National Institute for Health and Care Excellence

COVID-19 rapid guideline: managing the long-term effects of COVID-19

[A] Evidence reviews for risk factors

NICE guideline NG188

December 2020

Guideline version (Final)

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NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

COVID-19 rapid guideline: managing the long-term effects of COVID-19 (NG188)

Review question 1: risk factors

December 2020

Literature search

NICE's information services team identified relevant evidence through focused evidence searches between 22 and 28 October 2020 (see appendix 3). Additional studies were also considered from NICE surveillance up to 28 October 2020. Results from the literature searches and surveillance were screened using their titles and abstracts for relevance against the criteria from the protocol (see appendix 2). Four reviewers screened titles and abstracts. Having identified the evidence, four reviewers assessed the full text references of potentially relevant evidence to determine whether they met the inclusion criteria for this evidence review. All uncertainties were discussed amongst the reviewers and referred to an adviser if needed. See appendix 4 for the study flow chart of included studies.

Healthcare Improvement Scotland knowledge management team also conducted a search to identify qualitative evidence to support the questions in this review. See Managing the long-term effects of COVID-19: the views and experience of patients, their families and carers for more information. This review will be referred to in this document as "patient lived experience".

Methods and process

This evidence review was developed using the methods and processes described in the methods chapter.

Review question 1

What risk factors are associated with developing post-COVID-19 syndrome?

The review protocol is shown in appendix 2.

Included studies

In total 4,104 references were identified through the searches. Of these, 505 were included and ordered for full text assessment. A total of 58 references were included for the whole guideline, 13 of which were included for this review. Of these, 8 were cohort studies, 4 were cross-sectional studies and 1 was an international longitudinal survey.

See tables 1 and 2

Table 1 Included studies for review question 1: people who have symptoms of COVID-19 for 4 to 12 weeks

Study	Country, study design, dates	Population (n)	COVID-19 disease severity	Time of follow-up	Main risk factors reported
Aliae 2020	Egypt, Cross sectional, July to August 2020	444 patients – 336 (76%) were hospitalised 108 (24%) were non-hospitalised	Not reported	5 weeks since acute illness	Functional restrictions were affected by age, gender, periodic influenza vaccination, smoking, duration since symptoms onset, need for oxygen or ICU admittance, and lastly the presence of coexisting comorbidity.
Assaf 2020	International, Patient-led research, Survey,	640 self-selected people (age range 30 to 49, 62.7%)	Not reported	Limited to evidence from weeks 1 to 8 from acute COVID-19	The analyses suggested that pre-existing asthma might prolong recovery time.
Carvalho-Schneider 2020	France, prospective cohort, March 17 to June 3 2020	150 people with non-critical COVID-19	Non-critical	30 to 60 days from symptom onset	Persisting symptoms at Day 30 were significantly associated with hospital admission at symptom onset, initial clinical presentation, dyspnoea, and abnormal auscultation. Persisting clinical symptoms at Day 30 were associated with age class 40-60 years old but not pre-existing comorbid conditions. At Day 60, the associations remained for hospital admission and abnormal auscultation at symptom onset as well as the same age class 40 to 60 years old.
Cirulli 2020	USA, cross-sectional, April 2020 to September 2020	233 with positive COVID-19 test (out of a sample of 21,359, median age 58 years)	Mild	30, 60 and 90 days from symptom onset	The total number of initial symptoms was the strongest predictor of long-term symptoms. Dyspnoea was the most strongly associated with long-term symptoms after correction (p=0.001).
D'Cruz 2020	UK, prospective cohort, June to July 2020	119 COVID-19 survivors who had been hospitalised with PCR-confirmed severe COVID-19	Severe	4 to 6 weeks from discharge	There was no relationship between age groupings and persistent post-COVID symptoms, self-reported functional disability, or physiological impairment.

Study	Country, study design, dates	Population (n)	COVID-19 disease severity	Time of follow-up	Main risk factors reported
		pneumonia (mean age 58.7)			
Daher 2020	Germany, retrospective cohort, February to May 2020	33 people with COVID-19 who were discharged from the isolation ward (mean age 64 years)	Severe	6 weeks from discharge	Hospitalised patients with severe COVID-19, who did not require mechanical ventilation, are unlikely to develop pulmonary long-term problems after discharge but frequently suffer from symptoms of fatigue (45%).
Goertz 2020	Netherlands and Belgium, Cross sectional, 4 to 11 June 2020	2113 Facebook group members, Lung Foundation Netherlands website (median age 47 years)	Mild	79 days since onset of first symptoms	The multiple regression model statistically significantly predicted the number of symptoms at follow-up.
Kamal 2020	Egypt, Cross-sectional (date not reported)	287 COVID-19 survivors (mean age 32.3 years)	Mild	More than 20 days since last negative PCR	Severe cases expressed high severity manifestations compared with those suffering from mild conditions. Hence, the severity of manifestations is also related to the age and comorbidities of the involved subjects.
Sudre 2020	UK, USA, Sweden, Prospective cohort	4182 users of the COVID symptom study app	Not reported	Long (more than 28 days) [LC28] and short duration (reporting symptoms lasting less than 10 days).	Age was significantly associated with LC28, rising from 9.9% in 18 to 49-year olds to 21.9% in those aged 70 and over; clear escalation in OR by age decile with females aged 50 to 60 had the highest odds. LC28 disproportionately affected women (14.9%) compared to men (9.5%), although this sex effect was not significant in older age-groups. LC28 affected all socioeconomic groups. Asthma was the only/ unique pre-existing condition providing significant association with LC28 (OR 2.14 (1.55, 2.96). Fatigue (97.7%) and headache (91.2%) were the most reported symptoms in those with LC28, followed by anosmia and lower respiratory symptoms.
Vaira 2020	Italy, prospective cohort, (date not reported)	138 people with COVID-19 (mean age 51.2 years)	Most likely mild	Up to 60 days from COVID-19 diagnosis	The risk of developing a long-lasting disorder became significant at 10 days for taste (OR 40.2 (2.204, 733.2) and also for smell (OR 58.5 (3.278, 1043.5)

Table 2 Included studies for review question 1: people who have symptoms of COVID-19 beyond 12 weeks

Study	Country, study design, dates	Population (n)	COVID-19 disease severity	Time of follow-up	Main risk factors reported
Dennis 2020	UK, prospective cohort, April to August 2020	201 people (mean age 44) with previous SARS-COV-2 infection who had been hospitalised (n=164) and non-hospitalised (n=37)	Not reported	3 to 5 months after initial illness	Single (66%) and multi-organ (25%) impairment was observed and was significantly associated with risk of prior COVID-19 hospitalisation (p<0.05).
Cirulli 2020	USA, cross-sectional, April 2020 to September 2020	233 with positive COVID-19 test (out of a sample of 21,359, median age 58 years)	Mild	30, 60 and 90 days from symptom onset	The total number of initial symptoms was the strongest predictor of long-term symptoms. Dyspnoea was the most strongly associated with long-term symptoms after correction (p=0.001).
Xiong 2020	China, retrospective cohort, up to 1st March 2020	538 COVID-19 survivors who were discharged from hospital (median age 52 years)	Moderate	3 months after discharge	Dyspnoea during hospitalisation was associated with subsequent physical decline/fatigue, post-activity polypnoea and resting heart rate increases, but not specifically with alopecia. A history of asthma during hospitalisation was associated with subsequent post-activity polypnoea sequelae. A history of pulse 90 bpm during hospitalisation was associated with resting heart rate increase symptoms in convalescence.
Valiente-De Santis 2020	Spain, prospective cohort, 14th March to 15th April	108 people with previous acute SARS-CoV-2 infection (age >65 years 26.9%)	Mild to severe	12 weeks after acute phase	The persistence of symptoms in patients with COVID occurs in the majority of patients (75.9%) 12 weeks after the acute episode, especially in patients <65 years (p=0.026) and health-care workers (p-0.046). There was no association between severity of disease, Charlson >3, D-Dimer >500 ng/mL or specific treatment for COVID-19 with persistent symptoms.

Key results

Risk factors and symptoms of COVID-19 between 4 to 12 weeks

Mixed hospitalised and non-hospitalised people

Low quality evidence from 8 studies showed an association between the following risk factors and persistent symptoms at 4 to 12 weeks:

- asthma (2 studies: Assaf et al, 2020; Sudre et al, 2020)
- vitamin D deficiency (1 study: Assaf et al, 2020)
- symptoms associated with age (3 studies: Aliae et al, 2020; Carvalho-Schneider et al, 2020; Sudre et al, 2020)
- hospital admission, abnormal auscultation, dyspnoea (1 study: Carvalho-Schneider et al, 2020)
- severity of illness (2 studies: Aliae et al, 2020; Kamal et al, 2020)
- taste and smell disorders at 10 days (1 study: Vaira et al, 2020)
- number of symptoms (3 studies: Cirulli et al, 2020; Goërtz et al, 2020; Sudre et al, 2020)
- demographics and clinical characteristics (2 studies: Aliae et al, 2020; Sudre et al, 2020)

Hospitalised people

Low quality evidence from 1 study (Daher et al, 2020) found that people hospitalised with severe COVID-19 and not mechanically ventilated were unlikely to develop pulmonary or cardiac complications but did suffer from fatigue at 4 to 12 weeks.

Low quality evidence from 1 study (D'Cruz et al, 2020) found no relation between age and persistent symptoms at 4 to 12 weeks.

Risk factors and symptoms of COVID-19 beyond 12 weeks

Mixed hospitalised and non-hospitalised people

Low quality evidence from 1 study (Dennis et al, 2020) found prior COVID-19 hospitalisation was associated with single and multi-organ impairment at 3 to 5 months after initial illness.

Low quality evidence from 1 study (Valiente-De Santis et al, 2020) indicated that most hospital emergency attendees with COVID-19 exhibited at least one out of a broad range of potentially related symptoms 12 weeks after the acute episode; this was especially the case for patients under 65 years and healthcare workers. No association was found between severity of disease, Charlson score, D-Dimer or specific treatment for COVID-19 with persistent symptoms at 12 weeks.

Hospitalised people

Low quality evidence from 1 study (Xiong et al, 2020) indicated that dyspnoea during hospitalisation was associated with physical decline/fatigue, post-activity polypnoea and resting heart rate increase (at least 20 beats per minute more after COVID-19 than before) beyond 12 weeks.

Non-hospitalised people

Low quality evidence from 1 study (Cirulli et al, 2020) indicated that the total number of symptoms is the strongest predictor of long-term symptoms and the initial symptom of dyspnoea is also a significant predictor. Symptoms of low back pain, chest pain, blood types A and A+, were not found to be significant.

Strengths and limitations

Due to the novelty of the topic and the sparseness of the evidence base, the search was extended to include descriptive as well as analytic study designs, with inherent potential biases. The risk factor outcomes have been identified in observational studies of varying designs, but primarily the appropriate cohort study design. However, the primary aim of the studies was not necessarily to measure risk factors. People were recruited to the studies in different ways, some of which were only those active on social media and are less likely to be representative of the whole

population. All of the included studies were in adults, with no included studies covering children and no studies reporting extrapolation to children.

The risk of bias (RoB) for studies included in this review was assessed as high using the CASP critical appraisal checklist for cohort studies. See 'quality' for each study in Appendix 6 Evidence tables.

All 13 included studies, of either descriptive cohort or analytical cross-sectional design, were considered to have high RoB, except for Sudre et al (2020), with moderate RoB.

Expert panel discussion

This section describes how the expert panel considered the evidence in relation to the recommendations within the guidance.

The panel were interested in the extent to which risk factors are associated with post-COVID-19 syndrome (as defined by the study).

Quality of the evidence

In view of the diverse range of risk factors reported in the included studies and the low quality of the evidence, compounded by small sample sizes, the panel were unable to draw firm conclusions from the results on specific risk factors.

The panel noted the low quality of the evidence and agreed that they could not be confident in drawing firm conclusions on specific risk factors. The sampling techniques used in the included studies may have introduced selection bias and may not be representative of the population. The panel also raised concerns that a person's description of symptoms can be a confounder, resulting from factors such as cultural differences and individual perceptions of severity. Whilst evidence from patients' lived experience indicated that people could experience a large number of different symptoms which changed and fluctuated in severity during the course of long COVID-19, these qualitative studies did not specifically explore the relationship between risk factors and symptoms experienced.

Overall, the panel did not consider the evidence to be generalisable to the whole population.

Trade-off between benefits and harms

In view of the inconclusive evidence, the panel cautioned against a disproportionate focus on specific risk factors to the exclusion of others. The panel stressed the importance of ongoing monitoring of people who do not have the main risk factors under consideration. These people may be recovering as expected up to 12 weeks but might develop symptoms thereafter. Nevertheless, the panel emphasised the need for clinical suspicion of ongoing symptoms, with particular attention to the most common symptoms which include dyspnoea and fatigue. The panel noted that these symptoms, which were reflected in both the quantitative and patient lived experience evidence, can be considered 'warning signs' that should prompt follow up or assessment for post-COVID-19 syndrome. This was also supported by expert testimony.

Implementation and resource considerations

The panel noted resource implications of time and expertise needed to assess all the risk factors and whether this could be justified based on limited evidence.

The panel advised the need to avoid directing people along specific pathways inappropriately, for example where asthma is suspected but unconfirmed.

As described previously, the panel concluded that a research recommendation was needed to explore the question of risk factors further before conclusive recommendations could be made.

Other considerations

The panel suggested that returning to work may be a modifiable risk factor and in the absence of evidence should be considered as part of a research recommendation. The panel also advised that, since the studies were focused on adults, a research recommendation on children, young people and older people should be considered.

Appendix 1 Methods used to develop the guidance

Please see the methods chapter for details on how this guideline was developed.

