



Recovery from COVID-19: a sprint or marathon? 6-month follow-up data from online long COVID-19 support group members

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ABSTRACT

Background: It remains unknown whether and to what extent members of online “long COVID” peer support groups remain symptomatic and limited over time. Therefore, we aimed to evaluate symptoms in members of online long COVID peer support groups up to 6 months after the onset of coronavirus disease 2019 (COVID-19)-related symptoms.

Methods: Demographics, symptoms, health status, work productivity, functional status and health-related quality of life were assessed about 3 and 6 months after the onset of COVID-19-related symptoms in members of online long COVID peer support groups.

Results: Data from 239 patients with a confirmed COVID-19 diagnosis (83% women; median (interquartile range) age 50 (39–56) years) were analysed. During the infection, a median (interquartile range) of 15 (11–18) symptoms was reported, which was significantly lower 3 and 6 months later: 6 (4–9) and 6 (3–8), respectively ($p < 0.05$). From 3 to 6 months follow-up, the proportion of patients without symptoms increased from 1.3% to only 5.4% ($p < 0.001$). Patients also reported a significantly improved work productivity (work absenteeism and presenteeism: 73% versus 52% and 66% versus 60%, respectively), self-reported good health (9.2% versus 16.7%), functional status (mean \pm SD Post-COVID-19 Functional Status scale: 2.4 \pm 0.9 versus 2.2 \pm 1.0) and health-related quality of life (all $p < 0.05$).

Conclusion: Although patients with confirmed COVID-19, who were all members of online long COVID peer support groups, reported significant improvements in work productivity, functional status and quality of life between 3 and 6 months follow-up, these data clearly highlight the long-term impact of COVID-19, as approximately 6 months after the onset of COVID-19-related symptoms a large proportion still experienced persistent symptoms, a moderate-to-poor health, moderate-to-severe functional limitations, considerable loss in work productivity, and/or an impaired quality of life. Action is needed to improve the management and healthcare of these patients.



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Patients who are members of online #longCOVID peer support groups may still experience persistent symptoms about 6 months after the onset of symptoms, which can affect work productivity, functional status and quality of life <https://bit.ly/3vxPF2b>

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Introduction

Recovery from coronavirus disease 2019 (COVID-19) can take weeks up to months in previously hospitalised and non-hospitalised adult patients. Even though a large proportion recover fully, case reports and several cohort studies have shown that some patients have persistent symptoms (for >12 weeks after the COVID-19 related infection), such as fatigue, dyspnoea, chest tightness, headache and muscle pain [1–9]. Moreover, an impaired functional status, post-traumatic stress disorder and poor quality of life have been reported in previously hospitalised and non-hospitalised adults recovering from COVID-19 [4, 5, 7, 10, 11]. These data suggest the presence of a post-COVID-19 syndrome (*i.e.* long COVID or long-haul COVID, as called by several patient groups which refer to the long-lasting COVID-19 symptoms), which is defined by clusters of symptoms lasting for >12 weeks and may arise from any system in the body [1, 9, 12, 13]. The National Institute for Health Care Excellence (NICE) guideline for managing the long-term effects of COVID-19 defined the term “long COVID” for patients having signs and symptoms that continue or develop after acute COVID-19. It includes both ongoing symptomatic COVID-19 (from 4 to 12 weeks) and post-COVID-19 syndrome (≥ 12 weeks) [13].

It has been estimated that approximately 5–10% of the people experience prolonged symptoms after COVID-19 [3, 6, 14]. A growing number of these patients have gathered on online forums and social media, as they mostly feel unheard, perceive insufficient support from clinicians, and lack clearly defined healthcare pathways, especially when they were not admitted to the hospital [1, 15, 16]. These so-called long COVID peer support groups serve as source of support through shared experiences, knowledge and expertise, have taken the lead in generating evidence on COVID-19 with persisting symptoms and campaigning for better and more consistent healthcare [15, 16].

Our data from a first survey among members of online long COVID peer support groups about 3 months after the onset of COVID-related symptoms already highlighted the major impact of multiple persistent symptoms on patients’ daily lives [1, 10]. To date, it remains unknown whether and to what extent these patients with the so-called post-COVID-19 syndrome remain symptomatic and limited in daily functioning over time. Therefore, we aimed to evaluate symptoms in these COVID-19 patients up to 6 months after the onset of COVID-19 related symptoms. We hypothesised that patients still suffer from multiple symptoms and report limitations in work productivity, functional status, and quality of life after 6 months of follow-up, but to a lesser extent compared to 3 months after the onset of symptoms.

Methods

Study design, setting and participants

Between 4 June and 11 June 2020, 1939 members of two long COVID Facebook groups or an online COVID-19 panel (www.coronalongplein.nl) completed the first survey (T1) [1]. 1556 of these respondents consented to be approached for future research, and were invited to complete a second survey between 31 August and 8 September 2020 (T2). For all details see supplementary figure 1.

