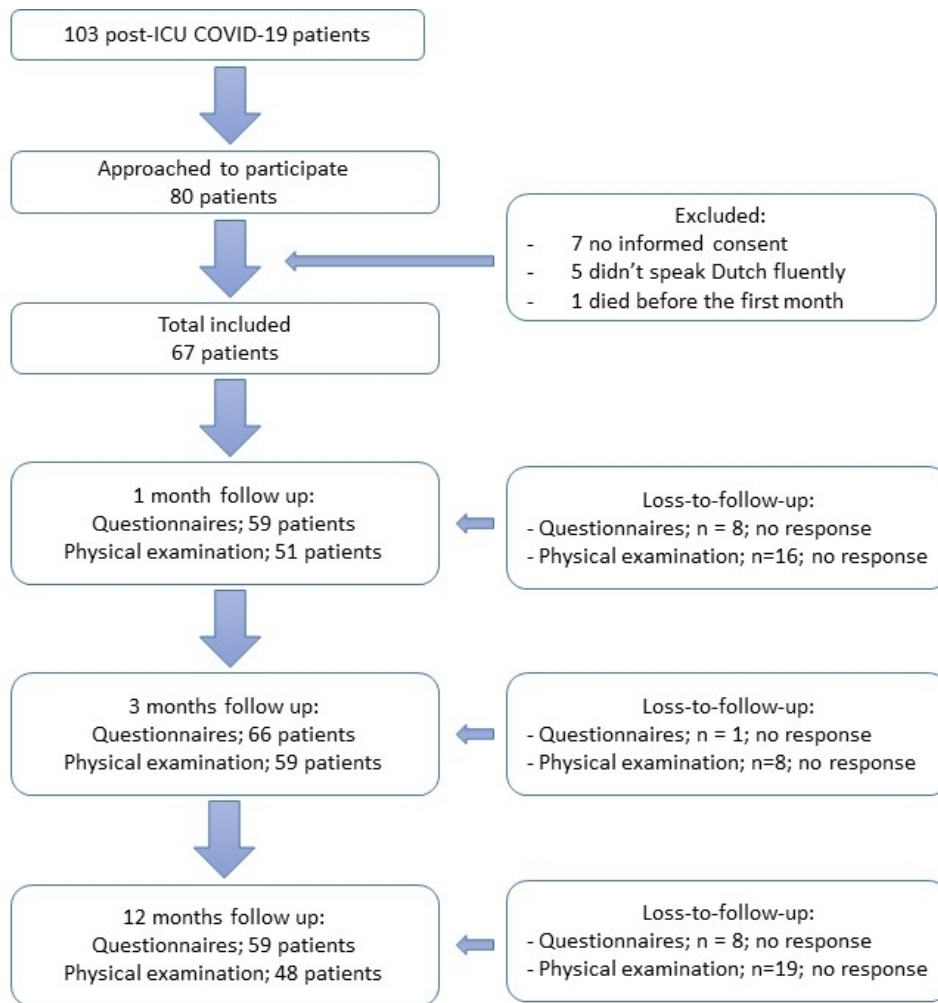


Figure 2; Subject recruitment flowchart.

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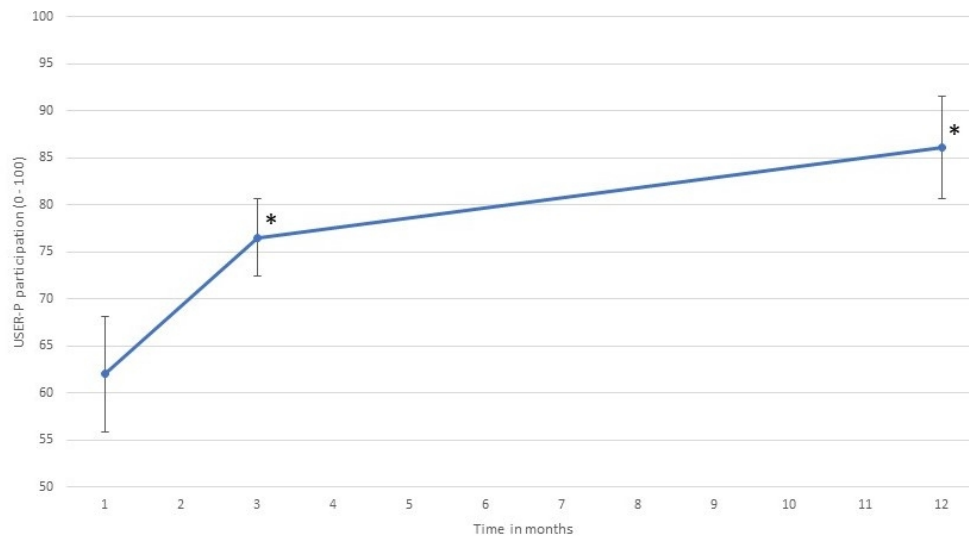


Figure 3; The recovery of participation levels (USER-P restriction subscale) in the first year after ICU discharge in post-COVID-19 patients. Results are expressed as mean with corresponding 95% confidence interval. \*  $p < 0.01$  (compared to previous measurement moment)