Appendix 2 Review protocols

Review question 1: What risk factors are associated with developing post-COVID-19 syndrome?

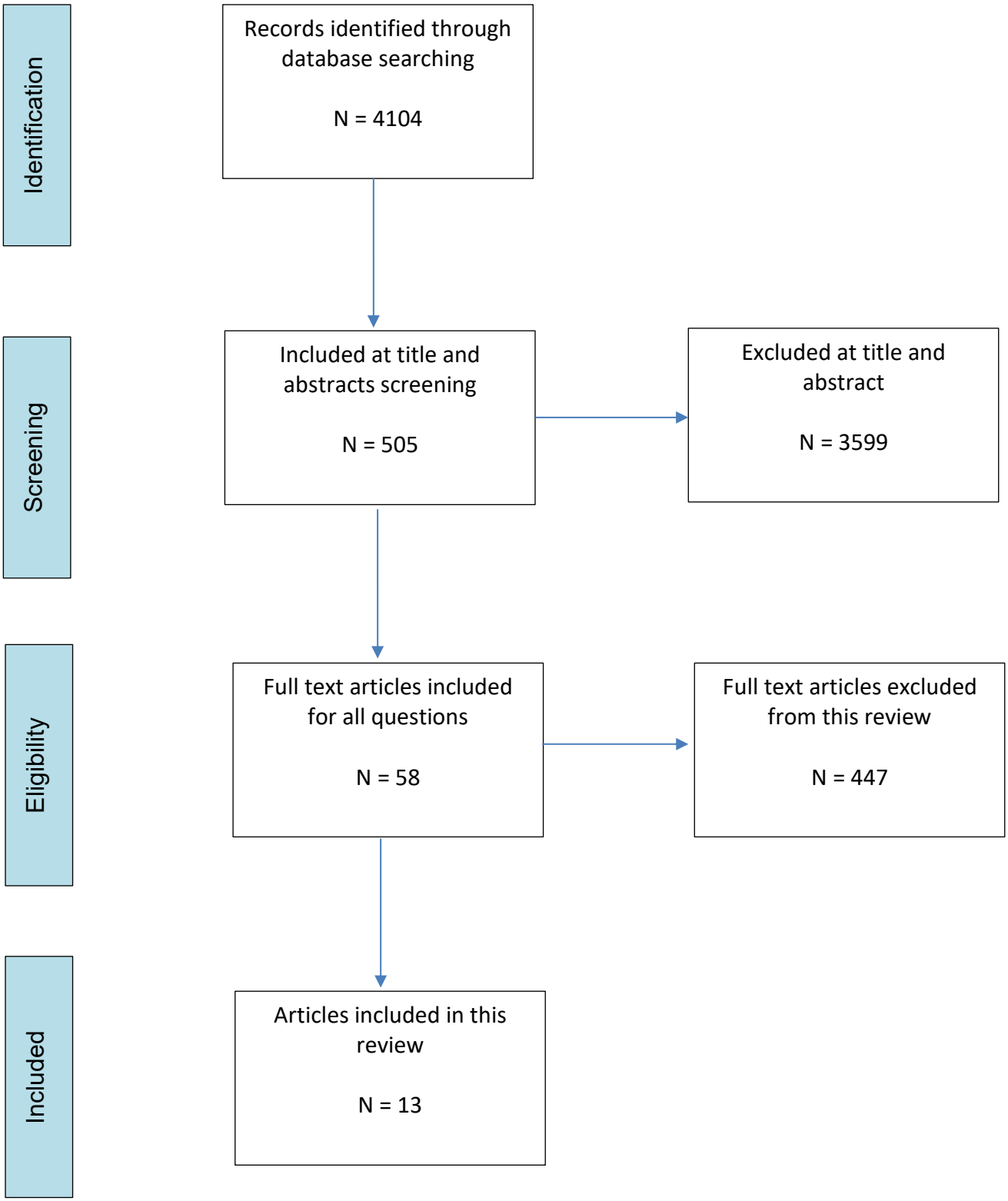
Criteria	Notes
Population	People experiencing symptoms or clusters of symptoms (ongoing physical and mental health) from the onset of acute COVID-19.
Exposure	Any
Comparators	Not applicable
Outcomes	Risk factors or factors that are associated with post-COVID-19 syndrome (as defined by the study)
Settings	Any
Subgroups	• Groups as defined in the EIA for example, age, sex, ethnicity • Diagnosis of COVID-19 (e.g. confirmed or high clinical suspicion)
Study types	Any The following study design types for this question are preferred. Where these studies are not identified, other study designs will be considered. Preferred: • Systematic reviews of cohort studies • Cohort studies (prospective or retrospective) • Cross-sectional studies
Countries	Any
Timepoints	Not applicable
Other exclusions	None

Appendix 3 Literature search strategy

Database strategies

Please refer to the search history record for full details of the search.

Appendix 4 Study flow diagram



Appendix 5 Included studies

Aliae, Mohamed-Hussein, Islam, Galal, Mahmoud, Saad et al. (2020) Post-COVID-19 Functional Status: Relation to age, smoking, hospitalization and comorbidities. MedRxiv

Carvalho-Schneider, Claudia, Laurent, Emeline, Lemaignen, Adrien et al. (2020) Follow-up of adults with non-critical COVID-19 two months after symptoms' onset. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases

Cirulli, Elizabeth T., Barrett, Kelly M. Schiabor, Riffle, Stephen et al. (2020) Long-term COVID-19 symptoms in a large unselected population. medRxiv: 2020100720208702

D'Cruz, Rebecca F., Waller, Michael D., Perrin, Felicity et al. (2020) Chest radiography is a poor predictor of respiratory symptoms and functional impairment in survivors of severe COVID-19 pneumonia. ERJ Open Research

Daher, Ayham, Balfanz, Paul, Cornelissen, Christian et al. (2020) Follow up of patients with severe coronavirus disease 2019 (COVID-19): Pulmonary and extrapulmonary disease sequelae. Respiratory Medicine: 106197 to 106197

Dennis, Andrea, Wamil, Malgorzata, Kapur, Sandeep et al. (2020) Multi-organ impairment in low-risk individuals with long COVID. medRxiv: 2020101420212555

Goërtz, Yvonne M. J., Herck, Maarten Van, Delbressine, Jeannet M. et al. (2020) Persistent symptoms 3 months after a SARS-CoV-2 infection: the post-COVID-19 syndrome? ERJ Open Research

Kamal, Marwa, Abo Omirah, Marwa, Hussein, Amal et al. (2020) Assessment and Characterization of Post-COVID-19 manifestations. International journal of clinical practice: e13746

Patient Led Research for, COVID-19 Report: What Does COVID-19 Recovery Actually Look Like? An Analysis of the Prolonged COVID-19 Symptoms Survey by Patient-Led Research Team.

Sudre, Carole H., Murray, Benjamin, Varsavsky, Thomas et al. (2020) Attributes and predictors of Long-COVID: analysis of COVID cases and their symptoms collected by the COVID Symptoms Study App. medRxiv: 2020101920214494

Vaira, L A, Hopkins, C, Petrocelli, M et al. (2020) Smell and taste recovery in coronavirus disease 2019 patients: a 60-day objective and prospective study. The Journal of laryngology and otology 134(8): 703 to 709

Valiente-De Santis, Lucia, Ines, Perez-Camacho, Beatriz, Sobrino et al. (2020) Clinical and immunoserological status 12 weeks after infection with COVID-19: prospective observational study. MedRxiv

Xiong, Qiutang, Xu, Ming, Li, Jiao et al. (2020) Clinical sequelae of COVID-19 survivors in Wuhan, China: a single-centre longitudinal study. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases

Appendix 6 Evidence tables

Aliae 2020

<table>
<tr><td>Bibliographic reference/s</td><td>Aliae, Mohamed-Hussein, Islam, Galal, Mahmoud, Saad et al. (2020) Post-COVID-19 Functional Status: Relation to age, smoking, hospitalization and comorbidities. medRxiv</td></tr>
<tr><td>Questions relevant to?</td><td>Investigations, risk factors, monitoring</td></tr>
<tr><td>Publication status</td><td>Preprint</td></tr>
<tr><td>Study type</td><td>Cross sectional</td></tr>
<tr><td>Quality</td><td>Low quality evidence
CASP critical appraisal checklist (cohort studies): High risk of bias</td></tr>
<tr><td>Objective</td><td>Assess the Post COVID-19 functional status in Egypt by the PCFS scale and to evaluate if age, gender, comorbidities have any effect on functional limitations</td></tr>
<tr><td>Study date</td><td>15th July to 13th August 2020</td></tr>
<tr><td>COVID-19 prevalence (high/low) if reported</td><td>Not reported</td></tr>
<tr><td>Country/Setting</td><td>Egypt</td></tr>
<tr><td>Population (including n)</td><td>444 who have had COVID-19 They were interviewed in our follow-up clinics or by calls</td></tr>
<tr><td>Time since acute COVID-19</td><td>35.31±18.75 days
4 to 12 weeks grouping</td></tr>
<tr><td>Investigations</td><td>Post-COVID-19 Functional Status Scale (PCFS) scale</td></tr>
<tr><td>Baseline characteristics</td><td>
<table>
<tr><td></td><td>N=444</td></tr>
<tr><td>Mean age</td><td>33.09±12.09 years</td></tr>
<tr><td>Male</td><td>192 (43.2%)</td></tr>
<tr><td>Female</td><td>252 (56.8%)</td></tr>
<tr><td>Reside in urban areas</td><td>316 (71.2%)</td></tr>
<tr><td>Reside in rural areas</td><td>125 (28.2%)</td></tr>
<tr><td>Non-smoker</td><td>346 (77.9%)</td></tr>
<tr><td>Smoker</td><td>58 (13.1%)</td></tr>
<tr><td>Former smoker</td><td>40 (9%)</td></tr>
<tr><td>Admitted to hospital</td><td>336 (75.7%)</td></tr>
<tr><td>Comorbidity</td><td>111 (25.5%)</td></tr>
</table>
</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>• Confirmed COVID-19 in the registry of Ministry of Health and Population in Egypt (positive or indeterminate COVID-19 PCR test or presumed presence of Covid-19 based on clinical & radiological criteria).</td></tr>
<tr><td>Follow up</td><td>Around 5 weeks</td></tr>
<tr><td>Main results</td><td>
<table>
<tr><td>Post COVID-19 Functional status scale</td><td>N=444</td></tr>
<tr><td>No limitation (Grade 0)</td><td>89 (20%)</td></tr>
<tr><td>Negligible limitation (grade 1)</td><td>280 (63.1%)</td></tr>
<tr><td>Slight limitation (Grade 2)</td><td>64 (14.4%)</td></tr>
<tr><td>Moderate limitation (Grade 3)</td><td>9 (2%)</td></tr>
</table>
</td></tr>
</table>

Severe (Grade 4)	2 (0.5%)

Association between Demographic and Clinical characteristics and POST COVID19 Functional Status Scale (PCFS)

Variable	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	P value
Age	30.06±10.28	33.11±11.73	36.62±14.12	37.33±18.35	32.50±6.36	**0.003**
Male	50 (26%)	120 (62.5%)	19 (9.9%)	2 (1.0%)	1 (0.5%)	**0.014**
Female	39 (15.5%)	160 (63.5%)	45 (17.9%)	7 (2.8%)	1 (0.4%)	
Residence: Urban	59 (18.7%)	212 (67.1%)	38 (12%)	6 (1.9%)	1 (0.3%)	0.069
Residence: Rural	30 (23.4%)	68 (53.1%)	26 (20.3%)	3 (2.3%)	1 (0.8%)	
Duration since symptoms onset in days	38.87±17.69	34.52±19.01	33.67±17.79	38.89±26.00	25.00±14.14	**<0.001**
Quarantine: Hospital	17 (14.9%)	76 (66.7%)	17 (14.9%)	3 (2.6%)	1 (0.9%)	0.516
Quarantine: Home	72 (21.8%)	204 (61.8%)	47 (14.2%)	6 (1.8%)	1 (0.3%)	
O_2 supplementation: Yes	0 (0%)	70 (76.1%)	19 (20.7%)	2 (2.2%)	1 (1.1%)	**<0.001**
O_2 supplementation: No	89 (25.3%)	210 (59.7%)	45 (12.8%)	7 (2%)	1 (0.3%)	
ICU admission: Yes	2 (3.3%)	42 (70%)	14 (23.3%)	1 (1.7%)	1 (1.7%)	**0.003**
ICU admission: No	87 (22.7%)	238 (62%)	50 (13%)	8 (2.1%)	1 (0.3%)	
Comorbidity: Yes	0 (0%)	36 (32.4%)	64 (57.7%)	9 (8.1%)	2 (1.8%)	**<0.001**
Comorbidity: No	89 (26.7%)	244 (73.3%)	0 (0%)	0 (0%)	0 (0%)	

Most of the COVID-19 recovered cases have diverse degrees of functional restrictions ranging from negligible to severe based on PCFS. These restrictions were affected by age, gender, periodic influenza vaccination, smoking, duration since symptoms onset, need for oxygen or ICU admittance, and lastly the presence of coexisting comorbidity.