The medical ethics committee of Maastricht University stated that the Medical Research Involving Human Subjects Act (WMO) did not apply for this study and that an official approval of this study by the committee was not required (METC2020-1978 and METC2020-2554). The medical ethics committee of Hasselt University (Diepenbeek, Belgium) formally judged and also approved the study (MEC2020/041). All adult respondents (aged ≥ 18 years) gave digital informed consent at the start of the second survey. Without the informed consent, the survey could not be continued. The study was registered before its start (trialregister.nl; NL8705).

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Measures

The survey contained questions regarding: demographics; pre-existing comorbidities; COVID-19 diagnosis (based on reverse transcriptase(RT)-PCR and/or computed tomography (CT) scan of the thorax, symptom-based medical diagnosis, no test/medical diagnosis); intensive care unit (ICU) or hospital admission; current self-reported health status (good/moderate/poor); and received care (help with personal care/physiotherapy/rehabilitation: yes/no, frequency). In addition, respondents were asked about the presence (yes/no) of a list of symptoms during the acute infection (retrospectively) and at time of completing the questionnaires (T1 and T2: “symptoms at this moment”). Scientists, methodologists, healthcare professionals and COVID-19 patients from the Facebook groups of The Netherlands and Flanders were closely involved in putting together the list of 29 symptoms that were studied: increased body temperature (37.0–37.9°C); fever (body temperature $\geq 38.0^\circ\text{C}$); cough; mucus; nose cold; sneezing; dyspnoea; sore throat; fatigue; muscle pain; joint pain; anosmia; ageusia; headache; dizziness; diarrhoea; nausea; vomiting; red spots on toes/feet; pain/burning feeling in the lungs; ear pain; chest tightness; pain between shoulder blades; heart palpitations; increased resting heart rate; eye problems; sudden loss of body weight; burning feeling in the trachea; and heat flushes. Moreover, there was the option of an open text field to add other symptoms. These data contained many different symptoms, including loss of concentration and cognitive function, hair loss, chills, rashes, and sleeping problems. However, these “other” symptoms were not analysed in detail due the large heterogeneity.

In addition, participants were asked to complete the following validated questionnaires. 1) The Work Productivity and Activity Impairment questionnaire to assess COVID-19-related absenteeism, presenteeism, overall work impairment (absenteeism and presenteeism combined), and impairment of regular activities during the preceding 7 days [17]. Scores are presented as percentages and higher percentages indicate greater impairment and compromised productivity, as described previously [18]. 2) The Post-COVID-19 Functional Status (PCFS) Scale to assess the impact on self-reported functional status at time of completing the questionnaire [19, 20]. The PCFS scale stratification is composed of five scale grades: grade 0 (no functional limitations); grade 1 (negligible functional limitations); grade 2 (slight functional limitations); grade 3 (moderate functional limitations); and grade 4 (severe functional limitations). A final scale, grade 5 (death), that is required to be able to use the scale as an outcome measure in clinical trials, was left out for this self-administered questionnaire. 3) The 5-level EuroQol-5 Dimensions version (EQ-5D-5L) to assess generic quality of life, providing an index score which ranges from -0.329 (worst quality of life) to 1 (best quality of life) [21]. The EQ-5D-5L includes a vertical visual analogue scale (VAS) ranging from 0 (the worst health you can imagine) to 100 points (the best health you can imagine) [22]. The reference values of GROCHTDREIS *et al.* [23] were used to calculate the proportion of patients with an EQ-5D index below the 5th percentile ($1.64 \times \text{SD}$) of the mean age/sex-based reference values.

Statistical methods

Continuous data are presented as mean \pm SD or median (interquartile range), as appropriate. Categorical data are presented as absolute and relative frequencies. The proportion of patients selecting “yes” per symptom was calculated, including “other” if selected. Sensitivity analyses were performed to identify potential differences between specific subgroups (hospitalised/non-hospitalised, responders/non-responders), using Chi-squared tests or Mann–Whitney U-Tests. Differences between 3 and 6 months follow-up were evaluated with the McNemar Test or Wilcoxon Signed Rank test. Initial analyses were performed in patients with a RT-PCR or CT confirmed diagnosis and a sensitivity analyses were performed to confirm the results for patients with no formal COVID-19 diagnosis. An exploratory analyses was performed to identify predicting variables of having persistent symptoms about 6 months after the onset of COVID-19 related symptoms, using the following predicting variables in a stepwise logistic regression analysis: age; sex; education level; marital status; body mass index; number of comorbidities; self-reported health status before the onset of COVID-19 related symptoms; and number of symptoms during the infection. Statistics were performed using SPSS version 25.0. *A priori*, the level of significance was set at $p < 0.05$.

Results

Of the initial 1556 patients who completed the first survey about 3 months after the onset of COVID-related symptoms (T1) and consented to be approached for future research, 1005 (65%) patients completed the second survey about 6 months after onset of the COVID-related symptoms (T2). Generally, the results from the first survey were comparable between the patients who did and did not complete the second survey (supplementary table 1).

