NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

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

Evidence reviews 2 and 3: prevalence

December 2020 – **Please note that this is a revised version from that originally published**

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 the methods chapter.

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Review question 2

What is the prevalence of symptoms or clusters of symptoms (physical and mental health) and problems carrying out usual activities, including work, education and leisure, among people who have symptoms of COVID-19 for a duration of 4 to 12 weeks?

The review protocol is shown in appendix 2.

Included studies

In total, 4104 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, 23 of which were included for this review. Of these 21, 12 were cohort studies and 9 were cross-sectional studies and 2 were published real world evidence analyses.

See tables 1 to 3 for more details on the identified studies.

Table 1: Included studies for review question 2: hospitalised people

Study	Country, study design, dates	Population (n)	COVID-19 disease severity	Time since acute COVID-19 illness	Main symptoms/conditions reported
Arnold 2020	UK, prospective cohort, 30th March to 3rd June 2020	110 people hospitalised with COVID-19 (median age 60 years)	Mild, moderate and severe	8 to 12 weeks from admission	Breathlessness (39%) Excessive fatigue (39%) Insomnia (24%)
D'Cruz 2020	UK, prospective cohort, June to July 2020	119 COVID-19 survivors who had been hospitalised with PCR-confirmed severe COVID-19 pneumonia (mean age 58.7)	Severe	4 to 6 weeks from discharge	Fatigue (67.8%) Sleep disturbance (56.5%) Pain (49.6%) Breathlessness (46.2%) Cough (42.6%)

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Study	Country, study design, dates	Population (n)	COVID-19 disease severity	Time since acute COVID-19 illness	Main symptoms/conditions reported
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	Fatigue (45%) Tiredness (45%) Dyspnoea (33%) Cough (33%)
Halpin 2020	UK, retrospective cohort, May to June 2020	100 hospitalised people diagnosed with COVID-19 (median age 70.5 years ward people; 58.5 years ICU people)	Moderate to severe	4-8 weeks from discharge	Fatigue (64%) Breathlessness (50%) PTSD (31%)
Landi 2020	Italy, prospective cohort, 21st April to 21st May 2020	109 people recovered from COVID-19 (mean age 55.8 years)	Moderate to severe	8 weeks from COVID-19 onset	Fatigue (51.3%) Short of breath (45.8%) Joint pain (25.6%)
Mazza 2020	Italy, cross-sectional, 6 April to 9 June 2020	402 people surviving COVID-19 who had previously been hospitalised (mean age 57.8 years)	Severe	31 days after discharge	Psychiatric symptoms: 55.7% scored in the clinical range in at least one psychopathological dimension, 36.8% in two, 20.6% in three, and 10% in four
Weerahandi 2020	USA, prospective cohort, from 15 April 2020	152 people recovering from severe COVID-19 (median age 62 years)	Severe	30 to 40 days after discharge	Dyspnoea (74.3%)
Xiong 2020	China, retrospective cohort, up to 1 March 2020	538 COVID-19 survivors who were discharged from hospital (median age 52 years)	Moderate	3 months after discharge	General symptoms (49.6%) Respiratory symptoms (39%) CVD symptoms (13%) Psychosocial symptoms (22.7%)

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Table 2: Included studies for review question 2: Non-hospitalised people

Study	Country, study design, dates	Population (n)	COVID-19 disease severity	Time since COVID-19 illness	Main symptoms/conditions reported
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 COVID-19 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.
Boscolo-Rizzo 2020	Italy, cross sectional, 19 March to 22 March	202 people who were mildly symptomatic of COVID-19 (median age 56 years)	Mild	4 weeks after positive test	Altered sense of smell/taste (51.3%) Dry cough (39.7%) Problems breathing (39%) Headache (23.7%)
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	Chest pain (13.1%) Dyspnoea (7.7%) Flu-like symptoms (21.5%) Anosmia/Ageusia (22.7%) Arthralgia (16.3%) Palpitations (10.9%)
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	Anosmia, ageusia, difficulty concentrating, dyspnoea, memory loss, headache, heart palpitations were significant after 30 days and 60 days in COVID-19+ cases. Tachycardia was significant at 60 days All symptoms except memory loss were significant at 90 days
Eiros 2020	Spain, cross-sectional, 25 May 2020 to 12 June 2020	139 health-care workers with confirmed past SARS-CoV-2 infection (median age 52 years)	Not reported	10 weeks after infection onset	Cardiac symptoms (42%) Dyspnoea (26%) Fatigue (27%) Chest pain (19%)
Fjaelstad 2020	Denmark, cross-sectional, 22	109 non-hospitalised people experiencing a sudden	Mild	33.5 days after symptom onset	Anosmia (28%) Ageusia (20%)