	It is recommended that Post COVID-19 monitoring programs should be implemented in specific clinical settings or as an out-patients program to follow the functional status of patients in 1, 3, 6 months visits to support the complete care for cases recovered from COVID-19. Furthermore, extended monitoring using simple scales as PCFS is necessary to determine whether these functional deficits after COVID- 19 recovery persist or not.
Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	Limitations: • Lack of data of functional status before COVID-19 • history of the symptoms both at the onset of COVID-19 and after recovery is not included • pharmacologic therapy given to the patients was not mentioned • random selection bias may be present • inability for personal face-to- face interview in some cases
Additional references	Clinicaltrial.gov: NCT04479293

Patient-Led Research Team

Bibliographic reference/s	**Assaf, G., Davis, H. et al (2020): An Analysis of the Prolonged COVID-19 Symptoms Survey by Patient-Led Research Team. https://patientresearchcovid19.com /research/report-1/**
Questions relevant to?	**Symptoms (including variation over time) and Prognostic (not sure we have a question on prognosis specifically?)**
Publication status	Published on a patient web site). "Survey questions and symptoms were aggregated and curated by patients themselves with expertise in research and survey design. Analysis was also conducted by patients themselves with expertise in both quantitative and qualitative data analysis."
Study type	Participatory research with patient-led analysis: Cross-sectional survey (Prolonged COVID-19 Symptoms Survey).
Quality	Very low quality JBI critical appraisal checklist rating (analytical cross-sectional studies): High risk of bias
Objective	To understand what Covid recovery looks like
Study date	11/5/20 (based on data at 2/5/20)
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	Most respondents are from the U.S. (71.7%), followed by the U.K. (12.7%), Netherlands (4.2%), Canada (1.9%), Belgium (1.7%), and France (1.4%). Other countries represented include Sweden, Ireland, Germany, Belgium, Scotland, Italy, Russia, Spain, South Africa, Greece, and India. N.B. It was an online survey of an online patient group.
Population (including n)	Online patient group – self-selected both as to who was in the group and who responded to the survey (n=640)
Time since acute COVID-19	Variable – up to 6 weeks
Interventions/ Prognostic factors	**Interventions:** not applicable **Prognostic factors:**

	Over half of respondents (57.8%) listed at least one pre-existing condition, with the most prevalent conditions being asthma and vitamin D deficiency.
Baseline characteristics	62.7% were aged between 30 and 49 years 76% were White/Caucasian 76.6% were female
Inclusion and exclusion criteria	None specific
Follow up	None
Main results	**Symptoms and natural course of illness** The vast majority of participants with symptoms experienced fluctuations both in the type (70% reporting) and intensity (89% reporting) of symptoms over the course of being symptomatic. At time they took the survey, 90.6% of the respondents had not recovered (self-interpreted recovery). For the 60 respondents who had recovered, the average length of time of being symptomatic was 27 days. Respondents who had not recovered had been experiencing symptoms for an average of 40 days, with a large proportion experiencing symptoms for 5-7 weeks. "Survival analysis" shows that the chance of full recovery by day 50 is smaller than 20%. **Prognostic factors:** "Our analyses suggest pre-existing asthma might prolong recovery time."
Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	Authors note: "When considering the results of this survey, it is important to keep in mind that this sample is not representative of all COVID-19 patients. Sampling bias is at work here: both in who would be willing and able to take a survey, and who would have exposure to the survey. We consider this sample to be disproportionately, white, cis-gender female and U.S.-based; we plan to intentionally conduct broader outreach to create a subsequent version of the survey and report with a more diverse group of respondents. Further, unless indicated, we have not completed significance testing on our findings. Therefore, our results should not be taken as being representative of the COVID-19 experience." Reviewer comments: Given the study type, including the nature of the sampling, it is not certain how representative and therefore generalisable this data is. Note that numerical data was not provided for symptoms in the report – only graphs
Additional references	https://docs.google.com/document/d/1KmLkOArlJem-PArnBMbSp-S_E3OozD47UzvRG4qM5Yk/edit# ('cleaned up' version of same report)

Carvalho-Schneider 2020

Bibliographic reference/s	**Carvalho-Schneider, Claudia, Laurent, Emeline, Lemaignen, Adrien et al. (2020) Follow-up of adults with non-critical COVID-19 two months after symptoms' onset. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases**
Questions relevant to?	**Prevalence, risk factors**

<table>
<tr><td>Publication status</td><td>Journal pre-proof</td></tr>
<tr><td>Study type</td><td>Prospective cohort</td></tr>
<tr><td>Quality</td><td>Low quality evidence
CASP critical appraisal checklist (cohort studies): High risk of bias</td></tr>
<tr><td>Objective</td><td>To describe the clinical evolution and predictors of symptom persistence during 2-month follow-up in adults with non-critical COVID-19.</td></tr>
<tr><td>Study date</td><td>March 17 to June 3, 2020</td></tr>
<tr><td>COVID-19 prevalence (high/low) if reported</td><td>Not reported</td></tr>
<tr><td>Country/ Setting</td><td>France</td></tr>
<tr><td>Population (including n)</td><td>150 patients with non-critical COVID-19</td></tr>
<tr><td>Time since acute COVID-19</td><td>30 to 60 days
4 to 12 weeks grouping</td></tr>
<tr><td>Interventions/ Prognostic factors</td><td>None</td></tr>
<tr><td>Baseline characteristics</td><td>See results</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>Inclusion criteria:
Adult patients (≥ 18 years old) with a confirmed diagnosis of COVID-19 (positive RT-PCR for SARS-CoV-2)
Received medical care in the hospital either via hospitalisation to after consultation at the hospital’s outpatient clinical evaluation centre
Exclusion criteria:
Patients deceased or admitted to the ICU (considered as critical disease according to the 90 WHO guidance for clinical management of COVID-19)
Residents of retirement/nursing homes or long-term care facilities
Patients transferred to another healthcare facility (i.e. other hospital, rehabilitation institution, retirement home).
Those unable to answer a phone questionnaire
Patients lost-to-follow-up patients at D30.</td></tr>
<tr><td>Follow up</td><td>30 and 60 days</td></tr>
<tr><td>Main results</td><td>Patient characteristics 30 and 60 days after symptom onset
<table>
<tr><td>--</td><td>--</td><td colspan="4">≥1 persisting symptom at 30 or 60 days</td></tr>
<tr><td>--</td><td>Total
N=150</td><td>30 days
N =103</td><td>P value</td><td>60 days
N=86</td><td>P value</td></tr>
<tr><td>Female</td><td>84 (56%)</td><td>59 (57.3%)</td><td>0.6</td><td>48 (55.8%)</td><td>0.3</td></tr>
<tr><td>Age (years), mean (SD)</td><td>49 (15)</td><td>--</td><td>0.06</td><td>--</td><td>0.026</td></tr>
<tr><td><30</td><td>16 (10.7%)</td><td>7 (6.8%)</td><td>--</td><td>4 (4.7%)</td><td>--</td></tr>
<tr><td>30 to 39</td><td>32 (21.3%)</td><td>21 (20.4%)</td><td>--</td><td>19 (22.1%)</td><td>--</td></tr>
</table></td></tr>
</table>

40 to 49	27 (18%)	24 (23.3%)	--	23 (26.7%)	--
50 to 59	37 (24.7%)	28 (27.2%)	--	21 (24.4%)	--
60 to 69	19 (12.7%)	11 (10.7%)	--	10 (11.6%)	--
≥70	19 (12.7%)	12 (11.7%)	--	9 (10.5%)	--
Healthcare professional	75 (50%)	49 (47.6%)	0.38	43 (50%)	0.6
Comorbid conditions	--	--	0.75	--	0.5
0	69 (46%)	46 (45.6%)	--	2 (48.8%)	--
1	52 (34.7%)	35 (34%)	--	25 (29.1%)	--
2 or more	28 (18.7%)	21 (20.4%)	--	19 (22.1%)	--
Initial hospitalisation	53 (35.3%)	43 (41.7%)	**0.017**	37 (43%)	**0.011**
Initial clinical presentation	--	--	**0.02**	--	0.2
Mild/moderate COVID	116 (77.3%)	74 (71.8%)	--	64 (74.4%)	--
Severe COVID	34 (22.7%)	29 (28.2%)	--	22 (25.6%)	--

Patient symptoms at onset, 30 days and 60 days

--	**Onset (n=150)**	**30 days (n=150**	**60 days (n=130)**
Fever (>38°C temperature)	76 (51.4%)	5 (3.6%)	0 (0%)
Dyspnoea/shortness of breath	49 (42.2%)	16 (10.7%)	10 (7.7%)
Chest pain	15 (14%)	27 (18%)	17 (13.1%)
Abnormal auscultation	46 (39.3%)	--	--
Flu-like symptoms	129 (87.2%)	54 (36%)	28 (21.5%)
Digestive disorders	48 (33.1%)	26 (17.3%)	15 (11.5%)
Including diarrhoea	44/48 (91.7%)	13 (50%)	5/15 (33.3%)
Weight, mean (SD)	78 (19.4)	77.2 (20.2)	75.6 (18.0)
Weight loss ≥5%	--	13 (15.9%)	15 (17.2%)
Anosmia/ageusia	89 (59.3%)	40 (27.8%)	29 (22.7%)
Palpitations	--	9 (6.5%)	14 (10.9%)
Arthralgia	--	13 (9.8%)	21 (16.3%)
Cutaneous signs	--	21 (15.47%)	15 (11.5%)
Sick leave	--	26 (19.7%)	14 (11.2%)

Predictors of persistent COVID-19 symptoms

Symptom	Day 30 OR (95% CI)	Day 60 OR (95% CI)
Oxygen therapy	3.4 [1.2 to 9.5]	1.8 [0.7 to 4.7]
Abnormal auscultation	3.3 [1.3 to 8.0]	2.5 [1.0 to 6.1]
Hospitalisation	2.8 [1.2 to 6.2]	2.9 [1.3 to 6.9]
Dyspnoea	2.4 [1.0 to 5.3]	1.6 [0.7 to 3.9]
Flu-like symptoms	1.3 [0.5 to 3.4]	1.3 [0.5 to 3.5]
Diarrhoea	1.2 [0.6 to 2.7]	1.0[0.5 to 3.5]
Fever	1.2 [0.6 to 2.4]	1.1 [0.5 to 2.2]
Chest pain	1.2 [0.4 to 3.7]	1.4 [0.4 to 5.0]
Anosmia/ageusia	0.9 [0.4 to 1.9]	1.6 [0.8 to 3.4]
Other respiratory signs	0.6 [0.2 to 2.3]	0.7 [0.2 to 2.8]
Female	1.2 [0.6 to 2.4]	1.5 [0.7 to 3.1]
Healthcare professional	0.7 [0.3 to 1.4]	0.8 [0.4 to 5.0]
1 comorbidity	1.0 [0.5 to 2.2]	0.8 [0.4 to 1.8]
2 comorbidities or more	1.5 [0.6 to 4.1]	1.7 [0.6 to 4.8]
Age 30 to 39	3.2 [0.9 to 11.1]	4.2 [1.0 to 17.8]
Age 40 to 49	13.3 [2.8 to 64.1]	15.3 [2.8 to 83.9]
Age 50 to 59	5.2 [1.5 to 18.3]	4.2 [1.0 to 17.3]
Age 60 to 69	2.3 [0.6 to 8.9]	2.9 [0.6 to 13.3]
Age ≥70	2.9 [0.7 to 11.3]	2.6 [0.5 to 12.2]

Summary

- Up to 2 months after symptom onset, two thirds of adults with non-critical COVID-19 had complaints, mainly anosmia/ageusia, dyspnoea or asthenia.
- Persisting symptoms at D30 were significantly associated with hospital admission at symptom onset, initial clinical presentation, dyspnoea, and abnormal auscultation.
- Persisting clinical symptoms at D30 were associated with age class 40 to 60 years old but not pre-existing comorbid conditions.
- At D60, the associations remained for hospital admission and abnormal auscultation at symptom onset as well as the same age class 40 to 60 years old.

Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	Funding: None Limitations: None reported by author
Additional references	N/A

Cirulli 2020

<table>
<tr><td>Bibliographic reference/s</td><td>Cirulli, Elizabeth T., Barrett, Kelly M. Schiabor, Riffle, Stephen et al. (2020) Long-term COVID-19 symptoms in a large unselected population. medRxiv: 2020100720208702</td></tr>
<tr><td>Questions relevant to?</td><td>Prevalence, risk factors</td></tr>
<tr><td>Publication status</td><td>Published</td></tr>
<tr><td>Study type</td><td>Retrospective cohort (survey administered at periodic intervals)</td></tr>
<tr><td>Quality</td><td>Low quality
JBI critical appraisal checklist rating (analytical cross-sectional studies): High risk of bias</td></tr>
<tr><td>Objective</td><td>To characterise the frequency, duration, and other properties of long-term COVID-19 symptoms</td></tr>
<tr><td>Study date</td><td>April 2020 to September 2020</td></tr>
<tr><td>COVID-19 prevalence (high/low) if reported</td><td>Not reported</td></tr>
<tr><td>Country/ Setting</td><td>USA/community</td></tr>
<tr><td>Population (including n)</td><td>General population, regardless of history of COVID-19 infection or test (n=21,359)</td></tr>
<tr><td>Time since acute COVID-19</td><td>30 to 90 days
4 to 12 weeks grouping
And 12+ weeks grouping</td></tr>
<tr><td>Interventions/ Prognostic factors</td><td>None</td></tr>
<tr><td>Baseline characteristics</td><td>See results</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>Inclusion criteria:
Adults
Exclusion criteria:
Children</td></tr>
<tr><td>Follow up</td><td>30,60 and 90 days from symptom onset. Surveys were administered at intervals of 4 to 6 weeks from April to September 2020.</td></tr>
<tr><td>Main results</td><td>Patient characteristics
<table>
<tr><td>Median age (range)</td><td>58 (18 to 89+)</td></tr>
<tr><td>N female (%*)</td><td>11,570 (63.6%)</td></tr>
<tr><td>Ancestry N (%*)
African
East Asian
European
Latinx
South Asian
Other / mixed ancestry</td><td>
367 (2.0%)
302 (1.7%)
15267 (83.7%)
1658 (9.1%)
121 (0.7%)
520 (2.9%)</td></tr>
<tr><td>N with COVID-19 test (%)
Positive (%)
Negative (%)</td><td>3885 (18.2%)
233 (6.0%)
3652 (94.0%)</td></tr>
</table></td></tr>
</table>

N reporting ≥1 symptom (%) ≥1 symptom lasting longer than 30 days (%**) ≥1 symptom lasting longer than 60 days (%**) ≥1 symptom lasting longer than 90 days (%**)	11,680 (54.7%) 1056 (10.1%) 682 (7.1%) 526 (5.6%)
--	--

* adjusted to remove individuals who do not have their sex and ethnicity available.
** adjusted to remove individuals who did not yet have enough days since their symptoms started to qualify.