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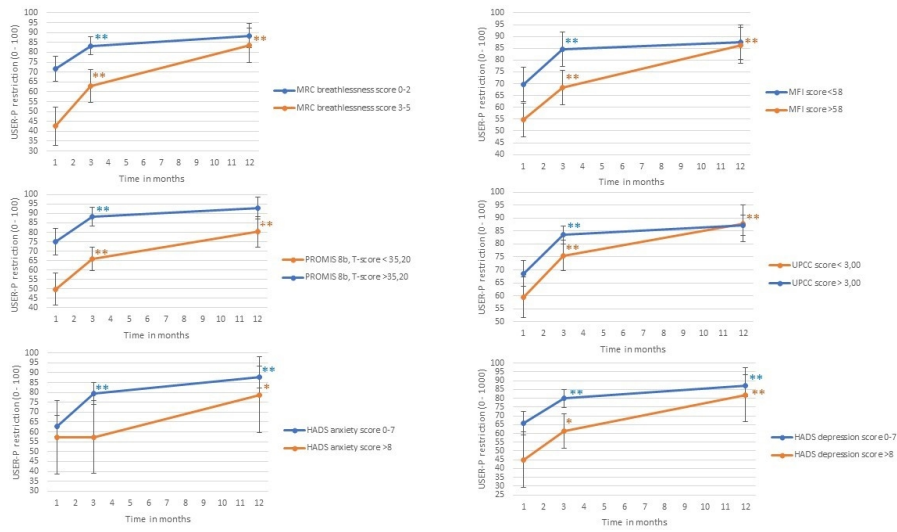


Figure 4; The influence of early levels of body function impairments, activity limitations and personal factors on the recovery of participation levels (USER-P restriction subscale). For illustrative purposes, subgroups have been created based on cut-off value (HADS) or the median if no specific cut-off 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).

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

	Item No	Recommendation	Page No
<b>Title and abstract</b>	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
<b>Introduction</b>			
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
<b>Methods</b>			
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  (b) For matched studies, give matching criteria and number of exposed and unexposed	5
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  (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	7
<b>Results</b>			
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
<b>Discussion</b>			
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
<b>Other information</b>			
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

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3 23 **Life after COVID-19 the road from intensive care back to living: a prospective cohort study**

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6 24 **Abstract**

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9 25 **Objectives:** The aim of the study was to evaluate recovery of participation in post-COVID-19 patients  
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11 26 during the first year after ICU discharge. The secondary aim was to identify the early determinants  
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13 27 associated with recovery of participation.

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16 28 **Design:** Prospective cohort study.

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19 29 **Setting:** COVID-19 post-ICU inpatient rehabilitation in the Netherlands, during the first epidemic wave  
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21 30 between April - July 2020, with one-year follow-up.

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24 31 **Participants:** COVID-19 ICU survivors  $\geq 18$  years of age needing inpatient rehabilitation.

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27 32 **Main outcome measures:** Participation in society was assessed by the 'Utrecht Scale for Evaluation of  
28  
29 33 Rehabilitation-Participation (USER-P) restrictions scale'. Secondary measures of body function  
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31 34 impairments (muscle force, pulmonary function, fatigue (MFI), breathlessness (MRC), pain (NRS)),  
32  
33 35 activity limitations (6MWT, PROMIS 8b), personal factors (coping (UPCC), Anxiety and depression  
34  
35 36 (HADS), post traumatic stress (GPS-PTSD-5), cognitive functioning (CLC-IC)) and social factors were  
36  
37 37 used. Statistical analyses: linear mixed-effects model, with recovery of participation levels as  
38  
39 38 dependent variable. Patient characteristics in domains of body function, activity limitations, personal  
40  
41 39 and social factors were added as independent variables

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44 40 **Results:** This study included 67 COVID-19 ICU survivors (mean age 62y, 78% male). Mean USER-P  
45  
46 41 restrictions scores increased over time; mean participation levels increasing from 62.0, 76.5 to 86.1 at  
47  
48 42 one, three and 12 months respectively. After one year, 50% had not fully resumed work and  
49  
50 43 restrictions were reported in physical exercise (51%), household duties (46%), and leisure activities  
51  
52 44 (29%). Self-reported complaints of breathlessness and fatigue, more perceived limitations in daily life,  
53  
54 45 as well as personal factors (less pro-active coping style and anxiety/depression complaints) were  
55  
56 46 associated with delayed recovery of participation (all p-value < 0.05).

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3 47 **Conclusions:** This study supports the view that an integral vision of health is important when looking  
4  
5 48 at the long-term consequence of post-IC COVID-19. Personal factors such as having a less proactive  
6  
7 49 coping style or mental impairments early on contribute to delayed recovery.  
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13 51 **Keywords:** COVID-19, Critical care, Rehabilitation medicine  
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19 53 **Strengths and limitations of this study**

- 20  
21 54 - This study only included the most severely affected post-ICU COVID-19 patients referred to  
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23 55 inpatient rehabilitation.  
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26 56 - This study used physical examination as well as questionnaires, which means that there was a  
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28 57 combination of objective and subjective measurements.  
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30 58 - Although the sample size is small, a large number of factors were studied for their effect on  
31  
32 59 the course of participation recovery.  
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34  
35 60 - Twenty-three patients were not approached in time for consent to participate.  
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37 61 - The lockdown and the inability to perform social and outdoor activities may have affected the  
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39 62 total USER-P score.  
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## 68 Introduction

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

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

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91

## 92 **Methods**

### 93 Study design and participants

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

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

109

### 110 Data collection

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

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3 117 and Health (ICF) that supports the classification of health and health-related conditions and their effect  
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5 118 on social participation (Figure 1) (14).