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	April to 4 May 2020	chemosensory loss (mean age 39 years)			
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	Fatigue (87%) Dyspnoea (71%) Headache (38%) Chest tightness (44%) Palpitations (32%) Cough (29%)
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	Fatigue (72.8%) Dyspnoea (28.2%) Depression (28.6%) Anxiety (38%) Cognitive impairment (28.6%) Headache (28.9%) Joint pain (31.4%)
Paderno 2020	Italy, prospective cohort, April 27 to May 5, 2020	151 home-quarantined SARS-CoV-2–positive people (mean 45 years)	Most likely mild	45 days since symptom onset	Olfactory dysfunction (16%) Gustatory dysfunction (12%)
Poyraz 2020	Turkey, cross-sectional, March 15 and May 15, 2020	284 adults who had received care (mean age 39.7 years)	Mild to moderate	48.7 days since COVID-19 diagnosis	Fatigue (40%) Muscle aches (22%) Alteration of taste (18%) Headache (17%) Alteration of smell (17%)
Taquet 2020	USA, prospective cohort	44,779 COVID-19 survivors with no prior psychiatric history (mean age 49.3 years)	Not reported	14 to 90 days from illness	At 3 months a diagnosis of COVID-19 led to significantly more first diagnoses of psychiatric illness vs six other health events (HR 1.58 to 2.24, all P values <0.0001). The most frequent diagnosis was anxiety disorder, and the other most common disorders were adjustment disorder, generalised anxiety disorder and PTSD to a lesser extent.
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	Dyspnoea (55.6%) Asthenia (44.9%) Cough (25.9%) Chest pain (25.9%) Palpitations (22.2%)
Vaira 2020	Italy, prospective	138 people with COVID-19	Most likely mild	Up to 60 days from	Anosmia/ageusia (7.2%)

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	cohort, (date not reported)	(mean age 51.2 years)		COVID-19 diagnosis	

Table 3: Included studies for review question 2: Real world evidence

Study	Country, study design, dates	Population (n)	COVID-19 disease severity	Time since COVID-19 illness	Main symptoms/conditions reported
Banda 2020	Country not reported, real world data,21 May 2020 to 10 July 2020	150 tweets from 107 users in the largest publicly available COVID-19 Twitter chatter dataset.	Not reported	Not reported	malaise and fatigue (62%) dyspnoea (19%) tachycardia/palpitations (13%) chest pain (13%), insomnia/sleep disorders (10%) cough (9%) headache (7%)
Singh 2020	Country not reported, real world data 20 July 2020 to 29th July 2020	165 tweets from 89 users were included in the final analysis	Not reported	Not reported	Fatigue 42 (47%) Shortness of breath (26%) Brain fog 15 (17%) Exercise intolerance (15%) Pain in the whole body (10%)

Key results

Hospitalised people

Outcomes: Symptoms and conditions

Evidence from 8 studies recorded various symptoms reported by participants between 4 to 12 weeks from onset of acute COVID-19 or hospital discharge. Prevalence of these symptoms were wide ranging. The most common symptoms reported across the studies are reported in Table 3.

Table 3: Common symptoms reported across studies in hospitalised people

Symptom	Number of studies	Number of people (n)	Prevalence (range, %)
Shortness of breath	6	619	32% to 74%
Fatigue	6	950	28% to 68%
Cough	4	795	7.% to 43%
Sleep disturbance	3	659	18% to 57%
Cognitive impairment	3	248	18% to 22%

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Sore throat	3	680	3% to 9%
Loss of smell	2	142	12% to 15%
Loss of taste	2	142	9% to 10%

Only 1 study (Xiong 2020) included a control group of people who had never had COVID-19. This study reported that when compared to people who had never had COVID-19 (n=184), COVID-19 survivors (n=583) were significantly more likely to report symptoms at 3 months after hospital discharge (all p values <0.01).

Landi 2020 included a subgroup analysis. They tested participants with a nasopharyngeal swab RT-PCR test (approximately 8 weeks from COVID-19 onset) for SARS-CoV-2 infection. 22/131 (16.7%) tested positive. Comparison of symptoms at follow-up between people with positive and negative tests showed that people with a positive test were significantly more likely to report sore throat (p=0.04) and rhinitis (p=0.05).

Outcomes: Carrying out usual activities (including work, education and leisure)

There were 3 studies highlighted difficulties in people being able to carry out usual activities, due to both physical and mental health symptoms.

Weerahandi 2020 reported that people experienced worse physical and mental health after COVID-19 illness compared to before (all p values <0.001) and also experienced worsened ability to carry out social activities (p <0.001) at 1 month from discharge.

Halpin 2020 reported that 44/100 (44%) people reported worsened ability to carry out usual activities and that 15/100 (15%) were off sick from work at 4 to 6 weeks from discharge).

Mazza 2020 (n=402) performed a psychiatric assessment around a month after hospital discharge. They found that a significant proportion of people self-rated symptoms in the pathological range: overall, 55.7% scored in the clinical range in at least one psychopathological dimension, 36.8% in two, 20.6% in three, and 10% in four. People with a previous psychiatric history reported a more significant impact on mental health (all p values <0.001).