239 (24%) patients had a RT-PCR and/or CT scan confirmed diagnosis. Patients were mostly middle-aged women with a slightly overweight body mass index (table 1). 62 (26%) patients were hospitalised (without

TABLE 1 Characteristics and outcomes of patients with confirmed coronavirus disease 2019 (COVID-19) diagnosis

Subjects n	239
Women	198 (82.8)
Age years	50.0 (39.0–56.0)
BMI kg·m⁻²	26.0 (23.4–30.5)
Married/living with partner	173 (72.4)
Pre-existing comorbidities	
0	142 (59.4)
1	62 (25.9)
≥2	35 (14.6)
Health status before infection	
Good	208 (87.0)
Moderate	28 (11.7)
Poor	3 (1.3)
Time between T0 and completion questionnaire weeks	
T1	10.4±2.4
T2	22.6±2.4
Number of symptoms	
T0	15 (11–18)
T1	6 (4–9)*
T2	6 (3–8)*.#
Work productivity and activity index	
Percentage of work time missed due to ill health (absenteeism)	
T1	72.9±35.2
T2	52.4±38.4 [#]
Percentage of impairment while working (presenteeism)	
T1	66.1±25.8
T2	59.7±24.0 [#]
Overall work impairment due to health (work productivity)	
T1	89.3±19.4
T2	78.6±26.0 [#]
Activity impairment	
T1	71.4±21.7
T2	59.7±22.8 [#]
Self-reported poor health	
T0	1.3
T1	25.5*
T2	10.5* [#]
Post-COVID-19 functional status scale	
Grade	
T1	2.4±0.9
T2	2.2±1.0 [#]
Quality of life	
EQ-5D index	
T1	0.645±0.181
T2	0.694±0.165 [#]
EQ-5D index < P5 reference values [23]	
T1	36.8
T2	26.8 [#]
Today's health status (VAS 0–100) points	
T1	49±19
T2	56±18 [#]
Received care	
Physiotherapy	
Between T0 and T1	31.8
Between T1 and T2	61.9 [#]
Rehabilitation	
Between T0 and T1	4.2
Between T1 and T2	11.7 [#]
Need for help with personal care	
From partner	
Before	5.0
Between T0 and T1	46.0*
Between T1 and T2	21.3* [#]

From family	
Before	1.7
Between T0 and T1	17.2*
Between T1 and T2	7.1* [#]
Data are presented as n (%), median (interquartile range), mean±SD or %, unless otherwise stated. BMI: body mass index; T0: symptom onset; T1: first questionnaire; T2: second questionnaire; P5: percentile five; VAS: visual analogue scale. *: p<0.05 <i>versus</i> before; [#] : p<0.05 <i>versus</i> T1.	

admission to the ICU) and 177 (74%) were not hospitalised at the time of the infection. Generally, results were comparable between hospitalised and non-hospitalised patients (supplementary table 2) The remaining 766 patients who also completed both surveys were suspected to have had COVID-19. They did not have a formal COVID-19 test at the time of the suspected infection.

Number of symptoms

During the COVID-related infection a median of 15 (11–18) symptoms were reported, which was significantly lower about 3 and 6 months later: 6 (4–9) and 6 (3–8), respectively (p<0.001) (table 1, figure 1). At all three time-points, fatigue was the most prevalent symptom (figure 2).

The proportion of patients with zero symptoms increased between 3 and 6 months follow-up, from 1.3% to 5.4% (p<0.001). After about 6 months, 98 (41.0%) patients reported one to five symptoms, 69 (40%) patients reported six to 10 symptoms, and 32 (13%) patients reported >10 symptoms (supplementary figure 2). In a stepwise logistic regression model, having persistent symptoms after about 6 months was significantly associated with female sex (OR 4.596 (95% CI 1.405–15.038); p=0.012) and number of symptoms during the infection (OR 1.168; (95% CI 1.022–1.334); p=0.022). To correct for the unequal sex distribution, analyses were repeated in female patients, showing that only the number of symptoms during the infection was associated with having persistent symptoms (OR 1.186 (95% CI 1.005–1.400); p=0.043).

Work productivity

The majority of patients (87.9%) reported having a job before the infection. The mean proportion of work time missed in the previous week due to ill health (absenteeism) and impairment while working (presenteeism) reduced from 73% to 52% and from 66% to 60%, respectively (both p<0.001) (table 1). In addition, average work productivity loss reduced from 89% to 79%, resulting in an overall working impairment of 71% and 60% after about 3 and 6 months follow-up, respectively (both p<0.001) (table 1).

Self-reported health, functional status and quality of life

Pre-infection, 87.0% of the patients had a good self-reported health-status. After 3 months follow-up, only 9.2% of the patients rated their health as “good”, which significantly increased up to 16.7% after about 6 months follow-up (p<0.001) (figure 3). Consequently, 83.3% of the patients still reported moderate-to-poor self-reported health after 6 months.