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8 119 Primary outcome variable: Participation in society was assessed by the 'Utrecht Scale for Evaluation of  
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10 120 Rehabilitation-Participation (USER-P) restriction subscale'. This subscale consists of 11 items on  
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12 121 restrictions in vocational, leisure and social activities. Items are rated from 0 'not possible' to 3 'without  
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14 122 difficulty' and a 'not applicable' option. The total score ranges from 0 to 100, higher scores indicating  
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16 123 fewer restrictions in participation (16,17).

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20 124 Data on age, sex, comorbidities and parameters related to critical illness were collected from the  
21  
22 125 medical transfer letters (T0). Comorbidities were classed into diabetes mellitus, hypertension,  
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24 126 cardiovascular disease, lung disease and psychiatric disorders. Parameters related to severity of the  
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26 127 critical illness were length of ICU stay, invasive mechanical ventilation (IMV) (yes/no) and duration of  
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28 128 invasive IMV. The duration of the inpatient rehabilitation was recorded.

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32 129 Physical examination: Assessment of muscle strength, functional exercise capacity and pulmonary  
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34 130 function were part of physical examination. To measure muscle strength, a handheld dynamometer  
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36 131 (HHD) was used (18) to assess the following muscle groups: shoulder abduction, elbow flexion, wrist  
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38 132 extension, hip flexion and knee extension, all on patient's dominant side. HHD values were measured  
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40 133 in Newtons and percentages of the norm compared with healthy persons of the same sex, age, and  
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42 134 weight (19,20). Severe muscle weakness was defined as <80% of the norm score. For the clinical  
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44 135 assessment of the functional exercise capacity, the 6-minute walk test (6-MWT) was used, displayed  
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46 136 in meters and percentage of the norm (21,22). To evaluate pulmonary function Quark PFT spirometry  
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48 137 (Cosmed, Italy) was used (23). Forced expiratory volume in the first second ( $FEV_1$ ), forced vital capacity  
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50 138 (FVC) and  $FEV_1/FVC$  ratio were included in the analysis, displayed in percentage of the norm.

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55 139 In addition, self-administered questionnaires were used. Breathlessness was assessed by the MRC  
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57 140 breathlessness scale, which comprises five statements that range from 0 'no trouble with  
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59 141 breathlessness' to 5 'I am too breathless to leave the house' (24). The Numerical Rating Scale (NRS)

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3 142 was used for assessing pain. Patients were asked to rate their mean pain intensities in the last seven  
4  
5 143 days, ranging from 0-10, with 0 indicating 'no pain' and 10 indicating 'the worst imaginable pain' (25).  
6  
7 144 The multidimensional Fatigue Inventory (MFI) is a 20-item metric for fatigue severity. It has 5  
8  
9 145 dimensions: general fatigue, physical fatigue, mental fatigue, reduced motivation and reduced activity.  
10  
11 146 Each item ranges from 1 'absence of fatigue' to 5 'severe fatigue'. A total score is calculated as the sum  
12  
13 147 of the subscale scores (20–100). Higher scores indicate higher levels of fatigue (26). The perceived  
14  
15 148 limitations in daily life were assessed using the PROMIS physical function shortform 8b. This survey  
16  
17 149 contains eight questions ranging from 1 'unable to do' to 5 'without any difficulty' (27). A web-based  
18  
19 150 scoring service was used to calculate T-scores (maximum score 60.1 and mean 50.0, corresponding to  
20  
21 151 the mean in the general population of the USA), whereas a higher scores indicates better physical  
22  
23 152 function (28). Anxiety and depression complaints were assessed with the Hospital Anxiety and  
24  
25 153 Depression Scale (HADS). A score  $\geq 8$  on either subscale was considered to be substantial anxiety or  
26  
27 154 depression symptoms (29). Post-traumatic stress was assessed using the Global Psychotrauma Screen  
28  
29 155 – Post Traumatic Stress Disorder (GPS-PTSD-5). The regular GPS consists of 22 items, item 1-5 can be  
30  
31 156 used to generate a GPS-PTSD-5 score (range 0-5), score  $\geq 3$  indicates PTSD (30). Cognitive functioning  
32  
33 157 was assessed using the Checklist for Cognitive consequences after ICU-admission (CLC-IC). The CLC-IC  
34  
35 158 consists of 10 items; higher scores indicate more cognitive problems experienced in daily life (range 0-  
36  
37 159 10). The CLC-IC is based on the CLCE-24 (31). Proactive coping skills were assessed at T3 with the  
38  
39 160 Utrecht Proactive Coping Scale (UPCC), which is a 21-item questionnaire scored on a 4-point scale  
40  
41 161 ranging from 'not competent at all' to 'competent'. The total score was the average for all item scores  
42  
43 162 (range 1–4), where higher scores indicate higher levels of proactive coping (32). Premorbid social- and  
44  
45 163 work situations were collected at T1.