Patients with at least 1 symptom at 30 days, 60 days and 90 days

--	30 days (%)	60 days (%)	90 days (%)
All patients	--	--	--
Positive test (%)	42.3	33.8	24.1
Negative test (%)	13.3	9.7	8.0
No test	8.6	8.6	6.0
Patients with 5 or less initial symptoms	--	--	--
Positive test (%)	14.3	11*	3.8
Negative test (%)	7*	4.5*	4*
No test	6	3	2
Patients with 5 or more initial symptoms	--	--	--
Positive test (%)	59*	47*	40.6
Negative test (%)	38*	32*	29.3
No test	29*	23*	22*

***Approximate data reported graphically**

Summary

- Respondents were queried about 32 different symptoms that can be indicative of COVID-19 and whether they occurred between Jan 1, 2020 and the survey date.
- Respondents answered surveys between April 2020 and September 2020, and those who responded were asked for longitudinal updates every 4 to 6 weeks.
- Respondents were additionally queried about whether they had taken a COVID-19 test and the result. Of the 21,359 respondents, 233 reported a positive COVID-19 test, 3,652 a negative test, and 17,474 were not tested.

Symptoms lasting longer than 30 days

- Respondents were asked about a set of 32 long-term symptoms, defined as symptoms that lasted longer than 30 days, with initial onset occurring since the start of the pandemic.
- The specific long-term symptoms of anosmia, ageusia, difficulty concentrating, dyspnoea, memory loss, confusion, headache, heart palpitations, chest pain, pain with deep breaths, tachycardia, and dry cough were significantly enriched after 30 days in COVID-19+ cases compared to controls ($p<0.001$). However, after adjusting for the initial number of symptoms in the illness as a covariate, only long-term anosmia, ageusia, memory loss, and headache remained significantly associated with COVID-19 status.

	• These symptoms remained significantly enriched in COVID-19+ cases after 60 days, at which point tachycardia also became significantly enriched in COVID-19+ cases. After 90 days, all of these 5 symptoms, except for memory less, remained significantly enriched in COVID-19+ cases. • Individuals who had more initial symptoms also had more long-term symptoms, regardless of whether they were COVID-19+ cases. • COVID-19+ cases had the highest incidence of continuing symptoms at the 30-, 60-, and 90-day marks, even in the less ill category. **Factors predisposing to long term symptoms** After accounting for the total number of initial symptoms, which was the strongest predictor of long-term symptoms, the only factors to maintain a nominal association were the initial symptoms of dyspnoea, lower back pain, chest pain, and blood type A as well as blood type A+ (marked with *). Dyspnoea was the most strongly associated with long-term symptoms after this correction, at p=0.001.
Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	Funding: None The authors used the total number of initial symptoms reported by each person as a proxy for their severity of illness. Limitations: • The study is a pre-print • Some data was only presented graphically • Due to the relatively low numbers of people with these long-term symptoms, analysis of each individual long-term symptom was underpowered, and a larger sample size is needed to determine which of the other long-term symptoms are truly enriched in individuals with COVID-19, as well as how long they last. • The study was underpowered to identify other factors predisposing to long-term symptoms (n=111 for positive patients with long term information). The population level design limited the ability to capture the rates of long-term symptoms in the most severely ill COVID-19 patients (only 3.4% were hospitalised) although this is also a strength in capturing data on people who were not admitted and included those not tested.
Additional references	N/A

D'Cruz 2020

Bibliographic reference/s	**D'Cruz RF, Waller MD, Perrin F, *et al*. Chest radiography is a poor predictor of respiratory symptoms and functional impairment in survivors of severe COVID-19 pneumonia. *ERJ Open Res* 2020; in press (https://doi.org/10.1183/23120541.00655-2020).**
Questions relevant to?	• Investigations • Monitoring • Risk Factors • Signs and symptoms/prevalence
Publication status	Accepted for publication
Study type	Cohort (prospective)

Quality	Low quality evidence CASP critical appraisal checklist (cohort studies): High risk of bias
Objective	To prospectively investigate clinical, radiological, functional, and psychological COVID-19 sequalae of severe COVID-19 pneumonia, and to identify factors associated with symptomatic and functional recovery
Study date	June to July 2020
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	Kings College Hospital, UK
Population (including n)	119 COVID-19 survivors who had been hospitalised with PCR-confirmed severe COVID-19 pneumonia
Time since acute COVID-19	Median (IQR) times between hospital admission and discharge to follow-up assessment were 76 (71 to 83) days and 61 (51 to 67) days, respectively (4-12 weeks grouping)
Investigations	• Chest radiography • Symptom questionnaires • Mental health screening • Physiological testing • Computed tomography and pulmonary angiography (CTPA)
Baseline characteristics	**Age (years)**: Mean 58.7 SD 14.4 **Sex**: Female 45/119 (37.8%); Male 74/119 (62.2%) **Ethnicity**: White 36/119 (30.3%); Black 52/119 (43.7%); Asian 18/119 (15.1%); Mixed race 5/119 (4.2%); Other 8/119 (6.7%) **BMI (kg/m^2):** 30.0 (25.9-35.2) **Comorbidities:** Any CVD 63/119 (52.9%); Diabetes 41/119 (34.5%); Immunosuppressed 16 (13.4%); Obstructive lung disease 13/119 (10.9%), Malignancy 12/119 (10.1%); End stage renal failure 8/119 (6.7%); Thyroid disease 7/119 (5.9%); Mental health condition 6/119 (5%); Cerebrovascular disease 5/119 (4.2%).
Inclusion and exclusion criteria	• Aged 18 years and above • PCR-confirmed COVID-19 by naso- and oro- pharyngeal swab between 5th March and 28th May 2020 • Severe COVID-19 pneumonia defined as requiring hospitalisation for ≥48 hours and a fraction of inspired oxygen (FiO_2) of ≥40% or intensive care unit (ICU) admission
Follow up	Face to face assessment 4 to 6 weeks post discharge

Main results	**At follow-up:** There was no relationship between age groupings and persistent post-COVID symptoms, self-reported functional disability, or physiological impairment. **Breathlessness**: (Medical Research Council Breathlessness Scale, mMRC): • 55/115 (46.2%) had not returned to pre-COVID mMRC • Of these, 11/55 (20%) had no pre-existing comorbidity • Comorbid obstructive lung disease was associated with failure of mMRC recovery to baseline (OR 5.06 95%CI 1.33 to 19.2) **Post-COVID Functional Status (PCFS)**: • ≥2 in 47/115 (40.9%) • Comorbid obstructive lung disease was associated with PCFS ≥2 (OR 2.84 95%CI 1.01 to 7.98) **Persistent symptoms:** • Median 4 IRQ (2-5) • 11% reported no persistent symptoms • Burdensome breathlessness (numerical rating scale, NRS ≥4): 37/115 (32.2%) • Persistent cough (NRS ≥1): 49/115 (42.6%) • Burdensome cough (NRS ≥4): 8/115 (7%) • Fatigue: 78/115 (67.8%) • Sleep disturbance: 65/115 (56.5%) • Pain (commonly reported in shoulder, chest, lower limbs and back): 57/115 (49.6%) • Pre-morbid obstructive lung disease was associated with persistent (NRS ≥1) breathlessness (OR 8.04 95%CI 0.19 to 21.4) and cough (OR 3.43 95% CI 0.98 to 12.0), but not burdensome (NRS ≥4) breathlessness or cough (OR 1.97 95%CI 0.60 to 6.47 and OR 2.27 95% CI 0.38 to 13.7, respectively) • There were no associations between the presence or absence of pre-existing comorbidities and persistent fatigue, sleep disturbance or pain **Mental health outcomes:** • PHQ-9 score ≥9: 20/115 (18%) • GAD-7 score ≥9: 25/113 (22.1%) • Trauma screen questionnaire ≥6: 28/113 (24.8%) • 6-item Cognitive impairment test ≥8: 21/97 (21.6%) **Physiological outcomes:** • 4-metre gait speed (4MGS): 44/115 (38.3%) had a 4MGS <0.8m/s; 71/115 (61.7%) • Sit to stand (STS): The number of repetitions performed were below the 2.5 percentile in 56/109 (52%) • There were no adverse events during physiological testing. • There were no associations between pre-morbid obstructive lung disease and physiological functional impairment (OR 0.68 95%CI 0.16 to 2.95) • Cardiovascular disease was associated with a 4MGS <0.8 m/s (OR 3.95 95%CI 0.42 to 2.49). **Chest radiography** • Evidence of COVID-related lung disease (RALE score >4): 15/119 (13%)

	CTPA (for patients with abnormal chest radiography, persistent respiratory symptoms or exercise desaturation) • Features of COVID-related interstitial lung disease and/or airways disease: 42/56 (37.5%) • No pulmonary emboli were identified on CT pulmonary angiography • Presence of COVID-related CT abnormalities were associated with mental health screening questionnaires (PHQ-9 ≥9, GAD-7 ≥9 and/or Trauma Screening Questionnaire ≥6) (χ^2 =3.98 p=0.046 95%CI -0.56 to -0.02) but not with any measure of patient reported or physiological functional impairment • Only 21% of patients with abnormal CT findings also had an abnormal follow-up chest radiograph • 78% of those with ≥4% desaturation during STS also had abnormal CT findings • 33 patients had a normal chest radiograph (RALE score 0-4) and an abnormal CT • 9 patients had both an abnormal chest radiograph (RALE score >4) and abnormal CT • Amongst those with abnormal CT scans, presence or absence of radiographic abnormalities was not predictive of any patient-reported or physiological outcome measure **Summary:** Persistent symptoms, adverse mental health outcomes and physiological impairment are common 2 months after severe COVID-19 pneumonia. Follow-up chest radiograph is a poor marker of recovery, therefore holistic face-to-face assessment is recommended to facilitate early recognition and management of post-COVID sequelae
Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	**Statistical analysis:** Group comparisons were performed using independent t-tests and Chi square (χ^2) tests. Ordinal logistic regression modelling was used to identify factors associated with measures of COVID-19 recovery. **Limitations:** • Unable to perform lung function testing in serial patients due to decontamination procedures required limiting conclusions on respiratory sequelae • Conventional field walking tests to evaluate exercise capacity (6-minute walk test (6MWT), incremental shuttle walk test (ISWT)) were impractical in the clinic setting. • Authors devised their own definition of “severe” COVID-19 pneumonia which may have missed some patients with persistent symptoms or functional disability. • Data collected from a single, urban teaching centre which may limit generalisability **Funding:** This study received no specific funding or grant from any agency in the public, commercial, or not-for-profit sectors. RFD is funded by a National Institute for Health Research (NIHR) Doctoral Research Fellowship (RFD)
Additional references	N/A

Daher 2020

<table>
<tr><td>Bibliographic reference/s</td><td>Daher, Ayham, Balfanz, Paul, Cornelissen, Christian et al. (2020) Follow up of patients with severe coronavirus disease 2019 (COVID-19): Pulmonary and extrapulmonary disease sequelae. Respiratory Medicine: 106197 to 106197</td></tr>
<tr><td>Questions relevant to?</td><td>Investigations, prevalence, risk factors</td></tr>
<tr><td>Publication status</td><td>Published</td></tr>
<tr><td>Study type</td><td>Cohort (retrospective)</td></tr>
<tr><td>Quality</td><td>Low quality evidence
CASP critical appraisal checklist (cohort studies): High risk of bias</td></tr>
<tr><td>Objective</td><td>To investigate pulmonary impairments, as well as the prevalence of other organ dysfunctions and psychological disorders in patients with COVID-19 six weeks after discharge from hospital</td></tr>
<tr><td>Study date</td><td>February to May 2020</td></tr>
<tr><td>COVID-19 prevalence (high/low) if reported</td><td>Not reported</td></tr>
<tr><td>Country/ Setting</td><td>Germany</td></tr>
<tr><td>Population (including n)</td><td>33 patients with COVID-19 who were discharged from the isolation ward and followed up 6 weeks after discharge
All 33 patients had a severe disease during their hospital stay</td></tr>
<tr><td>Time since acute COVID-19</td><td>Time from discharge to follow up 56 (48 to 71) days
4 to 12 weeks grouping</td></tr>
<tr><td>Investigations</td><td>• Pulmonary function tests (PFTs)
• Electrocardiography
• Transthoracic echocardiography
• Whole-body plethysmography
• Blood tests
• Heath-related quality of life
• 6min walk test</td></tr>
<tr><td>Baseline characteristics</td><td>
<table>
<tr><td>--</td><td>Patients (n=33)</td></tr>
<tr><td>Age (years)</td><td>64 ±3</td></tr>
<tr><td>Female</td><td>11 (33%)</td></tr>
<tr><td>Comorbidities</td><td>--</td></tr>
<tr><td>COPD</td><td>3 (9%)</td></tr>
<tr><td>Bronchial asthma</td><td>4 (13%)</td></tr>
<tr><td>Hypertension</td><td>19 (59%)</td></tr>
<tr><td>Heart failure</td><td>3 (9%)</td></tr>
<tr><td>Atrial fibrillation</td><td>3 (9%)</td></tr>
<tr><td>Chronic kidney disease</td><td>7 (22%)</td></tr>
<tr><td>Coronary artery disease</td><td>6 (19%)</td></tr>
<tr><td>Diabetes mellitus</td><td>8 (25%)</td></tr>
</table>
</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>Inclusion criteria</td></tr>
</table>