Compared to 3 months follow-up, patients had a significantly lower grading (*i.e.* better self-reported functional status) on the PCFS scale (2.4 (0.9) *versus* 2.2 (0.8); p<0.001) (table 1). Functional status improved in 26.8% of the patients, and deteriorated in 15.5% of the patients. The proportion of patients reporting to currently have no limitations in everyday life without infection-related symptoms increased significantly from 1.9% to 6.5% (p<0.001) (figure 4).

On the EQ-5D-5L questionnaire, the proportion of patients who had problems with mobility, self-care, and/or daily activities, who had pain or discomfort, or felt anxious or depressed reduced significantly between 3 and 6 months of follow-up (figure 5). Still, 62% of the patients had moderate-to-extreme problems with daily activities at 6 months, and 49% of the patients experienced moderate-to-severe pain or discomfort (figure 5). The mean EQ-5D index (from 0.645 (0.181) to 0.694 (0.165)) and the EQ-VAS (from 49 (19) to 56 (18)) improved significantly (p<0.001) (table 1). Compared to age/sex-matched reference values [23], the percentage of patients who had an EQ-5D index that was below the fifth percentile also significantly reduced from 36.8 to 26.8% (p<0.001) (table 1).

Received care

The proportion of patients receiving physiotherapy or rehabilitation between 3 and 6 months of follow-up was significantly higher compared to the period from the infection to 3 months of follow-up (61.9% *versus* 31.8% and 11.7% *versus* 4.2%, respectively, p<0.05) (table 1), and median (interquartile range) number of sessions increased significantly from 7 (4–10) to 12 (8–24) (p<0.001). The dependency on partner or

family for personal care significantly decreased from 3 to 6 months follow-up (from 46.0% to 21.3% and from 17.2% to 7.1%, respectively, $p < 0.05$), though the proportion of patients needing help from their partner or family was still significantly higher compared to before the infection (21.3% versus 5.0% and 7.1% versus 1.7%, respectively; $p < 0.05$). A subgroup analyses comparing patients who did and did not receive physiotherapy or rehabilitation is included in the supplementary material (supplementary table 3). In brief, 3 and 6 months after the onset of COVID-19 related symptoms, patients receiving physiotherapy reported more symptoms and a worse self-reported health, work productivity, functional status and quality of life compared to patients who did not receive physiotherapy or rehabilitation. Between 3 and 6 months of follow-up, significant improvements were found in both patients who did and did not receive physiotherapy or rehabilitation.