#### 164 Statistical analyses

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

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3 167 effects model for repeated measures. Patient characteristics in the domains body function, activity  
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5 168 limitations, personal and social factors at T0 and and 1 month after admission in the rehabilitation  
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7 169 centre (T1) were added to separate models that also included time and the interaction between that  
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10 170 covariate and time. Next, for illustrative purposes only, linear mixed-effects model analyses were  
11  
12 171 stratified according to patient characteristics that were significantly associated with the course of  
13  
14 172 recovery of participation levels to visualize different patterns of change over time. A  $p < 0.05$  was  
15  
16 173 considered as statistically significant. Statistical analyses were performed with IBM SPSS statistics 26.0  
17  
18  
19 174 (SPSS Inc. Chicago, IL).

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22 17523  
24  
25 176 **Results**

26  
27 177 During the first COVID-19 wave between April 2 and June 30, 2020, 103 post-ICU patients were  
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29 178 admitted for inpatient rehabilitation. Of these, twenty-three patients were missed since this study was  
30  
31 179 part of clinical practice in a very dynamic period and 13 patients were excluded excluded for reasons  
32  
33 180 given in figure 2. The study sample consisted of 67 patients (78% male) with a median age of 62 (IQR  
34  
35 181 57-68) and a median length of stay of 20 (12-33) days in the ICU and 19 (11-31) days inpatient  
36  
37 182 rehabilitation (Table 1). Overall, an improvement in muscle strength and functional exercise capacity  
38  
39 183 (6MWT) was found, whereas fatigue complaints and perceived limitations in daily life seem to decrease  
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41 184 in the first year after ICU discharge (Table 1).

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46 185 Participation restrictions improved in the first year after ICU discharge due to a COVID-19 infection  
47  
48 186 (Figure 3). Mean participation levels increased from 62.0 (95%CI 55.9-68.1), 76.5 (95%CI 71.9-81.1) to  
49  
50 187 86.1 (95%CI 80.6-91.6) at one, three and 12 months respectively. One year after ICU discharge, 50.8%  
51  
52 188 of the patients still reported restrictions in physical exercise, 45.8% in performing housekeeping and  
53  
54 189 28.8% in performing leisure activities. After one year work is not applicable in 42.4% of all patients,  
55  
56 190 which is comparable to the premorbid work situation, where 58% of all patients were employed. One  
57  
58 191 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)
<b>Baseline characteristics</b>				
Age, years; n=67; median (IQR)	62 (57 – 68)	-		
<b>Sex; n=67; No (%)</b>				
- Men	52 (77.6%)	-		
- Women	15 (22.5%)	-		
<b>Highest level of education; n=62; No (%)</b>				
- Lower education	42 (67.7%)	-		
- Higher education	20 (32.3%)	-		
<b>Work situation; n=62; No (%)</b>				
- Full-time job	26 (41.9%)	-		
- Parttime job	10 (16.1%)	-		
- Retired	18 (29.0%)	-		
- Not working otherwise	8 (12.9%)	-		
<b>Comorbidities; n=67; no (%)</b>				
- 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%)	-		
<b>Parameters related to severity critical illness</b>				
- 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%)	-		
<b>Duration inpatient rehabilitation, days; n=67; median (IQR)</b>	19 (11 – 31)			
<b>Coping style (UPCC); n=58; mean (SD)</b>	3.0 (0.2)			
<b>USER-P restriction subscale <sup>a</sup></b>				
- 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%
<b>Physical examination:</b>				
- 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)
<b>Self-administered questionnaires:</b>				
- 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)



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3 194 Table 1, overview of the baseline characteristics (T0) and the physical examination and self-administered questionnaires at T1, T2 and T3. Low educational level  
4 195 was determined as 'primary and secondary education and post-secondary school'. High educational level was determined as 'bachelor's degree, master's degree  
5 196 or doctorate or equivalent'. Abbreviations: IMV, Invasive mechanical ventilation; UPCC, Utrecht Proactive Coping Scale; USER-P, Utrecht Scale for Evaluation of  
6 197 Rehabilitation-Participation; HHD, handheld dynamometer; 6MWT, 6 minute walking test; FEV1, Forced expiratory volume in the first second; FVC, Forced vital  
7 198 capacity; n.a., not applicable; MFI, multidimensional Fatigue Inventory; HADS, Hospital Anxiety and Depression Scale; GPS, The Global Psychotrauma Screen; CLC-  
8 199 IC, Checklist for Cognitive consequences after an ICU-admission. \* Restriction items values are percentages of patients who are restricted or dissatisfied.