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Non-hospitalised people

Outcomes: Symptoms and conditions

Evidence from 13 studies recorded various symptoms reported by participants between 4 to 12 weeks from onset of acute COVID-19. Prevalence of these symptoms were wide ranging. The most common symptoms reported across the studies are reported in Table 4.

Table 4: Common symptoms reported across studies in non-hospitalised people

Symptom	Number of studies	Number of people (n)	Prevalence (range, %)
Loss of smell	8	3110	7% to 51%
Loss of taste	7	2960	5% to 51%
Shortness of breath	6	2999	8% to 71%
Chest pain	6	2999	6.9% to 44%
Joint pain	6	2999	2% to 31%
Headache	5	2849	5% to 38%
Fatigue	4	2823	27% to 87%
Palpitations	4	2510	10% to 32%
Fever	4	2710	2% to 11%
Cognitive impairment	2	679	2% to 29%

The following studies illustrate how these symptoms can vary across time and demonstrates their fluctuating nature. Some of these symptoms led to diagnoses of cardiac conditions or psychiatric illness.

Cirulli 2020 conducted longitudinal surveys on the general population in the USA regardless of history of COVID-19 infection or test. They found that 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 more common after 30 days in 233 people who had previously tested positive for SARS-CoV-2 compared to 3652 COVID-19 negative controls ($p<0.001$). However, after adjusting for initial numbers of symptoms, only long-term anosmia, ageusia, memory loss, and headache remained significantly associated with COVID-19 status. These symptoms remained significantly more common in people who had been COVID-19 positive after 60

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days. Tachycardia became significantly more common at 60 days. After 90 days, all of these 5 symptoms, except for memory loss, remained significantly more common in COVID-19 positive cases.

Goertz 2020 conducted a survey with 2113 participants from 2 Facebook groups and those registered on the Lung Foundation Netherlands website. They found that there was a median change of −7 (IQR −10 to −4) symptoms per person ($p<0.001$) at around 3 months from initial illness. The difference in median change of symptoms was highest in non-hospitalised patients with confirmed COVID-19 compared to hospitalised patients with COVID-19 and non-hospitalised suspected-based or symptom-based COVID-19 diagnosis ($p<0.001$).

Patient-led research (Assaf 2020) conducted a survey of 640 participants found that the majority of people with symptoms experienced fluctuations both in the type (70%) and intensity (89%) of symptoms over the course of being symptomatic.

Eiros 2020 carried out cardiac MRI investigations in health-care workers with previous COVID-19 illness. They found that cardiac MRI abnormalities were found in 104/139 (74.8%) 10 weeks after initial illness.

Taquet 2020 retrospectively analysed data for 44,779 people with a diagnosis of COVID-19 without prior psychiatric illness. They found that at 3 months a diagnosis of COVID-19 led to significantly more first diagnoses of psychiatric illness (HR 1.58 to 2.24, all P values <0.0001). The most frequent diagnosis was anxiety disorder, and the other most common disorders were adjustment disorder, generalised anxiety disorder and PTSD to a lesser extent. Those not requiring hospital admission for COVID-19 were still more at risk of psychiatric sequelae compared to people not requiring hospitalisation for other illnesses (influenza, other respiratory infections, skin infections, cholelithiasis, urolithiasis and fracture of a large bone; all p values <0.001).

Poyraz 2020 assessed psychological wellbeing of people with probable or confirmed COVID-19. They reported that 72/284 (25.4%) had moderate to severe PTSD symptoms at a mean of 48.7 days since diagnosis of COVID-19 illness.

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Outcomes: Carrying out usual activities (including work, education and leisure)

Poyraz 2020 assessed psychological wellbeing of patients with probable or confirmed COVID-19. They reported that 19/202 (9.4%) of working people were still on temporary disability leave at a mean of 48.7 days since diagnosis of COVID-19 illness.

Real world evidence studies

Evidence from 2 real world data studies provided analyses on social media posts (via Twitter) that contained information on symptoms reported as ongoing or new after acute COVID-19. Prevalence of these symptoms were wide ranging. The most common symptoms reported across the studies are reported in Table 5.

Table 5: Common symptoms reported in real world evidence studies

Rank	Banda (n=107)	Singh (n=89)
1	Malaise and fatigue (62%)	Fatigue (47.19%)
2	Dyspnoea (19%)	SOB (25.8%)
3	Chest pain (unspecified) (13%)	Brain fog (16.85%)
4	Tachycardia (unspecified) (13%)	Exercise intolerance (14.6%)
5	Insomnia (10%)	Pain in the whole body (10.11%)
6	Cough (9%)	Altered smell (7.86%)
7	Headache (7%)	Headache (7.86%)
8	Fever (unspecified) (6%)	Tachycardia (6.74%)
9	Pain (unspecified) (6%)	Altered taste (6.74%)
10	Pain in joint (6%)	Pain in chest (5.61%)

Strengths and limitations

Although these prevalence outcomes have been identified in cohort or cross-sectional studies, the primary aim of the studies was not necessarily to measure prevalence of symptoms. People were recruited to the studies in different ways, some of which were through self-selection and are subsequently less likely to be representative of the population. The sample sizes of the studies were also relatively

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small (majority with n <500) so may not be reliable to measure prevalence. Many studies were unable to obtain information of symptom history prior to initial COVID-19 illness. All studies were considered to be at high or moderate risk of bias (See evidence tables in appendix 6).