<table>
<tr><td></td><td>
COVID-19 confirmed by reverse-transcriptase–polymerase-chain-reaction (RT-PCR)
Symptomatic patients with severe disease needing hospitalization
Exclusion criteria
Patients with Acute Respiratory Distress Syndrome (ARDS) who needed mechanical ventilation in the intensive care unit (ICU) during their stay
</td></tr>
<tr><td>Follow up</td><td>6 weeks from discharge</td></tr>
<tr><td>Main results</td><td>
At follow up:
Laboratory findings
Majority had returned to normal
Median D-dimer was not elevated but those patients who did have elevated vales underwent ultrasound duplex scanning and V/Q scan, excluding VTE in all patients.
Symptoms:
<table>
<tr><th>--</th><th>Admission day (n=33)</th><th>Follow up (n=33)</th></tr>
<tr><td>Fever</td><td>22 (67%)</td><td>1 (3%)</td></tr>
<tr><td>Cough</td><td>23 (70%)</td><td>11 (33%)</td></tr>
<tr><td>Dyspnoea</td><td>16 (48%)</td><td>11 (33%)</td></tr>
<tr><td>Fatigue</td><td>21 (64%)</td><td>15 (45%)</td></tr>
<tr><td>Tiredness</td><td>15 (55%)</td><td>15 (45%)</td></tr>
<tr><td>Haemoptysis</td><td>1 (3%)</td><td>0 (%)</td></tr>
<tr><td>Rhinorrhoea</td><td>2 (6%)</td><td>4 (12%)</td></tr>
<tr><td>Sore throat</td><td>8 (24%)</td><td>3 (9%)</td></tr>
<tr><td>Pharyngalgia</td><td>4 (12%)</td><td>0 (0%)</td></tr>
<tr><td>Angina pectoris</td><td>4 (12%)</td><td>6 (18%)</td></tr>
<tr><td>Myalgia</td><td>12 (42%)</td><td>5 (15%)</td></tr>
<tr><td>Headache</td><td>7 (21%)</td><td>5 (15%)</td></tr>
<tr><td>Cognitive disorders</td><td>--</td><td>6 (18%)</td></tr>
<tr><td>Loss of smell</td><td>8 (24%)</td><td>4 (12%)</td></tr>
<tr><td>Loss of taste</td><td>9 (27%)</td><td>3 (9%)</td></tr>
<tr><td>Diarrhoea</td><td>13 (39%)</td><td>3 (9%)</td></tr>
<tr><td>Nausea</td><td>8 (24%)</td><td>2 (6%)</td></tr>
<tr><td>Emesis</td><td>2 (6%)</td><td>0 (0%)</td></tr>
<tr><td>Stomach pains</td><td>7 (21%)</td><td>1 (3%)</td></tr>
</table>
Pulmonary function parameters and ABGs
<table>
<tr><th></th><th>Follow up (n=33)</th></tr>
<tr><td>TLC, % of predicted</td><td>94 (85 to 105)</td></tr>
<tr><td>VC, % of predicted</td><td>93 (78 to 101)</td></tr>
<tr><td>RV, % of predicted</td><td>112 (98 to 127)</td></tr>
<tr><td>RV/TLC, % of predicted</td><td>109 (98 to 126)</td></tr>
<tr><td>FEV1, % of predicted</td><td>95 (72 to 103)</td></tr>
<tr><td>FEV1/FVC, %</td><td>79 (76 to 85)</td></tr>
<tr><td>R eff, % of predicted</td><td>86 (62 to 104)</td></tr>
<tr><td>DLCO, % of predicted</td><td>65 (53 to 73)</td></tr>
<tr><td>DLCO/VA, % of predicted</td><td>77 (69 to 95)</td></tr>
</table>
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ABG	--
paO2, mmHg	72 (67 to 79)
paCO2, mmHg	38 (35 to 38)
pH	7.4 (7.4 to 7.4)
Base excess, mmol/l	0.8 (-0.6 to +1.2)
COHb, vol%	0.9 (0.71)

6-min walk test

--	Follow up (n=33)
Distance, m	380 (180 to 470)
Distance < predicted value, n	26 (79%)
Distance < LLN, n	15 (45%)
Walk distance - predicted value, m	138 (-37 to -191)
Walk distance - LLN, m	1.5 (-52 to +130)
SpO2 before exercise, %	97 (94 to 98)
SpO2 after exercise, %	96 (94 to 98)
HR before exercise, bpm	76 (61 to 86)
HR after exercise, bpm	91 (74 to 100)
Dyspnoea on Borg scale before exercise	0 (0 to 2)
Dyspnoea on Borg scale after exercise	1 (0 to 4)
Fatigue on Borg scale before exercise	1 (0 to 3)
Fatigue on Borg scale after exercise	1 (0 to 4)

Electrocardiography and echocardiography

Echocardiography did not reveal deterioration of left or right ventricular function and there was no evidence of pulmonary hypertension on electrocardiogram (ECG) or in the echocardiograph [Right Ventricular Systolic Pressure (RVSP): median = 25 mmHg + Central venous pressure (CVP) (IQR: 22 to 31)]. There was no pericardial effusion in any patient.

Health status questionnaires

	Follow up (n=33)
PHQ-9	7 (4 to 11)
GAD-7	4 (1 to 9)
SRGQ total score (St. George's respiratory questionnaire)	26 (7 to 42)
EQ-5D-5L	--
Mobility (walking)	2 (1 to 3)
Self-Care	1 (1 to 1)
Usual Activities	2 (1 to 3)
Pain/Discomfort	2 (1 to 3)
Anxiety/Depression	2 (1 to 2)

	EQ VAS: 63 (53 to 80) Hospitalized patients with severe COVID-19, who did not require mechanical ventilation, are unlikely to develop pulmonary long-term impairments, thromboembolic complications or cardiac impairments after discharge but frequently suffer from symptoms of fatigue.
Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. No limitations reported
Additional references	N/A

Dennis 2020

Bibliographic reference/s	**Dennis, Andrea, Wamil, Malgorzata, Kapur, Sandeep et al. (2020) Multi-organ impairment in low-risk individuals with long COVID. medRxiv: 2020101420212555**
Questions relevant to?	**Investigations, prevalance, risk factors**
Publication status	Preprint
Study type	Prospective cohort (ongoing)
Quality	Low quality evidence CASP critical appraisal checklist (cohort studies): High risk of bias
Objective	In order to better understand the long-term impact of COVID-19 and ultimately inform preventive measures at health system level, we performed a pragmatic, prospective study in low-risk individuals with symptom assessment, multi-organ magnetic resonance imaging (MRI) and blood investigations for inflammatory markers at three months post-COVID-19 diagnosis.
Study date	April to August 2020
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	UK
Population (including n)	201 patients with previous SARS-CoV-2 infection and low risk for COVID-19 severity and mortality
Time since acute COVID-19	Around 3 to 5 months 12+ weeks grouping
Investigations	• Symptom assessment • Multi-organ MRI • Blood investigations for inflammatory markers
Baseline characteristics	See table below

	All (n=201) N (%)	Not hospitalised (n=164) N (%)	Hospitalised (n=37) N (%)

	Age (years, mean; sd)	44(11.0)	43(10.9)	50(10.0)
	Female (No, %)	140(69.7)	117(71.3)	23(62.2)
	BMI (kg/m^2, median; IQR)	25.7(22.7,28.1)	25.3(22.6,27.7)	27.2(23.1,31.0)
	Ethnicity	--	--	--
	White	174(86.6)	146(89.0)	28 (75.7)
	Mixed	3 (1.5)	3 (1.8)	0 (0)
	South Asian	8 (4.0)	5 (3.0)	3 (8.1)
	Black	5 (2.5)	3 (1.8)	2 (5.4)
	Comorbidities and risks	--	--	--
	Never smoked	132 (65.7)	108 (65.9)	24 (64.9)
	Current smoker	6 (3.0)	6 (3.7)	0 (0)
	Ex-smoker	63 (31.3)	50 (30.5)	13 (35.1)
	Health care worker	62 (30.8)	49 (29.9)	13 (35.1)
	Asthma	36 (17.9)	33(20.1)	3 (8.1)
	BMI ≥25 kg/m^2	112 (56.3)	87 (53.7)	25 (67.6)
	BMI ≥30 kg/m^2	40 (20.1)	28 (17.3)	12 (32.4)
	Hypertension	12 (6.0)	10 (6.1)	2 (5.4)
	Diabetes	4 (2.0)	4 (2.4)	0 (0.0)
	Previous heart disease	8 (4.0)	7 (4.3)	1 (2.7)
	Initial symptoms-to assessment (days: median, [IQR])	140 (105, 160) (n=1 missing)	140 (106, 162) (n=1 missing)	138 (97, 150)
	COVID-19 positive to-assessment (days: median, [IQR])	70 (42, 112) (n=3 missing)	67 (39, 109) (n=3 missing)	105 (59, 126)
Inclusion and exclusion criteria	Inclusion criteria: • Tested positive by the oro/nasopharyngeal throat swab forSARS-CoV-2 by reverse-transcriptase-polymerase-chain reaction or • positive antibody test or • had typical symptoms and were determined to have COVID-19 by two independent clinicians Exclusion criteria: • Symptoms of active respiratory viral infection (temperature >37.8°C or three or more episodes of coughing in 24 hours) • discharged from hospital in the last 7 days • contraindications to MRI, including implanted pacemakers, defibrillators, other metallic implanted devices; claustrophobia			
Follow up	Around 20 weeks			

Main results

At follow up

Symptoms	All (n=201) N (%)	Not hospitalised (n=164) N (%)	Hospitalised (n=37) N (%)
Fatigue	197 (98.0)	160 (97.6)	37 (100.0)
Muscle ache	176 (87.6)	145 (88.4)	31 (83.8)
Shortness of breath	175 (87.1)	140 (85.4)	35 (94.6)
Headache	175 (87.1)	139 (84.8)	27 (73.0)
Joint pain	157 (78.1)	128 (78.0)	29 (78.4)
Fever	151 (75.1)	127 (77.4)	24 (64.9)
Chest pain	147 (73.1)	116 (70.7)	31 (83.8)
Cough	148 (73.6)	119 (72.6)	29 (78.4)
Sore throat	143 (71.1)	120 (73.2)	23 (62.2)
Diarrhoea	119 (59.2)	92 (56.1)	27 (73.0)
Abnormal pain	108 (53.7)	91 (55.5)	17 (45.9)
Wheezing	97 (48.3)	74 (45.1)	23 (62.2)
Inability to walk	81 (40.3)	59 (36.0)	22 (59.5)
Runny nose	68 (33.8)	55 (33.5)	13 (35.1)

Blood investigations

- Triglycerides (p=0.002), cholesterol (p=0.021), LDL-cholesterol (p=0.005) and transferrin saturation (p=0.005) were more likely to be abnormal in hospitalised versus non-hospitalised individuals.
- Mean corpuscular haemoglobin concentration (26%), alanine transferase (14%), lactate dehydrogenase (16%), triglycerides (12%) and cholesterol (42%) were all abnormally high in ≥10% of all individuals (without separation by hospitalisation status).
- ESR (13%), bicarbonate (13%), uric acid (16%) and high-sensitivity CRP (13%) were abnormally high in ≥10% of individuals in the hospitalisation group
- Bicarbonate (10%), phosphate (13%), uric acid (11%), and transferrin saturation (19%) were abnormally low in ≥10% of individuals (without separation by hospitalisation status)

Single and multi- organ impairment

Heart	All (n=201) N (%)	Not hospitalised (n=164) N (%)	Hospitalised (n=37) N (%)	P value
LVEF (%)	--	--	--	--
Normal	155 (77.1)	129 (78.7)	26 (70.3)	0.079
Borderline impairment (50 to 55%)	38 (18.9)	31 (18.9)	7 (18.9)	
Definite impairment (<50%)	8 (4.0)	4 (2.4)	4 (10.8)	
Evidence of myocarditis	--	--	--	--

≥3 segments with high T1 (≥1264ms at 3T; ≥1015ms at 1.5T)	22 (10.9)	18 (11.0)	4 (10.8)	1

Lungs	All (n=201) N (%)	Not hospitalised (n=164) N (%)	Hospitalised (n=37) N (%)	P value
Deep Breathing Fractional area change <39%	63 (33.2) (n= 11 missing)	47 (30.1) (n= 8 missing)	16 (47.1) (n= 3 missing)	0.071

Pancreas	All (n=201) N (%)	Not hospitalised (n=164) N (%)	Hospitalised (n=37) N (%)	P value
Pancreatic inflammation (T1 in ms)	--	--	--	--
Normal (800ms)	157 (83.1)	136 (87.2)	21 (63.6)	0.003
Borderline (800 to 865ms)	20 (10.6)	11 (7.1)	9 (27.3)	
Significant (>865ms)	12 (6.3)	9 (5.8)	3 (9.1)	
Pancreatic fat	(n= 6 missing)	(n= 4 missing)	(n= 2 missing)	
Normal (<5%)	126 (64.6)	111 (69.4)	15 (42.9)	0.005
Borderline (5-10%)	44 (22.6)	33 (20.6)	11 (31.4)	
Significant (>10%)	25 (12.8)	16 (10.0)	9 (25.7)	

Liver	All (n=201) N (%)	Not hospitalised (n=164) N (%)	Hospitalised (n=37) N (%)	P value
Liver Inflammation (cT1 in ms)	(n= 1 missing)	(n= 1 missing)	--	--
Normal (800ms)	181 (90.5)	150 (92.0)	31 (83.8)	0.040
Borderline (800 to 865ms)	5 (2.5)	5 (3.1)	0 (0.0)	
Significant (>865ms)	14 (7.0)	8 (4.9)	6 (16.2)	
Liver fat	--	--	--	--

	Normal (<5%)	162 (80.6)	138 (84.1)	24 (64.9)	0.025
	Borderline (5 to 10%)	18 (9.0)	12 (7.3)	6 (16.2)	
	Definite (>10%)	21 (10.4)	14 (8.5)	7 (18.9)	

Spleen	All (n=201) N (%)	Not hospitalised (n=164) N (%)	Hospitalised (n=37) N (%)	P value
Splenic length (mm)	(n= 10 missing)	(n= 10 missing)	--	--
Normal	179 (9.4)	144 (9.5)	35 (9.5)	1
Borderline	12 (6.3)	10 (6.5)	2 (5.4)	

In a young, low-risk population with ongoing symptoms, almost 70% of individuals have impairment in one or more organs four months after initial symptoms of SARS-CoV-2 infection. There are implications not only for burden of long COVID but also public health approaches which have assumed low risk in young people with no comorbidities.

Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	**Funding**: This work was supported by the UK's National Consortium of Intelligent Medical Imaging through the Industry Strategy Challenge Fund, Innovate UK Grant, and also through the European Union's Horizon 2020 research and innovation programme **Limitations:** • Partly limited by access to laboratory testing during the pandemic • Causality of the relationship between organ impairment and infection cannot be deduced but may be addressed by longitudinal follow-up of individuals with organ impairment. • Study population was limited by ethnicity despite disproportionate impact of COVID-19 in non-white individuals • Pulse oximetry and spirometry were added later to the protocol and follow up; they were not included from the outset to limit interaction and exposure between trial team and patients • Did not include healthy controls or MRI assessment of brain or muscle function
Additional references	Ongoing study (https://clinicaltrials.gov/ct2/show/NCT04369807

Goërtz 2020

Bibliographic reference/s	**Goërtz, Yvonne M. J., Herck, Maarten Van, Delbressine, Jeannet M. et al. (2020) Persistent symptoms 3 months after a SARS-CoV-2 infection: the post-COVID-19 syndrome?. ERJ Open Research**
Questions relevant to?	**Prevalence, risk factors**

Publication status	Published
Study type	Cross sectional
Quality	Very low quality JBI critical appraisal checklist rating (analytical cross-sectional studies): High risk of bias
Objective	This study assessed whether or not multiple relevant symptoms recover following the onset of symptoms in hospitalised and non-hospitalised patients with COVID-19.
Study date	4 to 11 June 2020
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	Netherlands and Belgium
Population (including n)	2113 members of two Facebook groups for coronavirus patients with persistent complaints in the Netherlands and Belgium, and from a panel of people who registered on a website of the Lung Foundation Netherlands who were invited to complete an online survey
Time since acute COVID-19	4 to 12 weeks grouping
Interventions/ Prognostic factors	Not applicable
Baseline characteristics	<table><tr><td>--</td><td>Whole sample (n=2113)</td><td>Hospitalised (n=112)</td><td>Non-hospitalised (confirmed COVID-19) (n=345)</td><td>Non-hospitalised (symptom-based COVID-19) (n=882)</td><td>Non-hospitalised (suspected COVID-19) (n=774)</td><td>p value</td></tr><tr><td>Women</td><td>1803 (85.3%)</td><td>78 (69.6%)</td><td>314 (91%)</td><td>774 (87.8%)</td><td>637 (82.3%)</td><td><0.001</td></tr><tr><td>Age, years</td><td>47.0 (39.0–54.0)</td><td>53.0 (46.3 to 60.0)</td><td>47.0 (37.0 to 53.5)</td><td>46.0 (38.0 to 53.0)</td><td>47.0 (39.0 to 54.0</td><td><0.001</td></tr><tr><td>BMI kgm^{-2}</td><td>25.2 (22.6–28.8)</td><td>26.9 (24.5 to 30.9)</td><td>26.0 (23.2 to 29.4)</td><td>25.0 (22.3 to 28.7)</td><td>24.9 (22.5 to 28.4)</td><td><0.001</td></tr><tr><td colspan="7">Comorbidities (self-reported)</td></tr><tr><td>None</td><td>1293 (61.2)</td><td>51 (45.5)</td><td>225 (65.2)</td><td>523 (59.3)</td><td>494 (63.8)</td><td rowspan="3">0.007</td></tr><tr><td>1</td><td>541 (25.6)</td><td>40 (35.7)</td><td>77 (22.3)</td><td>240 (27.2)</td><td>184 (23.8)</td></tr><tr><td>≥2</td><td>279 (13.2)</td><td>21 (18.8)</td><td>43 (12.5)</td><td>119 (13.5)</td><td>96 (12.4)</td></tr><tr><td colspan="7">Health status before onset of symptoms (self-reported)</td></tr></table>

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<table>
<tr><td>Good</td><td>1799 (85.1%)</td><td>88 (78.6%)</td><td>316 (91.6%)</td><td>743 (84.6%)</td><td>652 (84.2%)</td><td rowspan="3">0.011</td></tr>
<tr><td>Moderate</td><td>301 (14.2%)</td><td>23 (20.5%)</td><td>27 (7.8%)</td><td>134 (15.2%)</td><td>117 (15.1%)</td></tr>
<tr><td>Poor</td><td>13 (0.6%)</td><td>1 (0.9%)</td><td>2 (0.6%)</td><td>5 (0.6%)</td><td>5 (0.6%)</td></tr>
</table>
</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>Exclusion criteria:
Patients admitted to ICU</td></tr>
<tr><td>Follow up</td><td>79 days since onset of first symptoms</td></tr>
<tr><td>Main results</td><td>
<table>
<tr><td>Symptoms at follow up</td><td>N=2113</td></tr>
<tr><td>Fatigue</td><td>87%</td></tr>
<tr><td>Dyspnoea</td><td>71%</td></tr>
<tr><td>Headache</td><td>38%</td></tr>
<tr><td>Chest tightness</td><td>44%</td></tr>
<tr><td>Cough</td><td>29%</td></tr>
<tr><td>Muscle pain</td><td>26%</td></tr>
<tr><td>Sore throat</td><td>26%</td></tr>
<tr><td>Increased body temp</td><td>22%</td></tr>
<tr><td>Pain between shoulder blades</td><td>33%</td></tr>
<tr><td>Pain/burning in lungs</td><td>24%</td></tr>
<tr><td>Heart palpitations</td><td>32%</td></tr>
<tr><td>Increased resting HR</td><td>28%</td></tr>
<tr><td>Dizziness</td><td>27%</td></tr>
<tr><td>Burning feeling in trachea</td><td>20%</td></tr>
<tr><td>Nose cold</td><td>18%</td></tr>
<tr><td>Fever</td><td>2%</td></tr>
<tr><td>Ageusia</td><td>11%</td></tr>
<tr><td>Diarrhoea</td><td>10%</td></tr>
<tr><td>Anosmia</td><td>13%</td></tr>
<tr><td>Joint pain</td><td>22%</td></tr>
<tr><td>Nausea</td><td>12%</td></tr>
<tr><td>Mucus</td><td>18%</td></tr>
<tr><td>Sneezing</td><td>12%</td></tr>
<tr><td>Hot flushes</td><td>13%</td></tr>
<tr><td>Eye problems</td><td>12%</td></tr>
<tr><td>Ear pain</td><td>8%</td></tr>
<tr><td>Sudden loss of body weight</td><td>3%</td></tr>
<tr><td>Vomiting</td><td>1%</td></tr>
<tr><td>Red spots on toes/feet</td><td>2%</td></tr>
<tr><td>Others</td><td>27%</td></tr>
</table>
<table>
<tr><td>--</td><td>During infection</td><td>At follow up</td></tr>
</table>
</td></tr>
</table>

	(n=2113)	(n=2113)
0 symptoms	0	0.7%
1 to 5 symptoms	2.9%	40.2%
6 to 10 symptoms	21.7%	41.5%
11 to 15 symptoms	37%	14.2%
16 to 20 symptoms	29.2%	3%
21 to 25 symptoms	8.3%	0.5%
26 to 30 symptoms	0.8%	0%

- There was a median change of −7 (−10 to −4) symptoms per respondent (p<0.001)
- The difference in median change of symptoms per subgroup was small but significant, being the highest in non-hospitalised patients with confirmed COVID-19 compared to hospitalised, non-hospitalised symptom-based COVID-19 and non-hospitalised suspected-based COVID-19 diagnosis (respectively −7 (−10 to −5) versus −7 (−9 to −5), −7 (−10 to −4), and −6 (−9 to −4); p<0.001)
- Self-reported health status at follow-up was significantly worse compared to before the infection (p<0.001)
- The multiple regression model including age, self-reported health status before the onset of symptoms, self-reported pre-existing comorbidities and the number of symptoms during the infection, statistically significantly predicted the number of symptoms at follow-up F(4, 2108)=293.818, p<0.001 (adjusted R2 =0.357)

Summary

In previously hospitalised and non-hospitalised patients with confirmed or suspected COVID19, multiple symptoms are present about 3 months after symptoms onset. This suggests the presence of a “post-COVID-19 syndrome” and highlights the unmet healthcare needs in a subgroup of patients with “mild” or “severe” COVID-19.

Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	Funding: The scientific work of Y.M.J. Goërtz is financially supported by Lung Foundation Netherlands grant 4.1.16.085, F.V.C. Machado is financially supported by European Union grant ZonMw ERACoSysMed 90030355 and R. Meys is financially supported by Lung Foundation Netherlands grant 5.1.18.232. Funding information for this article has been deposited with the Crossref Funder Registry. Limitations: • Excluded ICU patients • Mostly women responded • Only patients with COVID-19 from Facebook groups with persistent symptoms and who registered on www.coronalongplein.nl were included in the study. This most probably resulted in an overestimation of the true symptom burden in the non-hospitalised group of patients with COVID-19.
Additional references	N/A

Kamal

Bibliographic reference/s	**Kamal, M., Omirah, M. et al (2020): Assessment and characterisation of post-COVID-19 manifestations. Int J Clin Pract. 2020;00:e13746. https://doi.org/10.1111/ijcp.13746**
Questions relevant to?	**Symptom prevalence and risk factors**
Publication status	Published
Study type	Cross-sectional
Quality	Low (or very low?) quality JBI critical appraisal checklist rating (analytical cross-sectional studies): High risk of bias
Objective	To investigate and characterise the manifestations which appear after eradication of the coronavirus infection and its relation to disease severity. Also, to link these symptoms with several factors (age, weight, disease severity or other comorbidities).
Study date	Not reported
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	Egypt, no setting specified, but appears to cover all Covid survivors with range of severity from mild to severe
Population (including n)	Covid survivors (n=287)
Time since acute COVID-19	Unclear – authors reported all patients were showing one or more 'manifestations' persisting for more than 20 days from last negative PCR
Interventions/ Prognostic factors	Not applicable.
Baseline characteristics	103 male, 184 female Age 32.3 (mean) SD +/-8.5, range 20 to 60 Weight 77kg (mean) SD +/-16.4 Height 162.9cm (mean) SD +/-15.3 BMI 28.5 (mean) SD +/-5.2 27.2% of males smokers, no females 70.7% no known history of other illness, 7.7% hypertension 5.2% diabetic Severity of COVID-19 symptoms: Mild (isolated at home) 80.2% Moderate (received oxygen therapy) 14.9% Severe (required ICU admission) 4.9%
Inclusion and exclusion criteria	'Recovered Egyptian subjects from COVID-19' (nothing else stated)
Follow up	None reported
Main results	**Symptoms** Authors' summary:

“Only 10.8% of all subjects have no manifestation after recovery from the disease while a large percentage of subjects suffered from several symptoms and diseases.

The most common symptom reported was fatigue (72.8%), more critical manifestations like stroke, renal failure, myocarditis, and pulmonary fibrosis were reported by a few percent of the subjects. There was a relationship between the presence of other comorbidities and severity of the disease. Also, the severity of COVID-19 was related to the severity of post-COVID-19 manifestations.”

Post-COVID-19 manifestations were recorded for about 90% of the recovered subjects, with a wide range of symptoms and conditions that varied from a low-critical symptom like a headache to more critical conditions such as stroke, renal failure and pulmonary fibrosis.

Each subject reported one or more manifestations, those manifestations persisted with all subjects for more than 20 days from the last negative PCR.

Most of the reported manifestations were mild reversible symptoms that could be relieved without medical interventions such as fatigue and headache which could be related to COVID-19 symptoms. Other mild symptoms like joint and muscle pain were also reported by many subjects and it could be classified as mild manifestations. It was noted that many manifestations are related to the central nervous system such as continuous headache, migraine, depression, anxiety, and obsessive-compulsive disorder. Few percent of subjects have suffered from critical complications such as stroke, myocarditis, renal failure and pulmonary fibrosis which could be reversible and required extra investigation.

Manifestation of post-COVID-19 recorded during this study could be classified as mild or critical, the critical manifestations are those affecting organ functions such as pulmonary fibrosis, renal failure, myocarditis, arrhythmia, and stroke.

In addition to fatigue, neuropsychiatric symptoms were documented for a large percent of COVID-19 subjects.