8 200

9 201 Regarding the second aim, in the ICF domain body functions, breathlessness (MRC breathlessness),  
10 202 regression coefficient: 0.60 (95%CI 0.23-0.97; p-value <0.01) and fatigue (MFI), regression coefficient:  
11 203 0.07 (95%CI 0.03-0.09; p-value <0.01) were the only physical variables that influenced participation  
12 204 recovery over time. For the ICF domain activities, perceived limitations in daily life (PROMIS 8b)  
13 205 showed a different pattern in the recovery of participation restriction levels, regression coefficient: -  
14 206 0.11 (95%CI -0.12 to -0.05; p-value <0.01). In addition, personal factors like coping style (UPCC)  
15 207 regression coefficient: -2.39 (95%CI -4.20 to -0.06; p-value 0.01), anxiety (HADS anxiety) regression  
16 208 coefficient: 0.17 (95%CI 0.02-0.31; p-value 0.03) and depression (HADS depression) regression  
17 209 coefficient: 0.19 (95%CI 0.07-0.31; p-value <0.01) showed different paths in resuming the level of  
18 210 participation over time. Other early determinants show no significant difference in the recovery of  
19 211 participation (Table 2).

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Table 2	Estimate (95% CI)	p-value
<b>Baseline characteristics</b>		
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*
<b>ICU-stay specific parameters</b>		
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
<b>Physical examination</b>		
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
<b>Self-administered questionnaires</b>		
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.

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

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3 229 between 3 and 12 months. For depressive symptoms, both groups improved significantly in  
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5 230 participation levels between 1 to 3 months and between 3 to 12 months, although a steeper curve is  
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7 231 seen in recovery of participation levels at 3 to 12 months in patients with more depressive symptoms.  
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12 234 **Discussion**

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15 235 In this prospective cohort study, recovery of participation during the first year after ICU discharge in  
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17 236 COVID-19 ICU survivors who needed inpatient rehabilitation was evaluated and the association  
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19 237 between early levels of body function impairments, activity limitations and personal and social factors  
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21 238 on recovery were estimated. It is seen that in the first year after ICU discharge patients were able to  
22  
23 239 improve their participation levels. Nevertheless, after one year, there are still important limitations in  
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25 240 daily life, mainly in resuming work, physical exercise, housekeeping and leisure activities. As early  
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27 241 determinants for a delay in the resumption of patient's habitual level of participation levels over the  
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29 242 first year, higher levels of self-experienced breathlessness and fatigue complaints, more perceived  
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31 243 limitations in daily life as well as personal factors (having a passive coping style, anxiety complaints or  
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33 244 depression complaints) were found.  
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38 245 In previous Dutch studies focusing on overall post-ICU COVID-19 survivors, an average age of 61-63  
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40 246 was found, 69-72% men, with a median length of stay of 18-20 days in the ICU (33,34). These  
41  
42 247 demographic data seem to correspond with findings of current study, taking into account that in the  
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44 248 first COVID-19 wave, 83% of all post-ICU COVID-19 patients were transferred to a rehabilitation centre  
45  
46 249 (34). Heesakker et al. reported that in patients who survived one year following ICU treatment for  
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48 250 COVID-19, physical, mental, or cognitive symptoms were often reported (33). This corresponds with  
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50 251 the findings of the current study, whereas various physical, mental and cognitive impairments were  
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52 252 seen one year after ICU admission. However, to our knowledge, this is the first study to report  
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54 253 differences in the resumption of participation levels in post-ICU COVID-19 patients. Mean participation  
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56 254 levels increased to 86.1 one year after ICU discharge. As a reference, in other non-COVID patients (i.e.  
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3 255 stroke, acquired brain injury, progressive neurologic diseases, spinal cord injury and acute coronary  
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5 256 syndrome), participation levels between 70.6-83.5 have been observed (35–37). In all non-COVID  
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7 257 patient groups, patients mainly reported restrictions in work/education, housekeeping, physical  
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10 258 exercise and performing leisure activities, which is in accordance with restrictions in participation  
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12 259 reported in current study (36,37).

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14 260 Moreover, these results showed that higher scores of self-experienced breathlessness or fatigue and  
15  
16 261 more perceived limitations in daily life in the early phase of rehabilitation were associated with a  
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18 262 delayed recovery of participation levels over the first year. Furthermore, patients with a less active  
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20 263 coping style, those that were more anxious or reported to perceive more depressive complaints had a  
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22 264 delayed recovery of their level of participation over the first year. For all these determinants,  
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24 265 participation levels also appeared to be lower in the early phase of rehabilitation. These findings  
25  
26 266 indicate that patients with a higher level of anxiety and those with a higher level of depression had a  
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28 267 significantly slower improvement in participation levels during the first months, followed by a more  
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30 268 progressive recovery, especially in the last months. In addition, patients with more breathlessness  
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32 269 complaints, more fatigue complaints or more perceived limitations in daily life in the early phase of  
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34 270 rehabilitation and patients with a passive coping style showed a more progressive recovery of  
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36 271 participation levels especially in the last months. Poor baseline situation may also have provided more  
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38 272 opportunity to improve. However, with a mean participation restriction level of 86.1 one year after  
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40 273 ICU discharge, the maximum score of 100 of the USER-P restriction subscale has not been reached.