The real world evidence studies also had their own limitations. As this data came from social media, it is often incomplete, requires self-selection of users with a lack of objective validations of reported symptoms. The reporting of sociodemographic information and symptomatology were often vague or non-exact. Both studies included analysed data from the same social media platform so have potentially missed data from other platforms. These studies did not report the time since acute COVID-19 that the symptoms were being experienced so it is not possible to relate specifically to the case definition of post-COVID-19 syndrome.

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Review question 3 (published evidence)

What is the prevalence of symptoms or clusters of symptoms (physical and mental health) and problems carrying out usual activities, including work and leisure, among people who have symptoms of COVID-19 beyond 12 weeks?

The review protocol is shown in appendix 1.

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, 3 of which were included for this review. Of these 3, one was a cohort study and 2 were cross-sectional studies.

See table 6 and table 7.

Table 6: Included studies for review question 3: hospitalised people

Study	Country, study design, dates	Population (n)	COVID-19 disease severity	Time since COVID-19 illness	Main symptoms/conditions reported
Dennis 2020	UK, prospective cohort, April to August 2020	164 people with previous SARS-COV-2 infection who had been hospitalised (mean age 50 years)	Not reported	3 to 5 months after initial illness	Fatigue (97.6%) Muscle ache (87.6%) Shortness of breath (85.4%) Headache (84.8%) Joint pain (78%)
Tomasoni 2020	Italy, cross-sectional, April to June 2020	105 people clinically and virologically recovered from COVID-19 (mean age 55 years)	Not reported	>3 months from virological clearance	Asthenia (31.4%) Breathlessness (6.7%) Pain (10.5%) Cognitive impairment (17.1%) Loss of smell/taste (5.7%)

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Table 7: Included studies for review question 3: non-hospitalised people

Study	Country, study design, dates	Population (n)	COVID-19 disease severity	Time since COVID-19 illness	Main symptoms/conditions reported
Dennis 2020	UK, prospective cohort, April to August 2020	164 people with previous SARS-COV-2 infection who had been hospitalised (mean age 50 years)	Not reported	3 to 5 months after initial illness	Fatigue (87.1%) Muscle ache (87.6%) Shortness of breath (87.1%) Headache (87.1%) Joint pain (78.1%)
Klein 2020	Israel, cross-sectional, April 2020 to October 2020	112 Israeli residents with positive COVID-19 RT-PCR recruited via social media (mean age 35 years)	Most likely mild	Around 6 months after initial illness	Fatigue (20.5%) Loss of smell (13.4%) Breathlessness (8.9%) Myalgia (7.41%)

Key results

Hospitalised people

Outcomes: Symptoms and conditions

Very low-quality evidence from 2 studies recorded various symptoms reported at 12+ weeks from onset of acute COVID-19 by participants who were previously hospitalised. Prevalence of these symptoms were wide ranging. The symptoms most commonly reported across both studies were breathlessness (6.7% and 94.6%) and pain (10.5% and 45.9%).

Dennis 2020 reported that 164 (100%) of hospitalised people were experiencing fatigue at 3 to 5 months from initial illness. The majority of this cohort also reported cough, fever, myalgia headache joint pain, chest pain, wheezing and worsened mobility.

Tomasoni 2020 assessed their cohort with a HADS questionnaire (n=100). They found that 29% had abnormal results for anxiety and 11% were abnormal or depression. 33% had abnormal results for both anxiety and depression. Patients with

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abnormal HADS showed a higher proportion (77% vs 43%; P = 0.002) of physical symptoms persistence, compared to subjects displaying normal HADS.

Outcomes: Carrying out usual activities (including work, education and leisure)

No evidence was identified.

Non-hospitalised people

Outcomes: Symptoms and conditions

Very low-quality evidence from 2 studies recorded various symptoms at 12+ weeks from onset of acute COVID-19 reported by participants who had not previously been hospitalised for COVID-19. Prevalence of these symptoms varied across the studies. The symptoms most commonly reported across both studies were breathlessness (8.9% and 87.1%), fatigue (20.5% and 97.6%), myalgia (7.1% and 87.6%) and headache (3.6% and 87.1%).

Klein 2020 noted that fatigue, breathing difficulty, memory disorders and hair loss, were not typically reported during the 6-weeks follow-ups and were therefore new symptoms. Other symptoms such as muscle aches, headache and chemosensory changes were usually reported at earlier timepoints.