Characterisation of post-COVID-19 manifestations (Table 2 in paper):

Item	**Percent**
Manifestations	--
Fatigue	72.8%
Anxiety	38%
Joint pain	31.4%
Continuous headache	28.9%
Chest pain	28.9%
Dementia	28.6%
Depression	28.6%
Dyspnoea	28.2%

		Blurred vision	17.1%
		Tinnitus	16.7%
		Intermittent fever	11.1%
		Obsessive -compulsive disorder	4.9%
		Pulmonary fibrosis	4.9%
		Diabetes mellitus	4.2%
		Migraine	2.8%
		Stroke	2.8%
		Renal failure	1.4%
		Myocarditis	1.4%
		Arrythmia	0.3%
	Risk factors Majority of subjects were overweight or obese but there is no significant effect on the severity grade or type of post-COVID-19 symptoms. Relationship between severity of post-COVID-19 manifestations and severity of disease: severe cases expressed high severity manifestations compared with those suffering from mild condition. Hence, the severity of manifestations is also related to the age and comorbidities of the involved subjects.		
Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	Authors' conclusions: "The post-COVID-19 manifestation is largely similar to the post-SARS syndrome. All subjects recovered from COVID-19 should undergo long-term monitoring for evaluation and treatment of symptoms and conditions that might be precipitated with the new coronavirus infection." Timing/timescales for symptoms is vague; the authors merely state: "Each subject reported one or more manifestations, those manifestations persisted with all subjects for more than 20 days from the last negative PCR."		
Additional references	N/A		

Sudre 2020

Bibliographic reference/s	**Sudre, Carole H., Murray, Benjamin, Varsavsky, Thomas et al. (2020) Attributes and predictors of Long-COVID: analysis of COVID cases and their symptoms collected by the Covid Symptoms Study App. medRxiv: 2020101920214494**
Questions relevant to?	**Signs and symptoms**
Publication status	Preprint
Study type	Prospective cohort
Quality	Low quality evidence CASP critical appraisal checklist (cohort studies): Moderate risk of bias
Objective	To ascertain the duration of illness and prevalence of long-lasting symptoms
Study date	--
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	UK, USA, Sweden
Population (including n)	4182 users of the COVID symptom study app.
Time since acute COVID-19	Compared cases of long (more than 28 days) and short duration (reporting symptoms lasting less than 10 days).
Interventions/ Prognostic factors	Not applicable
Baseline characteristics	Not reported
Inclusion and exclusion criteria	People who tested positive for SARS CoV-2 by PCR swab testing who logged as feeling physically normal before the start of illness (up to 14 days before testing)
Follow up	Not reported
Main results	Age was significantly associated with LC28, rising from 9.9% in 18 to 49-year olds to 21.9% in those aged 70 and over; clear escalation in OR by age decile with females aged 50 to 60 had the highest odds. LC28 disproportionately affected women (14.9%) compared to men (9.5%), although this sex effect was not significant in older age-groups LC28 affected all socioeconomic groups Asthma was the only/ unique pre-existing condition providing significant association with LC28 (OR 2.14 (1.55, 2.96) Fatigue (97.7%) and headache (91.2%) were the most reported symptoms in those with LC28, followed by anosmia and lower respiratory symptoms. Whilst fatigue was reported continuously, other symptoms such as headache were reported intermittently. Analysis of free text responses that were more common in LC28 (81%) compared to short COVID (45%): - cardiac symptoms (palpitations, tachycardia) were overrepresented in LC28 group (6.1%) compared to short COVID (0.5%) (p<0.000) - concentration or memory issues (4.1% v 0.2%) (p=0.005) - tinnitus and earache (3.6% v 0.2%) (p=0.0005)

Bibliographic reference/s	**Sudre, Carole H., Murray, Benjamin, Varsavsky, Thomas et al. (2020) Attributes and predictors of Long-COVID: analysis of COVID cases and their symptoms collected by the Covid Symptoms Study App. medRxiv: 2020101920214494**
Questions relevant to?	**Signs and symptoms**
Publication status	Preprint
	- peripheral neuropathy symptoms (pins and needles and numbness) (2% v 0.5% (p=0.004) Different symptomology within long COVID? - 2 main patterns: 1. those reporting exclusively fatigue, headache, and upper respiratory complaints (SO< sore throat, persistent cough, loss of smell) 2. those with multisystem complaints including ongoing fever and GI symptoms. In people with long duration COVID (LC28) ongoing fever (OR 2.16 (1.50, 3.13) and skipped meals (OR 2.52 (1.74, 3.65\0 were strong predictors of subsequent hospital visits. Individuals with long COVID were more likely to report relapses compared to those not reporting long symptom duration (16% v 8.4%, p=<0.0005) Exploration of how to predict Long COVID from data available early in the disease course: - Individuals reporting more than 5 symptoms in the first week (the median number reported) significantly more likely to go onto experience LC28 (OR 3.95 (3.10, 5.04). Predictive in both sexes and all age groups. - Every symptom in isolation was positively predictive of longer illness duration. - The 5 symptoms experienced during the first week most predictive of long COVID were: 1. fatigue OR (95%CI) 2.83 (2.09, 3.83) 2.headache OR (95%CI) 2.62 (2.04, 3.37) 3.dyspnoea OR (95%CI) 2.36 (1.91, 2.91) 4.hoarse voice OR (95%CI) 2.33 (1.88, 2.90) 5. myalgia OR (95%CI) 2.22 (1.80, 2.73) Similar patterns observed in men and women In adults aged over 70, most predictive of long COVID: - loss of smell OR (95%CI) 7.35 (1.58, 34.22) - fever OR (95%CI) 5.51 (1.75, 17.36) - hoarse voice OR (95%CI) 4.03 (1.21, 13.42) Random Forest prediction models created using combination of 1st weeks symptoms reporting, personal characteristics and comorbidities - using all features, ROC AUC was 76.7% (SD2.5) In classification between short COVID and LC28 the strongest predictors were: - age (29.2%) - number of symptoms during the first week (16.3%) - BMI (10.8 - hoarse voice (4.1%)

Bibliographic reference/s	**Sudre, Carole H., Murray, Benjamin, Varsavsky, Thomas et al. (2020) Attributes and predictors of Long-COVID: analysis of COVID cases and their symptoms collected by the Covid Symptoms Study App. medRxiv: 2020101920214494**
Questions relevant to?	**Signs and symptoms**
Publication status	Preprint
	- SOB 3.8 (3.8%) - gender (3.7%) Ranking of feature importance relatively similar across the age group models. In the over 70s group appears that early features such as fever, loss of smell and comorbidities (especially heart and lung disease) were important and thus could be considered 'red flags' in older adults. Simplified prediction model that included only symptom number in first week, age and sex – ROC of AUC of 76.7% (SD2.5). Specificity of 73.4% (SD 9.7), sensitivity 68.7% (SD 9.9). Key predictive findings of analysis validated in dataset of 2472 people who were antibody positive. - number of symptoms in first week strongest predictor of long COVID OR?5.12 (3.65, 7.19) - predictive model of number of symptoms in first week, age and sex similarly predictive of LC28 with ROC AUC of 76.3% (SD 3.7%).
Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	Limitations: - confined to app users - disproportionally female -under-represented those >70 years which could increase or decrease estimate of extent of long COVID -population restricted to PCR positive, excludes people diagnosed on basis of clinical picture without PCR (given lack of testing early in pandemic, this could underestimate long COVID) and not fully capture the affected population.
Additional references	N/A

Vaira 2020

Bibliographic reference/s	**Vaira, L A, Hopkins, C, Petrocelli, M et al. (2020) Smell and taste recovery in coronavirus disease 2019 patients: a 60-day objective and prospective study. The Journal of laryngology and otology 134(8): 703 to 709**
Questions relevant to?	**Signs and symptoms** **Prevalence**
Publication status	Published

Study type	Prospective cohort
Quality	Low quality evidence CASP critical appraisal checklist (cohort studies): High risk of bias
Objective	To understand the longer- term recovery of chemosensitive functions to aid the counselling of patients and guide if and when appropriate to start a specific therapy.
Study date	Not reported
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	Milan/ Bologna
Population (including n)	N=138 Adults over 18 years, presented within 4 days of symptom onset, diagnosis of SARS-CoV-2 confirmed with PCR
Time since acute COVID-19	Patients were evaluated every 10 days from inclusion up to 60 days.
Interventions/ Prognostic factors	Psychophysical tests to assess olfactory and gustatory function. First (baseline evaluation) was performed within 4 days of clinical onset of COVID-19 symptoms. Home quarantined patients assessed by self-administered olfactory and gustatory psychophysical tests. Validated for home use and can be executed remotely by the operator. Hospitalized patients tested with Connecticut Chemosensory Clinical Research Centre orthonasal olfaction tests
Baseline characteristics	49.3% male; mean (SD) age 51.2 (8.8); 23.2% inpatients.
Inclusion and exclusion criteria	Patients with a history of previous trauma, surgery or radiotherapy in oral or nasal cavities, allergic rhinitis or rhinosinusitis, psychiatric or neurological diseases were excluded from the study.
Follow up	Up to 60 days 4- to 12-week group
Main results	60 days after symptom onset, 7.2% still had severe dysfunctions. The risk of developing a long-lasting disorder became significant at 10 days for taste (OR 40.2 (2.204, 733.2) and also for smell (OR 58.5 (3.278, 1043.5) Any association between age, gender, need for hospitalisation, cardiovascular and pulmonary comorbidities, diabetes and obesity and the persistence of chemosensitive disorders at 60 days were assessed with logistic regression and no significant relationships were found.
Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	--
Additional references	--

Valiente-De Santis 2020

<table>
<tr><td>Bibliographic reference/s</td><td>Lucia Valiente-De, Santis, Ines, Perez-Camacho, Beatriz, Sobrino et al. (2020) Clinical and immunoserological status 12 weeks after infection with COVID-19: prospective observational study. medRxiv</td></tr>
<tr><td>Questions relevant to?</td><td>Risk factors, prevelance, investigations</td></tr>
<tr><td>Publication status</td><td>Preprint</td></tr>
<tr><td>Study type</td><td>Prospective cohort</td></tr>
<tr><td>Quality</td><td>Low quality evidence
CASP critical appraisal checklist (cohort studies): High risk of bias</td></tr>
<tr><td>Objective</td><td>A multidisciplinary follow-up of all COVID-19 patients seen at a hospital to determine their functional and immunoserological status, assess the presence of possible sequelae and evaluate their course.</td></tr>
<tr><td>Study date</td><td>14th March to 15th April</td></tr>
<tr><td>COVID-19 prevalence (high/low) if reported</td><td>Not reported</td></tr>
<tr><td>Country/ Setting</td><td>Spain</td></tr>
<tr><td>Population (including n)</td><td>108 patients with previous acute SARS-CoV-2 infection contacted by telephone</td></tr>
<tr><td>Time since acute COVID-19</td><td>12 weeks after acute phase
(4 to 12 weeks grouping)</td></tr>
<tr><td>Investigations</td><td>• Blood test
• Chest radiograph
• Chest CT
• Spirometry
• Serological test</td></tr>
<tr><td>Baseline characteristics</td><td>During acute episode
<table>
<tr><td>Characteristic</td><td>Total (N=108)</td><td>Symptomatic (n=82)</td><td>Asymptomatic (n=26)</td><td>P value</td></tr>
<tr><td>Age > 65 years</td><td>29 (26.9%)</td><td>17 (20.7%)</td><td>12 (46.2%)</td><td>0.011</td></tr>
<tr><td>Female</td><td>60 (55.6%)</td><td>47 (57.3%)</td><td>13 (50%)</td><td rowspan="2">NS</td></tr>
<tr><td>Male</td><td>48 (44.4%)</td><td>35 (42.7%)</td><td>12 (50%)</td></tr>
<tr><td>Health care worker</td><td>30 (27.8)</td><td>28 (34.1)</td><td>2 (7.7)</td><td>0.009</td></tr>
<tr><td>Mild acute symptoms</td><td>64 (59.3)</td><td>48 (58.5)</td><td>16 (61.5)</td><td rowspan="2">NS</td></tr>
<tr><td>Severe acute symptoms</td><td>44 (40.7)</td><td>34 (41.5)</td><td>10 (38.5)</td></tr>
<tr><td>ICU during acute episode,</td><td>4 (3.7)</td><td>3 (3.7)</td><td>1 (3.8)</td><td>NS</td></tr>
</table></td></tr>
</table>