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42 274 Complaints of fatigue or breathlessness may be due to underlying medical problems or to the  
43  
44 275 contribution of personal factors. Previous study's showed significant recovery of respiratory function  
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46 276 and physical performance in the first year after ICU discharge due to COVID-19. Nevertheless, patients  
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48 277 still experience breathlessness and fatigue complaints after one year (38,39). Another finding in  
49  
50 278 current study was that early determinants related to the severity of the COVID-19 infection period  
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52 279 itself (such as ICU stay-specific parameters and physical parameters as age, sex, muscle strength,  
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54 280 functional exercise capacity and pulmonary function) did not individually explain progress in recovery  
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3 281 of participation over time. Contrary to expectations, this may indicate that non-physical factors such  
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5 282 as coping style, subjectively experienced physical impairments (including fatigue and breathlessness)  
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7 283 and mental health issues (such as anxiety and depressive symptoms) seem more important to  
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10 284 determine progress in recovering the level of participation. Previous literature on post-ICU patients  
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12 285 indicated that critical care recovery has focused on post-ICU impairments experienced by patients.  
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14 286 Whereas the positive aspects of recovery within the rehabilitation phase, including coping style and  
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16 287 resilience seems to be ignored (40,41). Resilience refers to the ability to face the challenges and  
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18 288 difficulties of life in a positive and adaptive manner, as well as the capacity to recover from an adverse  
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21 289 event (42). Higher levels of resilience have been linked to improved mental and physical health (43). It  
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23 290 is possible to improve the level of resilience. Which implies that resilience can be used to improve  
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25 291 (emotional) well-being, with the possible consequence of improving participation levels.  
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### 29 293 Implications for clinical practice and further research

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32 294 This study underlines the importance of looking at long-term consequence of COVID-19 ICU survivors  
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34 295 with an integral vision of health. Whether identical variables can be used to identify a delay in recovery  
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36 296 in patients who had a milder infection is currently still unclear. In this study, conclusions can be made  
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38 297 for a selected group (with ICU admission) of patients. Extrapolation to other populations needs to be  
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41 298 done with caution. Early detection of a passive coping style or mental impairments seems important  
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43 299 and should therefore be included in screening during early multidisciplinary rehabilitation. Further  
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45 300 research is needed to study the effect of early screening of a patients' level of coping/ resilience during  
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48 301 the first months after ICU discharge. As a consequence, an early intervention to increase  
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50 302 resilience/strengthen coping on indication could be promising to further strengthen social  
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52 303 participation, but needs to be further studied.  
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### 55 56 305 Strengths and limitations

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3 306 A strength of the study is that it only included the most severely affected post-ICU COVID-19 patients  
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5 307 referred to inpatient rehabilitation. In addition, this study used physical examination as well as  
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7 308 questionnaires, which means there was a combination of objective and subjective measurements. It is  
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10 309 notable that even in the most severely affected COVID-19 patients delayed recovery of participation is  
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12 310 associated with self-experienced physical impairments, mental impairments and coping style.  
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14 311 Nevertheless, some limitations of the current study need to be considered. First, sample size is limited  
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16 312 and a number of factors were studied for their effect on the course of participation recovery. The  
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18 313 limited sample size contributed to relatively wide confidence intervals. The risk of type II error should  
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20 314 therefore be considered while interpreting the data. A post-hoc power calculation revealed however  
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22 315 that the study had 90% power to detect an effect size of 0.2 for changes in participation levels over  
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24 316 time ( $\alpha = 0.05$ , mean correlation between repeated measures = 0.53). Still, p-values of the multiple  
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26 317 tests of association should be interpreted cautiously, because we cannot exclude erroneous  
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28 318 interpretations of statistical significant findings (i.e. type I error). However, since our results support a  
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30 319 certain pattern, we believe that the main conclusions of this study are solid. Second, number of  
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32 320 variables available to describe the acute illness severity were limited. Patients referred for inpatient  
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34 321 multidisciplinary rehabilitation were included in this study. Generalisation of the results to all ICU  
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36 322 survivors needs to be performed with caution, and needs further study. Third, due to high workload  
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38 323 on the ward, 23 patients were not approached in time for consent to participate. In our opinion, this  
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40 324 is unlikely to have led to selection bias, but this cannot be excluded. Finally, the lockdown and the  
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42 325 inability to perform social and outdoor activities may have affected the total USER-P score as this scale  
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44 326 allows the rating of 'not applicable'. Since the study- and lockdown period were similar for all patients,  
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46 327 we expect no difference in the study patients. Although it may have affected the recovery course of  
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48 328 participation recovery for the entire patient group, it is not expected to have affected the predictors.  
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### 330 Conclusion

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3 331 For patients admitted to an ICU for COVID-19, participation levels improves in the first year after ICU  
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5 332 discharge. However, at one year after discharge, many patients still experience limitations in daily life,  
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7 333 mainly in resuming work, physical exercise, housekeeping and leisure activities. Our results indicate  
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9 334 that progress of recovery in participation in the first year after discharge is associated with early  
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11 335 determinants in coping style, subjectively experienced physical impairments (breathlessness and  
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13 336 fatigue) and mental impairments (anxiety and depression) rather than medical variables. This study  
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15 337 supports the need for an integral perspective on health to facilitate the identification of factors that  
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17 338 delay the recovery trajectory for participation in the first year after ICU discharge. Personal factors  
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19 339 such as a passive coping style and more anxiety- or depression complaints seem relevant to this.  
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21 340 Rehabilitation care needs to anticipate on these topics, starting in the early rehabilitation phase of  
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23 341 post-ICU COVID-19 care.  
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35  
36