Outcomes: Carrying out usual activities (including work, education and leisure)

No evidence was identified.

Strengths and limitations

Although these prevalence outcomes have been identified in cohort or cross-sectional studies, the primary aim of the studies was not necessarily to measure prevalence of symptoms. 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. Only 3 studies were identified and the sample sizes of the studies were relatively small (all n<200) so may not be reliable to measure prevalence. The studies were unable to obtain information of symptom

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history prior to initial COVID-19 illness. All studies were considered to be at high or moderate risk of bias (See evidence tables in appendix 6).

Expert panel discussion (for both review questions 2 and 3)

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

Relative value of different outcomes

The outcomes the expert panel expected to see in the evidence were prevalence of symptoms or clusters of symptoms experienced by people at 4-12 weeks and 12+ weeks from acute COVID-19 onset. By identifying the most common symptoms experienced after acute COVID-19, it might be possible to use these to help differentially diagnose ongoing and post-COVID-19 syndrome, particularly if there are symptoms prevalent after 12 weeks or more.

The panel also wanted to consider how these symptoms impact on usual activities (including both work and leisure activities) in order to understand the wider implications of the long-term effects of COVID-19 such as loss of identity or sense of self.

Quality of the evidence

Whilst there was evidence of prevalence reported in the studies, the range of symptoms reported across the studies was very broad and there was a lack of clear evidence for differences in symptoms at the 4 to 12 week and 12+ weeks timepoints. Therefore, the panel could not draw strong conclusions from the data. There was high prevalence of some symptoms reported in individual studies and some evidence of association, but most studies did not identify many confounders or adjust for any that they did find so this data is unreliable. However, the published evidence and real world evidence analysis was consistent with the patient lived experience evidence and the panel's own experience in terms of which symptoms were the most common amongst those people with new and ongoing symptoms after COVID-19. These symptoms, for example included fatigue and breathlessness. The patient lived experience evidence supports the panel's experience of people reporting many

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symptoms that can fluctuate and affect them differently at different times. While the panel were unable to identify an exhaustive list of symptoms, due to the uncertainty in the evidence, they were able to recommend people are made aware of what they might expect in the time following their acute illness. The panel thought that it would be helpful to have a list of the most common symptoms, so these were drawn from the studies and the patient experience. There was no evidence identified that reported outcomes on clustering of symptoms so the panel considered making a research recommendation which is outlined in the guideline.

Whilst there was some quantitative evidence on the impact of symptoms on returning to work and other activities, it was very limited, and the panel could not draw firm conclusions in order to extrapolate to the wider population from this data. The panel thought that these outcomes will be affected by individual needs and characteristics so any support or advice given should be given based on holistic approach to assessment.

The overall certainty in the evidence was low to very low. People were recruited to the studies in different ways, some of which were through self-selection and are less likely to be representative of the population. The evidence showed a consistent pattern of people who were predominantly female and most likely middle-aged and of white ethnicity. The panel did not consider the evidence to be generalisable to the whole UK population. It highlighted expected over-representation in demographics for those more likely to seek help and those who use social media. The sample sizes of the studies were also relatively small so may not be reliable to measure prevalence. Most studies did not report symptoms prior to onset of acute COVID-19 and adjust for confounders or include a control group who had not had COVID-19. The panel would have liked to have had a better understanding of symptom history prior-to COVID-19 to determine the significance of these ongoing symptoms. Only one study compared reported symptoms to a COVID-19 free control group so the panel could not be confident in the findings.

Trade-off between benefits and harms

Although the panel acknowledged that new, ongoing or recurring symptoms 12 weeks or more from acute illness onset might be more indicative of post-COVID-19

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syndrome, they also thought it important to consider symptoms presenting earlier. This is to ensure symptoms that could indicate an acute complication are assessed as early as possible.

Implementation and resource considerations

Resource impact in relation to symptoms is covered in the evidence review on investigations.

Other considerations

The panel discussed that some reported symptoms, including dizziness, light-headedness and 'brain-fog', were not well reported in the published quantitative literature, despite it being reported in the patient lived experience evidence and the panel seeing these commonly in practice. However, they acknowledged that people may describe these symptoms in different ways and there could be limited ways in which data is recorded in the literature.

The patient lived experience data supported the panel's experience of people feeling dismissed when seeking help for their symptoms, and symptoms being mis-attributed to psychological causes. The panel discussed that this could increase anxiety levels.

The panel noted that there was no evidence identified for long term effects of COVID-19 in children and older people. They discussed that older people and children may present with atypical symptoms that could be overlooked. For example, older people can present with gradual decline, deconditioning, worsening frailty or dementia and may not be eating and drinking which can have a variety of causes. It would be reasonable to consider post-COVID-19 syndrome as a cause of these symptoms.