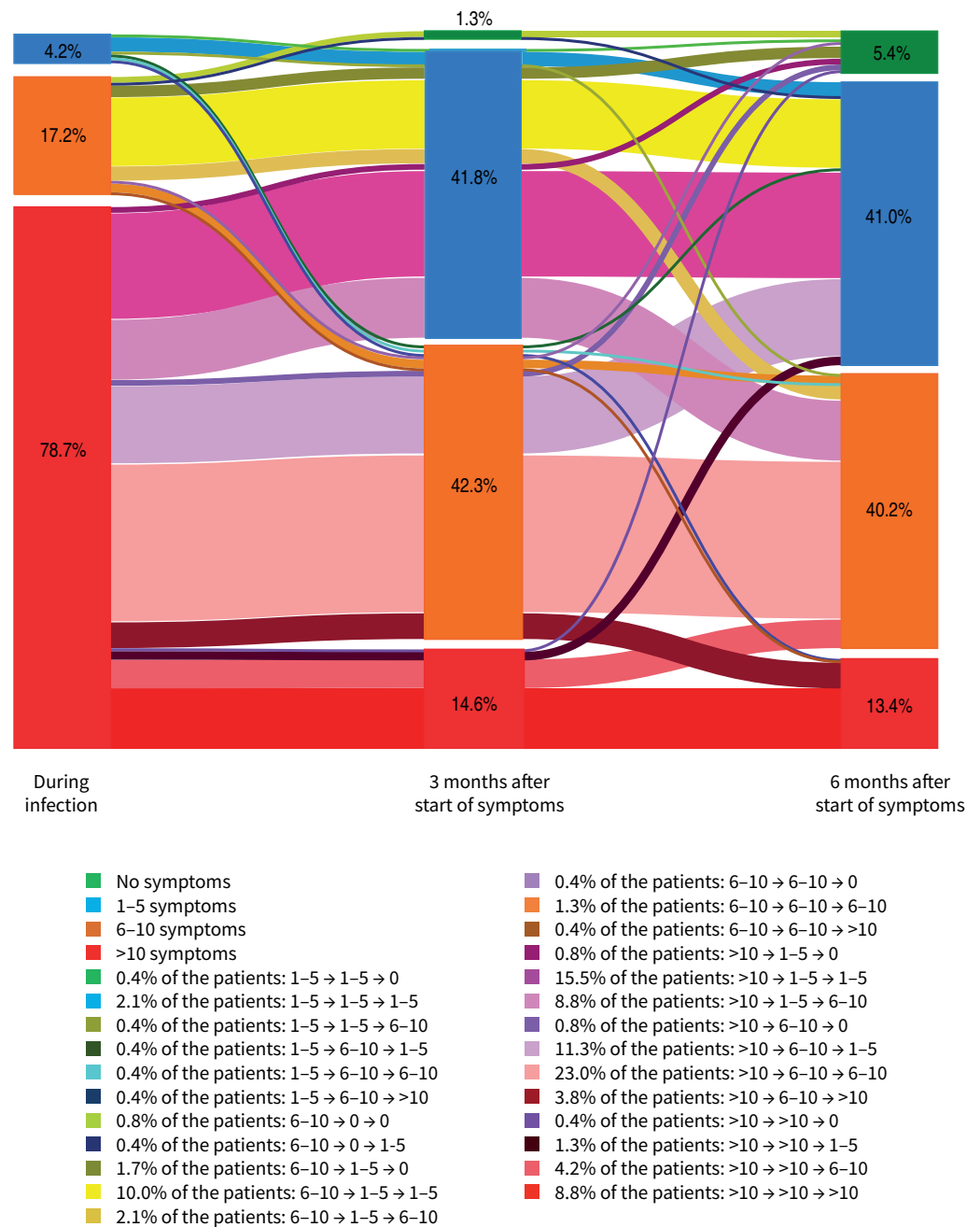


FIGURE 1 Prevalence and change in the total number of symptoms during the infection and after 3 and 6 months of follow-up. The width of lines is proportional to the flow rate.

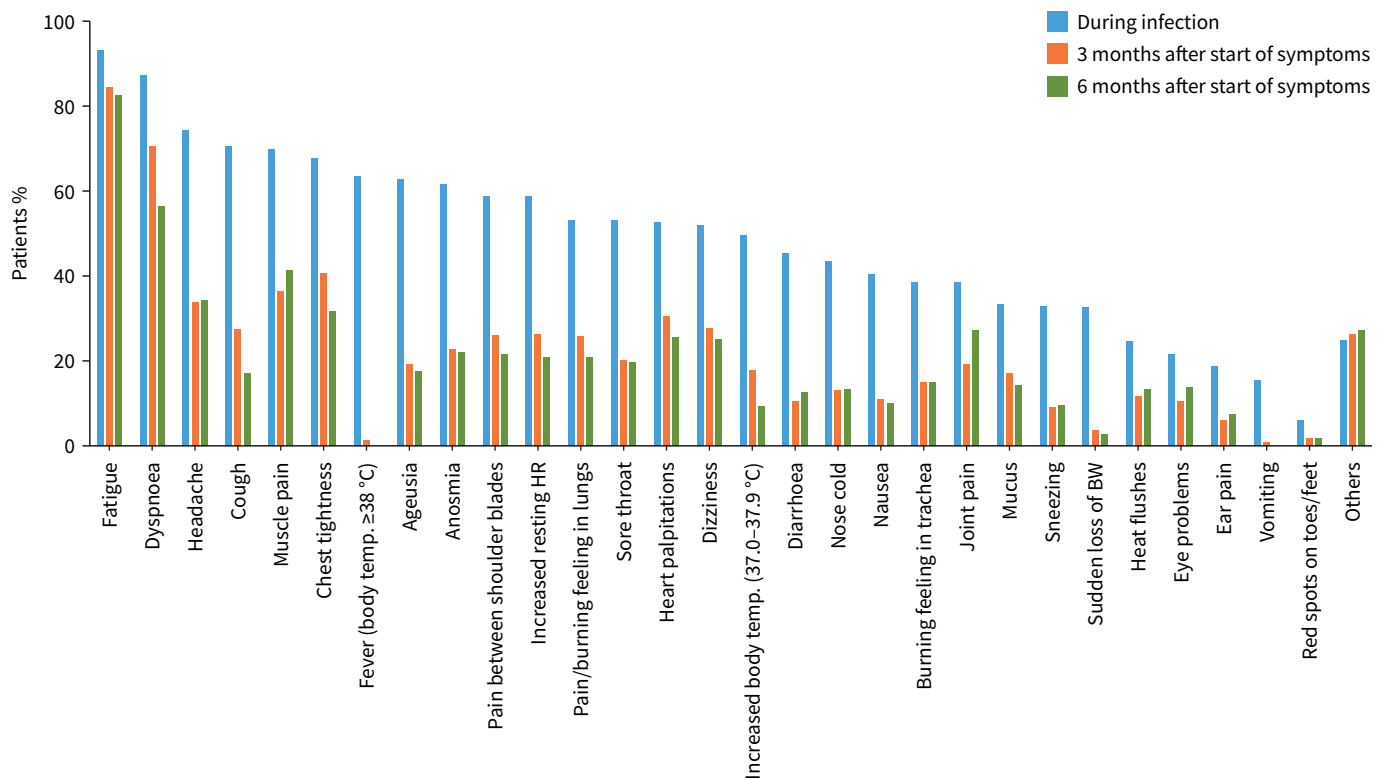


FIGURE 2 Prevalence of symptoms during the infection and after 3 and 6 months of follow-up. HR: heart rate; BW: body weight.