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38  
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40  
41 348 SvK. Practical implication was done by CW, SvS and YH. The first draft of the paper was written by CW  
42  
43 349 and all co-authors reviewed and approved it for submission. CW and JV are the guarantors. The  
44  
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46  
47 351 meeting the criteria have been omitted.  
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4  
5 357 submitted work in the past three years; no other relationships or activities that could appear to have  
6  
7 358 influenced the submitted work  
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10 359 Patient consent for publication: Not required.  
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13 360 Dissemination to participants and related patient and public communities: The study results will be  
14  
15 361 disseminated to the public through our media channels or national and international conferences.  
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18 362 Ethical approval: The local medical ethics committee Zuyderland METC (METCZ20200086) approved  
19  
20 363 the study.  
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23 364 Data availability statement: To guarantee the confidentiality of personal and health information, only  
24  
25 365 the authors have had access to the data during the study. Data is available (anonymised), but the  
26  
27 366 corresponding author must be contacted to request these data. Data will be kept for 15 years  
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3 492 **Figure Legend:**  
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- 5 493 - Figure 1: ICF model and measurement instruments used.  
6 494 - Figure 2: Subject recruitment flowchart.  
7 495 - Figure 3: The recovery of participation levels (USER-P restriction subscale) in the first year  
8 496 after ICU discharge in post-COVID-19 patients.  
9 497 - Figure 4: The influence of early levels of body function impairments, activity limitations and  
10 498 personal factors on the recovery of participation levels (USER-P restriction subscale).  
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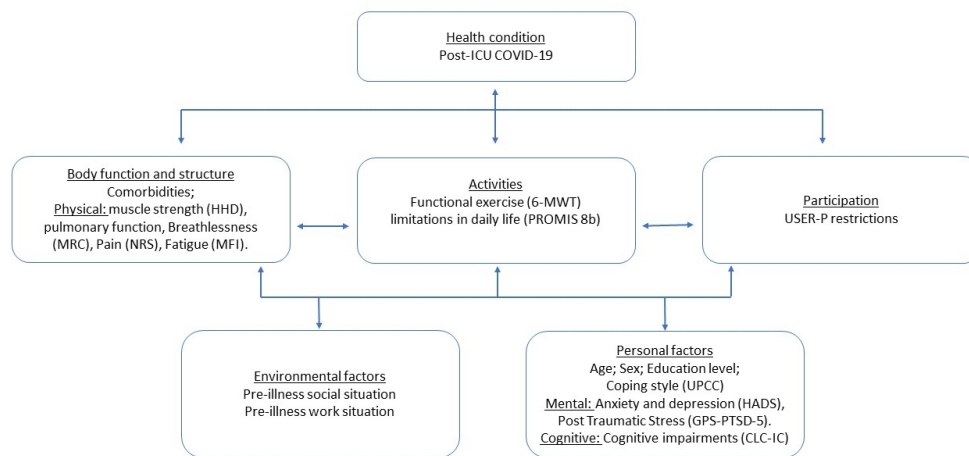


Figure 1. ICF model and measurement instruments used.

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

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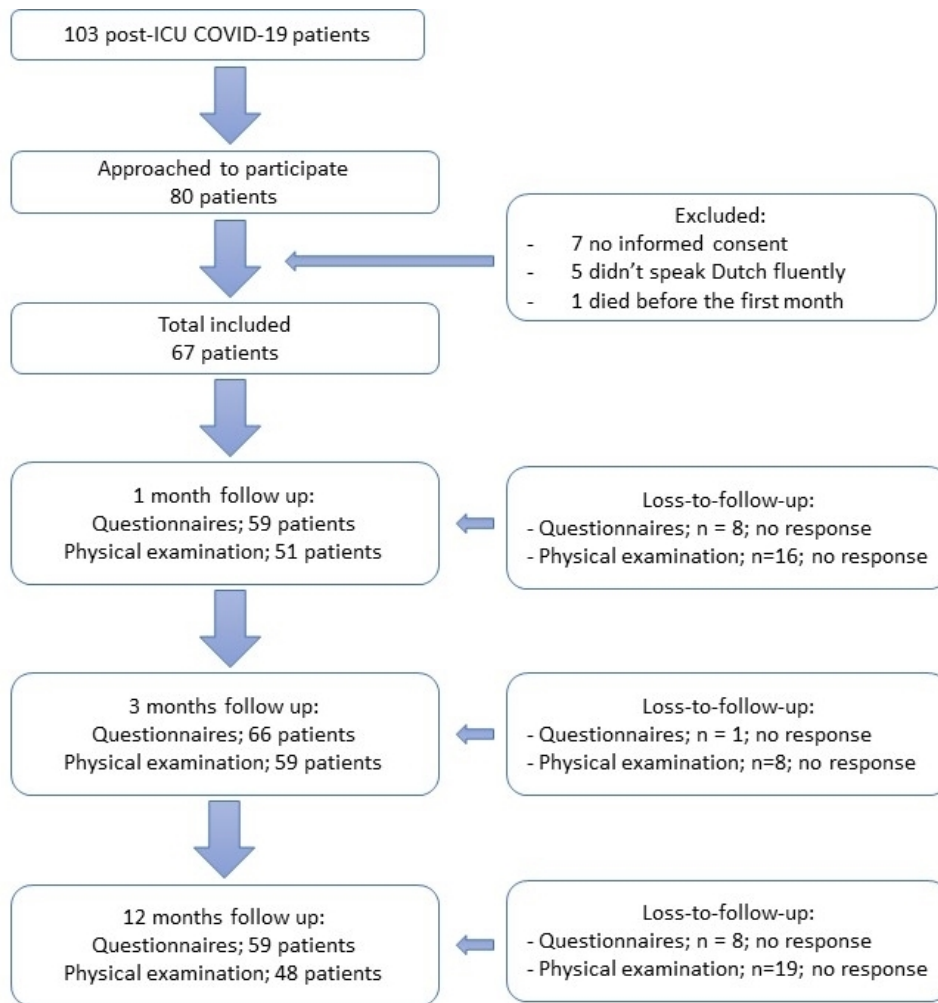