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Appendix 1 Methods used to develop the guidance

Please see the methods chapter for details of how this guidance was developed.

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Appendix 2 Review protocols

RQ 2: What is the prevalence of symptoms or clusters of symptoms (physical and mental health) and problems carrying out usual activities, including work, education and leisure, among people who have symptoms of COVID-19 for a duration of 4 to 12 weeks?

Criteria	Notes
Population	People experiencing symptoms or clusters of symptoms (ongoing physical and mental health) from 4 to 12 weeks after the onset of acute COVID-19.
Interventions/service configuration/information and support [delete/amend as appropriate]	Not applicable
Comparators	Not applicable
Outcomes	Prevalence of symptoms or clusters of symptoms (ongoing physical and mental health) reported 4-12 weeks following onset of acute COVID-19 including, but not limited to: Signs and symptoms: • respiratory symptoms such as chronic cough, shortness of breath, cardiovascular symptoms, and disease such as chest tightness, tachycardia, palpitations, protracted loss or change of smell and taste • mental health problems including but not limited to depression, anxiety and PTSD symptoms and cognitive difficulties • Neuropsychiatric or psychiatric symptoms • Neurological symptoms including weakness, numbness, continuing headaches, seizures, cognitive symptoms visual loss, autonomic symptoms, vestibular symptoms • Myalgia or joint pain • Evidence of end organ damage across a range of organs • Gastrointestinal disturbance with diarrhoea • Fatigue, weakness and sleeplessness • Skin rashes • Evidence of systemic inflammation • Conditions • Autonomic conditions • Respiratory conditions such as lung inflammation and fibrosis • Cardiovascular conditions such as myocarditis and heart failure • Liver and kidney dysfunction • Clotting disorders and thrombosis • Lymphadenopathy • Neurological disorders including neuropathy

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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) • Duration of symptoms
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. • Systematic reviews of observational studies • Prospective and retrospective observational studies • Descriptive studies; case series, case reports • Mixed method study designs
Countries	Any
Timepoints	Any
Other exclusions	None

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RQ 3: What is the prevalence of symptoms or clusters of symptoms (physical and mental health) and problems carrying out usual activities, including work and leisure, among people who have symptoms of COVID-19 beyond 12 weeks?

Criteria	Notes
Population	People experiencing symptoms or clusters of symptoms (ongoing physical and mental health) continuing after 12 weeks from the onset of acute COVID-19
Interventions/service configuration/information and support [delete/amend as appropriate]	Not applicable
Comparators	Not applicable
Outcomes	Prevalence of symptoms or clusters of symptoms (ongoing physical and mental health) reported 12+ weeks following onset of acute COVID-19 including, but not limited to: Signs and symptoms: • Respiratory symptoms such as chronic cough, shortness of breath, cardiovascular symptoms, and disease such as chest tightness, tachycardia, palpitations, protracted loss or change of smell and taste • Mental health problems including but not limited to depression, anxiety and PTSD symptoms and cognitive difficulties • Neuropsychiatric or psychiatric symptoms • Neurological symptoms including weakness, numbness, continuing headaches, seizures, cognitive symptoms visual loss, autonomic symptoms, vestibular symptoms • Myalgia or joint pain • Evidence of end organ damage across a range of organs • Gastrointestinal disturbance with diarrhoea • Fatigue, weakness and sleeplessness • Skin rashes • Evidence of systemic inflammation conditions • Autonomic conditions • Respiratory conditions such as lung inflammation and fibrosis • Cardiovascular conditions such as myocarditis and heart failure • Liver and kidney dysfunction • Clotting disorders and thrombosis • Lymphadenopathy • Neurological disorders including neuropathy
Settings	Any
Subgroups	• Groups as defined in the EIA for example, age, sex, ethnicity

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	• Diagnosis of COVID-19 (e.g. confirmed or high clinical suspicion) • Duration of symptoms
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. • Systematic reviews of observational studies • Prospective and retrospective observational studies • Descriptive studies; case series, case reports • Mixed method study designs
Countries	Any
Timepoints	Any
Other exclusions	None

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Appendix 3 Literature search strategy