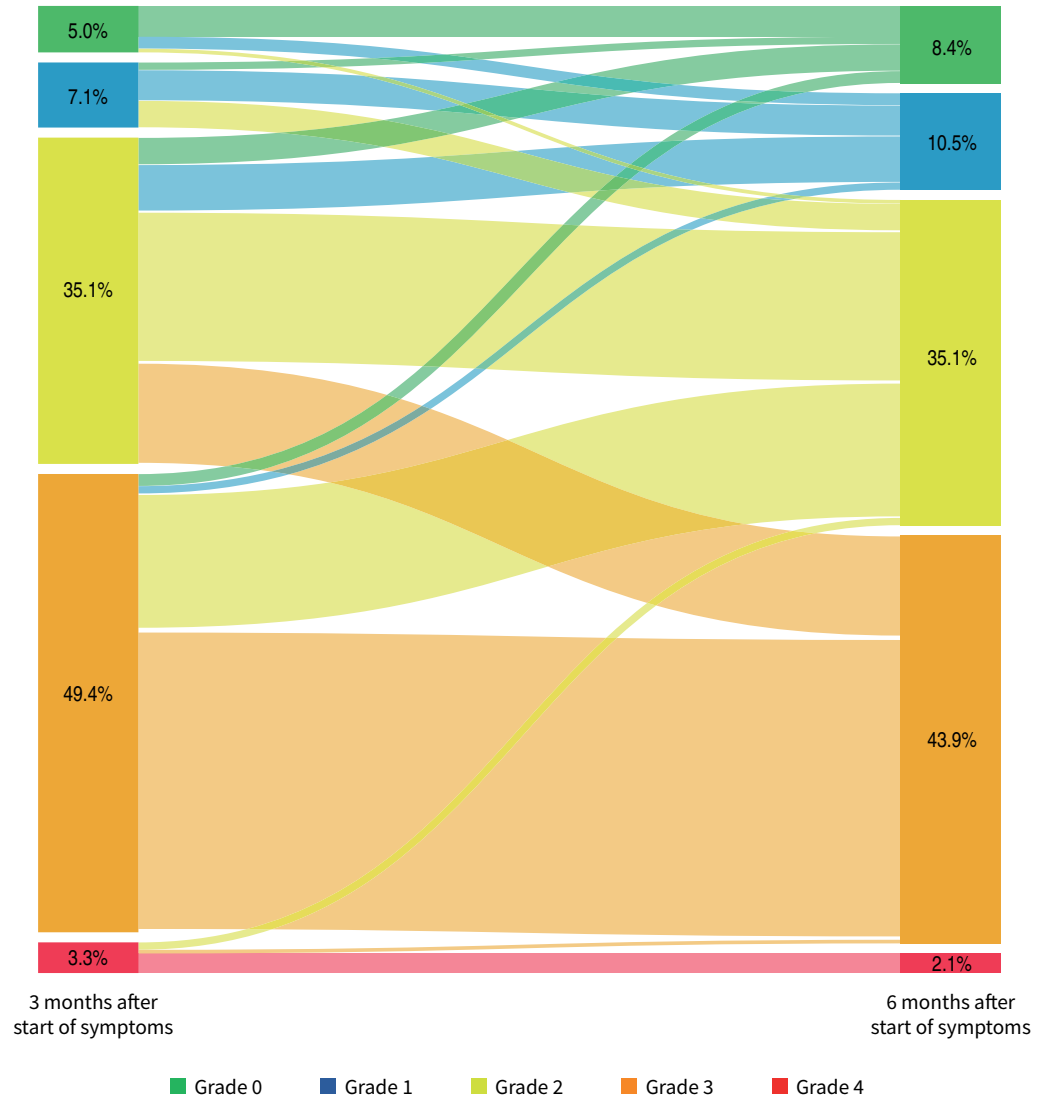
Patients with suspected COVID-19 diagnosis

The results of the 766 patients with suspected COVID-19 show similarities to those of the patients with a confirmed COVID-19 diagnosis (supplementary material).

Discussion

This is the first study to demonstrate that about 6 months after the onset of COVID-19-related symptoms, patients who are members of online long COVID support groups still suffer from a median of six symptoms. Although significant improvements in health status, work productivity and functional status were found between 3 and 6 months of follow-up, these data clearly highlight the long-term impact of COVID-19 and support the existence of a post-COVID-19 syndrome in a subset of patients [1, 7, 12, 13]. Indeed, the vast majority of patients (94.6%) still experienced one or more symptoms 6 months after being infected. Moreover, 83% of patients still reported moderate-to-poor self-reported health, and about half of the patients (49%) reported moderate-to-severe functional limitations. Furthermore, there was a considerable loss in work productivity, and about a quarter of the patients had an impaired quality of life.