<table>
<tr><td>Inclusion and exclusion criteria</td><td>Confirmed case (symptoms compatible with COVID-19 and positive result for the SARS-CoV-2 polymerase chain reaction (PCR) in respiratory samples, or a suspected case (symptoms compatible with COVID-19 and negative PCR)</td></tr>
<tr><td>Follow up</td><td>12 weeks</td></tr>
<tr><td>Main results</td><td>Symptoms 12 weeks after the acute episode
<table>
<tr><td>Symptom</td><td>N= 82 (75.9%)</td></tr>
<tr><td>Dyspnoea</td><td>60 (55.6)</td></tr>
<tr><td>Asthenia</td><td>48 (44.9)</td></tr>
<tr><td>Cough</td><td>28 (25.9)</td></tr>
<tr><td>Chest pain</td><td>28 (25.9)</td></tr>
<tr><td>Palpitations</td><td>24 (22.2)</td></tr>
<tr><td>Headache</td><td>10 (9.3)</td></tr>
<tr><td>Anosmia</td><td>10 (9.3)</td></tr>
<tr><td>Dysgeusia</td><td>5 (5.6)</td></tr>
<tr><td>Fever</td><td>4 (3.7)</td></tr>
<tr><td>Chills</td><td>4 (3.7)</td></tr>
<tr><td>Arthomyalgia</td><td>3 (2.8)</td></tr>
<tr><td>Hair loss</td><td>3 (2.8)</td></tr>
<tr><td>Diarrhoea</td><td>2 (1.9)</td></tr>
<tr><td>Anxiety</td><td>7 (6.4)</td></tr>
<tr><td>Sadness</td><td>7 (6.4)</td></tr>
<tr><td>Insomnia</td><td>2 (1.9)</td></tr>
<tr><td>Loss of memory</td><td>2 (1.9)</td></tr>
<tr><td>Difficulty concentrating</td><td>2 (1.9)</td></tr>
</table>
Main results of the laboratory studies
<table>
<tr><td>Parameters</td><td></td></tr>
<tr><td>Leukopenia (leukocytes <4000)</td><td>6 (5.8)</td></tr>
<tr><td>Lymphopenia (lymphocytes <900)</td><td>7 (6.8)</td></tr>
<tr><td>CD4/CD8 ratio <1</td><td>6 (5.8)</td></tr>
<tr><td>D-dimer >500 ng/mL</td><td>32 (31.3)</td></tr>
<tr><td>LDH > 246 U/L</td><td>7 (6.8)</td></tr>
<tr><td>CRP >2.9 mg/dL</td><td>25 (24.5)</td></tr>
<tr><td>Ferritin >252 ng/mL</td><td>9 (8.8)</td></tr>
<tr><td>IL-6 >40 pg/mL</td><td>4 (3.9)</td></tr>
<tr><td>IgM <40 mg/dL</td><td>6 (5.8)</td></tr>
<tr><td>IgG <600 mg/dL</td><td>11 (10.7)</td></tr>
</table>
Chest radiograph at 12 weeks
<table>
<tr><td>--</td><td>N = 89 (82.4%)</td></tr>
<tr><td>Normal</td><td>56 (62.9%)</td></tr>
<tr><td>Favourable evolution</td><td>24 (26.0%)</td></tr>
<tr><td>Persistent or worsened</td><td>9 (10.1%)</td></tr>
</table>
Chest CT scan
<table>
<tr><td>--</td><td>N = 37 (41.5%)</td></tr>
</table></td></tr>
</table>

Normal	7 (18.9%)
Pathological	24 (64.9%)

Spirometry

--	N = 32 (29.6%)
Normal	23 (71.9%)
Obstructive pattern	4 (12.5%)
Mixed pattern	2 (6.3%)

None of the baseline characteristics was associated with radiological or respiratory function changes.

Serological response

Antibodies, N (%)	Total	Symptomatic	Asymptomatic	P value
IgM positive	60 (57.1)	45 (56.3)	15 (60)	NS
IgM negative	35 (33.3)	28 (35.5)	7 (28)	NS
IgM indeterminate	10 (9.5)	7 (8.8)	3 (12)	NS
IgG positive	103 (98.1)	79 (98.8)	24 (96)	NS
IgG negative	2 (9.1)	1 (1.3)	1 (4)	NS
IgM and IgG positive	58 (55.5)	44 (55)	14 (56)	NS

Risk factors for persistence of symptoms

Variable	OR multivariate analysis (95% CI)	P value
Age >65 years	0.33 (0.12-0.87)	0.026
Healthcare worker	4.79 (1.02-22.38)	0.046
Mild or severe acute episode	--	0.087
Charlson >3	--	0.130
D-dimer >500 ng/mL	--	0.317
Specific treatment for COVID-19	--	0.435

The persistence of symptoms in patients with COVID is usual 12 weeks after the acute episode, especially in patients <65 years and health-care workers. All our patients had developed antibodies by 12 weeks.

Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	No limitations reported by author
Additional references	N/A

Xiong 2020

<table>
<tr><td>Bibliographic reference/s</td><td>Xiong, Qiutang, Xu, Ming, Li, Jiao et al. (2020) Clinical sequelae of COVID-19 survivors in Wuhan, China: a single-centre longitudinal study. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases</td></tr>
<tr><td>Questions relevant to?</td><td>Prevalence, risk factors</td></tr>
<tr><td>Publication status</td><td>Preprint</td></tr>
<tr><td>Study type</td><td>Retrospective cohort</td></tr>
<tr><td>Quality</td><td>Low quality evidence
CASP critical appraisal checklist (cohort studies): High risk of bias</td></tr>
<tr><td>Objective</td><td>To describe the prevalence, nature and risk factors for the main clinical sequelae in coronavirus disease 2019 (COVID-19) survivors who have been discharged from the hospital for more than 3 months</td></tr>
<tr><td>Study date</td><td>Up to 1st March 2020</td></tr>
<tr><td>COVID-19 prevalence (high/low) if reported</td><td>Not reported</td></tr>
<tr><td>Country/ Setting</td><td>China</td></tr>
<tr><td>Population (including n)</td><td>538 COVID-19 survivors who were discharged from hospital prior to 1 March 2020 and 184 controls COVID-free volunteers living in Wuhan</td></tr>
<tr><td>Time since acute COVID-19</td><td>3 months
4 to 12 weeks grouping</td></tr>
<tr><td>Interventions/ Prognostic factors</td><td>Not applicable</td></tr>
<tr><td>Baseline characteristics</td><td>
<table>
<tr><td>Characteristic</td><td>COVID-19 survivors (n=538)</td><td>Comparison group (n=184)</td><td>P value</td></tr>
<tr><td>Sex</td><td>--</td><td>--</td><td>0.12</td></tr>
<tr><td>Male</td><td>245 (45.5%)</td><td>96 (52.2%)</td><td>--</td></tr>
<tr><td>Female</td><td>293 (54.5%)</td><td>88 (47.8%)</td><td>--</td></tr>
<tr><td>Median age (IQR)</td><td>52.0 (41-62)</td><td>--</td><td>--</td></tr>
<tr><td>Age group</td><td>--</td><td>--</td><td>0.19</td></tr>
<tr><td>20-40 years</td><td>117 (21.7)</td><td>51 (27.7)</td><td>--</td></tr>
<tr><td>41-60 years</td><td>250 (46.5)</td><td>84 (45.7)</td><td>--</td></tr>
<tr><td>61-80 years</td><td>171 (31.8)</td><td>49 (26.6)</td><td>--</td></tr>
<tr><td>Comorbidity</td><td>177 (32.9)</td><td>63 (34.2)</td><td>0.74</td></tr>
<tr><td>Hypertension</td><td>82 (15.2)</td><td>32 (17.4)</td><td>0.49</td></tr>
<tr><td>Diabetes</td><td>40 (7.4)</td><td>16 (8.7)</td><td>0.58</td></tr>
<tr><td>Chronic obstructive lung disease</td><td>22 (4.1)</td><td>6 (3.3)</td><td>0.62</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><td></td><td>
<table>
<tr><td>Coronary heart disease</td><td>18 (3.3)</td><td>9 (4.9)</td><td>0.34</td></tr>
<tr><td>Chronic kidney disease</td><td>12 (2.2)</td><td>3 (1.6)</td><td>0.77</td></tr>
<tr><td>Carcinoma</td><td>5 (0.9)</td><td>3 (1.6)</td><td>0.43</td></tr>
<tr><td>Other</td><td>32 (5.9)</td><td>7 (3.8)</td><td>0.27</td></tr>
</table>
</td></tr>
<tr><td>Inclusion and exclusion criteria</td><td>Inclusion criteria:
diagnosed with COVID-19 according to World Health Organization interim guidance and
cured and discharged from the hospital by 1 March 2020
All participants in the comparison group should have been completely quarantined at home for more than 3 months and had not done much physical work during the outbreak
Exclusion criteria:
those who had a complex illness, were currently undergoing medical intervention or were unable to provide detailed related information</td></tr>
<tr><td>Follow up</td><td>3 months</td></tr>
<tr><td>Main results</td><td>Characteristics and prevalence of residual or new symptoms
<table>
<tr><th>Characteristic</th><th>COVID-19 survivors (n=538)</th><th>Comparison group (n=184)</th><th>P value</th></tr>
<tr><td>General symptoms</td><td>267 (49.6)</td><td>22 (12.0)</td><td><0.01</td></tr>
<tr><td>– Physical decline/fatigue</td><td>152 (28.3)</td><td>17 (9.2)</td><td><0.01</td></tr>
<tr><td>– Sweating</td><td>127 (23.6)</td><td>3 (1.6)</td><td><0.01</td></tr>
<tr><td>– Myalgia</td><td>24 (4.5)</td><td>0 (0.0)</td><td><0.01</td></tr>
<tr><td>– Arthralgia</td><td>41 (7.6)</td><td>0 (0.0)</td><td><0.01</td></tr>
<tr><td>– Chills</td><td>25 (4.6)</td><td>0 (0.0)</td><td><0.01</td></tr>
<tr><td>– Limb oedema</td><td>14 (2.6)</td><td>0 (0.0)</td><td>0.03</td></tr>
<tr><td>– Dizziness</td><td>14 (2.6)</td><td>3 (1.6)</td><td>0.58</td></tr>
<tr><td>Respiratory symptoms</td><td>210 (39)</td><td>11 (6.0)</td><td><0.01</td></tr>
<tr><td>– Post-activity polypnoea</td><td>115 (21.4)</td><td>10 (5.4)</td><td><0.01</td></tr>
<tr><td>– Non-motor polypnoea</td><td>25 (4.7)</td><td>0 (0.0)</td><td><0.01</td></tr>
<tr><td>– Chest distress</td><td>76 (14.1)</td><td>0 (0.0)</td><td><0.01</td></tr>
<tr><td>– Chest pain</td><td>66 (12.3)</td><td>0 (0.0)</td><td><0.01</td></tr>
<tr><td>– Cough</td><td>38 (7.1)</td><td>1 (0.5)</td><td><0.01</td></tr>
<tr><td>– Sputum</td><td>16 (3)</td><td>1 (0.5)</td><td>0.09</td></tr>
<tr><td>– Throat pain</td><td>17 (3.2)</td><td>0 (0.0)</td><td><0.01</td></tr>
</table>
</td></tr>
</table>

Cardiovascular-related symptoms	70 (13)	1 (0.5)	<0.01
– Resting heart rate increase*	60 (11.2)	0 (0.0)	<0.01
– Discontinuous flushing	26 (4.8)	1 (0.5)	<0.01
– Newly diagnosed hypertension	7 (1.3)	0 (0.0)	0.2
Psychosocial symptoms	122 (22.7)	14 (7.6)	<0.01
– Somnipathy	95 (17.7)	9 (4.9)	<0.01
– Depression	23 (4.3)	2 (1.1)	0.04
– Anxiety	35 (6.5)	3 (1.6)	0.01
– Dysphoria	9 (1.7)	1 (0.5)	0.47
– Feelings of inferiority	3 (0.6)	0 (0.0)	0.57
Specific symptoms	154 (28.6)	0 (0.0)	<0.01
– Alopecia	154 (28.6)	0 (0.0)	<0.01

* an increased resting heart rate was defined as an increase of resting heart rate of more than 20 bpm compared to the rate before COVID-19

Subgroup data by most common sequelae

Characteristic	Physical decline/fatigue		
	Yes (n=152)	No (n=386)	P value
Sex	--	193 (50%)	<0.01
Male	52 (34%)	193 (50%)	
Female	100 (66%)	193 (50%)	--
Age	--	--	<0.01
20 to 40 years	16 (11%)	101 (26%)	--
41 to 60 years	72 (47%)	178 (46%)	--
61 to 80 years	64 (42%)	107 (28%)	--

Characteristic	Post activity polypnoea		
	Yes (n=115)	No (n=423)	P value
Sex	--	--	0.04
Male	43 (37%)	202 (47%)	--
Female	72 (63%)	221 (52%)	--
Age	--	--	0.14
20 to 40 years	18 (16%)	99 (23%)	--
41 to 60 years	54 (47%)	196 (46%)	--
61 to 80 years	43 (37%)	128 (30%)	--

Characteristic	Resting heart rate increase		
	Yes (n=60)	No (n=478)	P value

Sex	--	--	0.75
Male	26 (43%)	219 (46%)	--
Female	34 (57%)	259 (54%)	--
Age	--	--	0.69
20 to 40 years	12 (20%)	105 (22%)	--
41 to 60 years	26 (43%)	224 (47%)	--
61 to 80 years	22 (37%)	149 (31%)	--

Characteristic	Alopecia		
	Yes (n=154)	No (n=384)	P value
Sex	--	--	<0.01
Male	12 (8%)	233 (61%)	--
Female	142 (92%)	151 (39%)	--
Age	--	--	0.01
20 to 40 years	21 (14%)	96 (25%)	--
41 to 60 years	82 (53%)	168 (44%)	--
61 to 80 years	51 (33%)	120 (31%)	--

- In an additional exploratory analysis, dyspnoea during hospitalisation was associated with subsequent physical decline/fatigue, post activity polypnoea and resting heart rate increases, but not specifically with alopecia.
- A history of asthma during hospitalization was associated with subsequent post activity polypnoea sequelae
- A history of pulse 90 bpm during hospitalization was associated with resting heart rate increase symptoms in convalescence.
- The duration of virus shedding after COVID-19 onset and hospital length of stay were longer in survivors with physical decline/fatigue or post activity polypnoea than in those without.

The most common early clinical sequelae in COVID-19 survivors include physical decline/fatigue post activity polypnoea, resting heart rate increases, somnipathy and alopecia. These sequelae may be related to gender, age and clinical characteristics during hospitalisation.

Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)

Limitations:

- This study may have obtained less accurate information mainly because of the nature of telephone follow-up compared to face-to-face communication or physical examination
- Only a small number of patients were included in the study, and most of them had general or severe cases. Sequelae of COVID-19 patients with critical illness or patients undergoing complex life support treatment were not reflected in this study

Additional references

N/A

Appendix 7 Excluded studies

Please refer to the full list of excluded studies for this guideline.