Figure 2; Subject recruitment flowchart.

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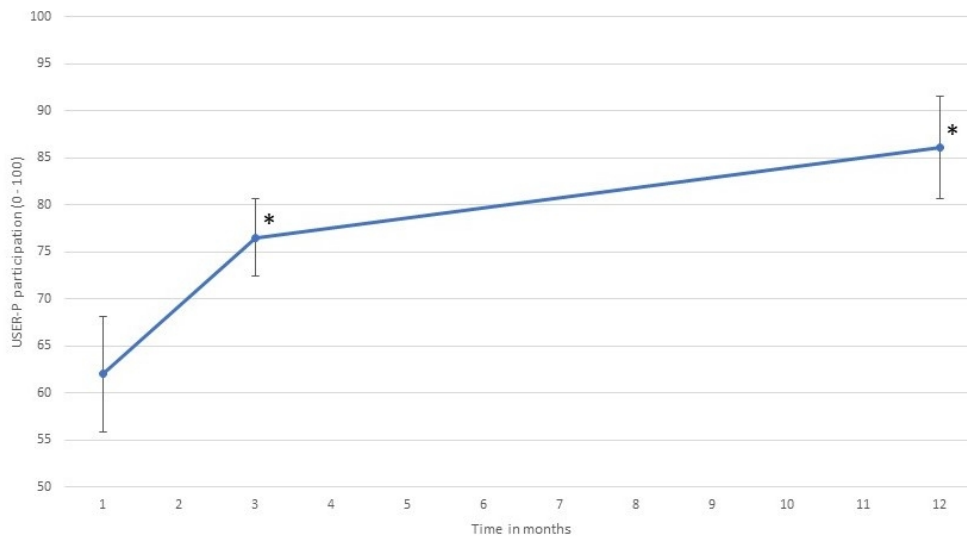


Figure 3; The recovery of participation levels (USER-P restriction subscale) in the first year after ICU discharge in post-COVID-19 patients. Results are expressed as mean with corresponding 95% confidence interval. \*  $p < 0.01$  (compared to previous measurement moment)

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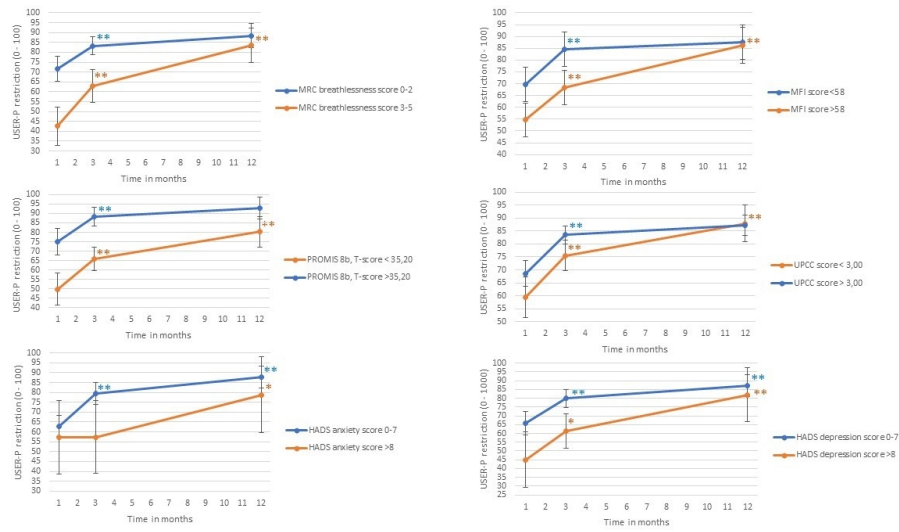


Figure 4; The influence of early levels of body function impairments, activity limitations and personal factors on the recovery of participation levels (USER-P restriction subscale). For illustrative purposes, subgroups have been created based on cut-off value (HADS) or the median if no specific cut-off 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).

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

	Item No	Recommendation	Page No
<b>Title and abstract</b>	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
<b>Introduction</b>			
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
<b>Methods</b>			
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	
<b>Results</b>			
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
<b>Discussion</b>			
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
<b>Other information</b>			
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>.