Data from the COVID-19 Symptom Study suggest that most people recover from COVID-19 within 2 weeks [6], though it is increasingly recognised that a subgroup of patients with COVID-19 may develop long-term symptoms. Our findings clearly demonstrate that a subset of patients with persistent symptoms 3 months after the onset of the infection still suffer from a median of six symptoms 6 months after being infected, including non-respiratory-related symptoms like fatigue, pain at different body locations and a loss of smell and/or taste. Remarkably, these patients are generally middle aged, with no or few other underlying chronic conditions before the infection and a good self-reported health. These symptoms seriously limit patients' daily life, as patients experience functional limitations and impaired work productivity, or are even unable to return to work. Fallout from work can not only result in a high financial burden for these patients, but can even have global consequences for the economy and society in the long run. Indeed, this middle-aged population is considered the back-bone of most modern economies as they have high shares of labour participation, tax payment and contribute significantly to countries' gross domestic product. Therefore, the involvement of occupational medicine or even interdisciplinary rehabilitation in the patients' return to work seems a necessity to minimise the post-COVID-19 societal impact. Importantly, the impact of COVID-19 in general on work productivity is likely underestimated in this study, as many patients with persistent symptoms may have no test-confirmed COVID-19 diagnosis,



3.3% of the patients: Grade 0 → Grade 0
 1.3% of the patients: Grade 0 → Grade 1
 0.4% of the patients: Grade 0 → Grade 2
 0.8% of the patients: Grade 1 → Grade 0
 3.3% of the patients: Grade 1 → Grade 1
 2.9% of the patients: Grade 1 → Grade 2
 2.9% of the patients: Grade 2 → Grade 0
 5.0% of the patients: Grade 2 → Grade 1
 16.3% of the patients: Grade 2 → Grade 2
 10.9% of the patients: Grade 2 → Grade 3
 1.3% of the patients: Grade 3 → Grade 0
 0.8% of the patients: Grade 3 → Grade 1
 14.6% of the patients: Grade 3 → Grade 2
 32.6% of the patients: Grade 3 → Grade 3
 0.8% of the patients: Grade 4 → Grade 2
 0.4% of the patients: Grade 4 → Grade 3
 2.1% of the patients: Grade 4 → Grade 4

FIGURE 4 Post-coronavirus disease 2019 functional status scale after 3 and 6 months of follow-up. The width of lines is proportional to the flow rate.

show that there are patients with persistent symptoms about 3 and 6 months after the infection who do not experience substantial limitations in their daily lives. To date, it remains unclear why these patients report less/no impact of the persistent symptoms on their daily activities.

The current findings show the major impact of COVID-19 on individual patients and justify a close follow-up by healthcare professionals of hospitalised and non-hospitalised COVID-19 patients. To date, there is no consistent approach for the diagnosis, management and follow-up of these patients with the so-called long COVID or post-COVID-19 syndrome. Through online long COVID peer support groups, patients aim to create broader awareness for their unmet care needs [1, 15, 16]. Indeed, an accurate diagnosis and treatment of the possible underlying causes of the persistent symptoms seems very