Database strategies

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

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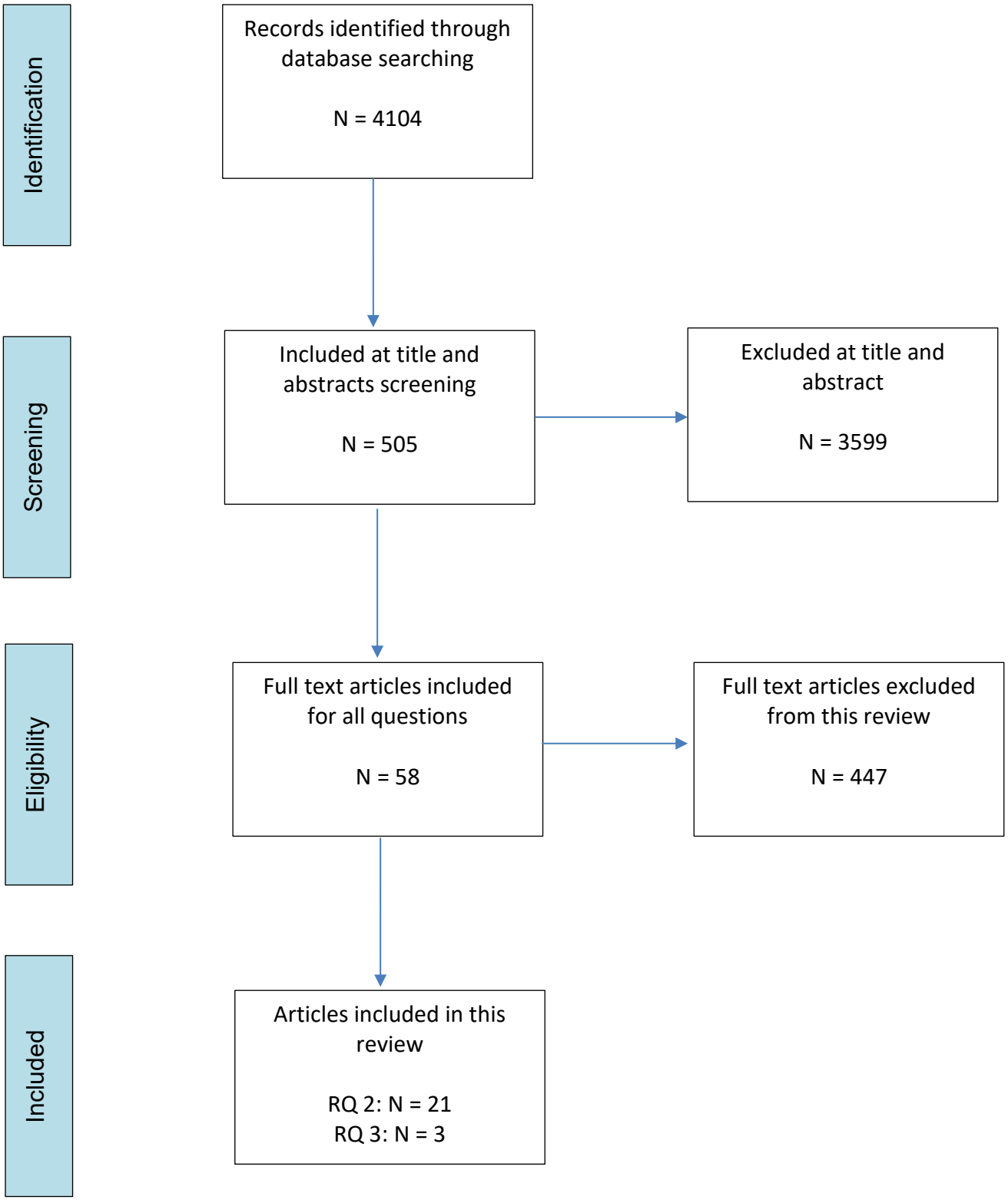
Appendix 4 Study flow diagram



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Appendix 5 Included studies

Review question 2: Symptom prevalence for people with ongoing symptoms in 4 to 12-week period post-acute Covid-19

Arnold, David T., Hamilton, Fergus W., Milne, Alice et al. (2020) Patient outcomes after hospitalisation with COVID-19 and implications for follow-up; results from a prospective UK cohort. medRxiv: 2020081220173526

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/

Boscolo-Rizzo, Paolo, Borsetto, Daniele, Fabbris, Cristoforo et al. (2020) Evolution of Altered Sense of Smell or Taste in Patients With Mildly Symptomatic COVID-19. JAMA Otolaryngology-Head & Neck Surgery 146(8): 729 to 732

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

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Eiros, Rocio, Perez Manuel, Barreiro-Perez, Garcia Ana, Martin-Garcia et al. Pericarditis and myocarditis long after SARS-CoV-2 infection: a cross-sectional descriptive study in health-care workers. medrxiv preprint

Fjaeldstad, Alexander Wieck (2020) Prolonged complaints of chemosensory loss after COVID-19. Danish medical journal 67(8)

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

Halpin, Stephen J, McIvor, Claire, Whyatt, Gemma et al. (2020) Post-discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. Journal of medical virology

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

Landi, Francesco, Carfi, Angelo, Benvenuto, Francesca et al. (2020) Predictive Factors for a New Positive Nasopharyngeal Swab Among Patients Recovered From COVID-19. American journal of preventive medicine

Mazza, Mario Gennaro, De Lorenzo, Rebecca, Conte, Caterina et al. (2020) Anxiety and depression in COVID-19 survivors: Role of inflammatory and clinical predictors. Brain, behavior, and immunity 89: 594 to 600