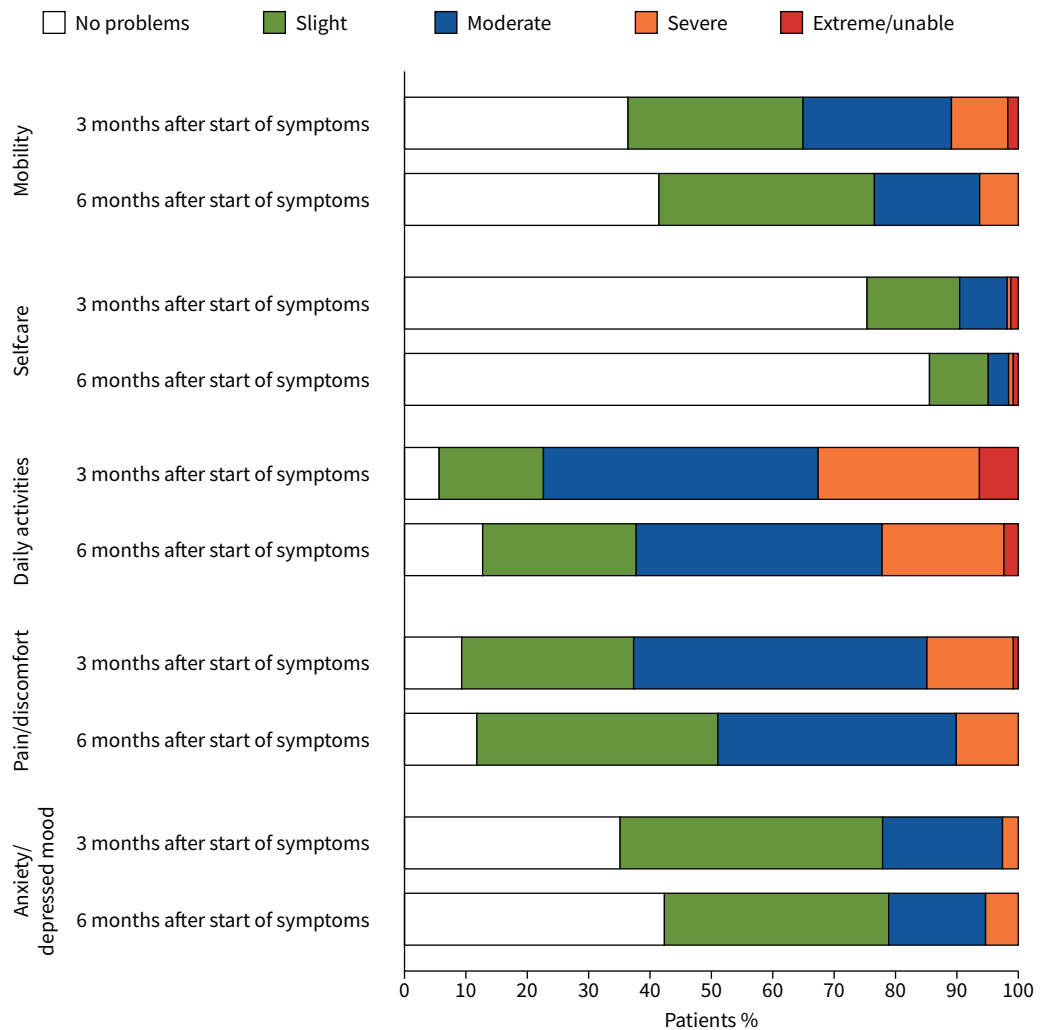


FIGURE 5 Problems on the 5-level EuroQol-5 Dimensions version domains after 3 and 6 months of follow-up.

important to restore patients’ health and quality of life. Identification of physical, emotional, cognitive and social treatable traits may play an important role towards interim guidance for pharmacological and/or non-pharmacological treatment options. Currently, many COVID-19 patients experience that they do not have access to appropriate healthcare and/or continuity of care is often lacking [15]. Although more than half of the patients in this study received physiotherapy, many of them still experienced multiple symptoms 6 months after being infected, and the number of symptoms was even higher compared to patients not receiving physiotherapy. It can be argued that the patients receiving physiotherapy are probably the more impaired patients with more symptoms and poorer health status, yet our findings indicate that physiotherapy alone may not be sufficient for a full recovery. Indeed, it has already been recognised that COVID-19 is not limited to the respiratory system, but is considered as a systemic disease, including cardiovascular, neurological, haematological, gastrointestinal, renal and skin manifestations [26, 27]. Therefore, a multidisciplinary approach will most probably be needed for providing optimal care of these patients. Healthcare professionals, employers, insurers and society need to take action to improve the management and healthcare of these patients.

The following methodological limitations need to be considered. Some questions may have been affected by recall bias. Additionally, we cannot rule out that the patients who completed the baseline and follow-up questionnaires are the ones who experienced the most symptoms. Then again, the median number of reported symptoms 3 months after the onset of symptoms was comparable between patients who completed the survey twice (June and September) and patients who only completed the survey in June (supplementary table 1). The majority of respondents were female, though, this is consistent with the sex distribution of previous studies [6, 15, 16, 28, 29], and can at least partly be explained by the higher number of women in online long COVID support groups [15, 16]. Moreover, it has been suggested that

persistent symptoms after COVID-19 are more common in women than men [6]. Obviously, long-term follow-up data from COVID-19 patients are lacking, and therefore, little is known about different recovery trajectories in these patients. More insight in COVID-19 is needed to identify patients at risk for post-COVID-19 syndrome and to develop targeted treatment plans. Similar to our findings, previous studies indicated that experiencing more than five symptoms during the first week of infection is associated with long-term health complaints [6, 8]. From influenza A (H7N9) and acute respiratory distress syndrome survivors it is already known that impaired health-related quality of life, functional disability and psychological problems persisted up to 2 years of follow-up [30–32]. Finally, this study aimed to evaluate the natural course of symptoms among members of online long COVID peer support groups. Therefore, our findings cannot be generalised to all COVID-19 patients.

In conclusion, patients who are all members of online long COVID peer support groups may still experience persistent symptoms 6 months after the onset of symptoms, which can affect work productivity, functional status and quality of life. These findings support the existence of a post-COVID-19 syndrome. More research is needed to better understand the long-term consequences of COVID-19 and to improve guidance and care of these patients.

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