Paderno, Alberto, Mattavelli, Davide, Rampinelli, Vittorio et al. (2020) Olfactory and Gustatory Outcomes in COVID-19: A Prospective Evaluation in Nonhospitalized Subjects. Otolaryngology--Head and Neck Surgery: Official Journal of American Academy of Otolaryngology-Head and Neck Surgery: 194599820939538

Poyraz, B., Poyraz, C. et al (2020): Psychiatric morbidity and protracted symptoms in recovered COVID-19 patients. medRxiv preprint doi: https://doi.org/10.1101/2020.10.07.20208249

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Taquet, M., Luciano, S. et al (2020): Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62 354 COVID-19 cases in the USA. Lancet Psychiatry 2020. Published Online November 9, 2020 https://doi.org/10.1016/ S2215-0366(20)30462 to 4

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

Vaira, L.A., Hopkins, C. et al (2020): Smell and taste recovery in coronavirus disease 2019 patients: a 60-day objective and prospective study. J Laryngol Otol 2020;1 to 7. https://doi.org/10.1017/S0022215120001826

Weerahandi, H., Hochman, K. et al (2020): Post-discharge health status and symptoms in patients with severe COVID-19. medRxiv preprint doi: https://doi.org/10.1101/2020.08.11.20172742

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

Review question 3: Symptom prevalence for people with ongoing symptoms in 12 week-plus period post-acute Covid-19

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

Klein, Hadar, Asseo, Kim, Karni, Noam et al. Onset, duration, and persistence of taste and smell changes and other COVID-19 symptoms: longitudinal study in Israeli patients. medrxiv preprint

Tomasoni, Daniele, Bai, Francesca, Castoldi, Roberto et al. Anxiety and depression symptoms after virological clearance of COVID-19: A cross-sectional study in Milan, Italy. Journal of Medical Virology na(na)

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Appendix 6 Evidence tables

Review question 2 (4 to 12-week period)

Arnold 2020

Bibliographic reference/s	**Arnold, David T., Hamilton, Fergus W., Milne, Alice et al. (2020) Patient outcomes after hospitalisation with COVID-19 and implications for follow-up; results from a prospective UK cohort. medRxiv: 2020081220173526**
Questions relevant to?	**Investigations, risk factors, prevalance**
Publication status	Preprint
Study type	Prospective cohort
Quality	Low quality evidence CASP critical appraisal checklist: High risk of bias
Objective	To assess the prevalence of complications from COVID-19 within a UK cohort of hospitalised patients with COVID-19 to inform appropriate follow up in secondary or primary care.
Study date	30 March to 3 June 2020
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	UK
Population (including n)	110 patients hospitalised with COVID-19
	8 to 12 weeks 4 to 12 weeks grouping
Investigations	At 8 to 12 week follow up: • Face to face review with a respiratory or infectious disease clinician • Chest radiograph • Spirometry • Exercise testing (sit to stand) • Routine bloods • Routine observations • HRQoL questionnaires • Health status questionnaire
Baseline characteristics	

Characteristic	Severity of COVID-19 illness		
	Mild (n = 27)	Moderate (n = 65)	Severe (n =18)
Age (years)	47 (32,61)	57 (48, 67)	62 (54, 71)
BAME	5 (19%)	15 (23%)	3 (19%)
Male	13 (48%)	15 (23%)	3 (19%)
BMI (mean)	31.2	32.5	32.5

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T1DM	1 (3.7%)	1 (1.5%)	1 (5.6%)
T2DM	2 (7.4%)	12 (18%)	2 (11%)
Heart Disease	6 (22%)	11 (17%)	3 (17%)
Chronic lung disease	4 (15%)	16 (25%)	8 (44%)
Severe liver disease	0 (0%)	1 (1.5%)	0 (0%)
Severe kidney disease	1 (3.7%)	4 (6.2%)	2 (11%)
Hypertension	4 (15%)	16 (25%)	7 (39%)
HIV	0 (0%)	0 (0%)	1 (5.6%)
SARS CoV-2 PCR +ve (as inpatient)	21 (78%)	50 (77%)	10 (56%)
SARS-CoV-2-IgG +ve (Abbott) (at follow-up)	18 (67%)	56 (86%)	15 (83%)

Inclusion and exclusion criteria

Inclusion criteria:

- Positive PCR result for SARS-CoV-2 or a clinico-radiological diagnosis of COVID-19 disease

Exclusion criteria:

- Age <18 years
- Inability to give informed consent to study participation

Follow up

- 28 days after admission (remotely to review hospital/ GP notes)
- 8 to 12 weeks (face to face at respiratory outpatient clinic)

Main results

8 to 12 weeks follow-up:

Ongoing symptoms:

Total (n=110)	Mild (n = 27)	Moderate (n =65)	Severe (n =18)
81 (74%)	16 (59%)	49 (75%)	16 (89%)

Symptoms reported:

The most common symptoms at follow-up were breathlessness, excessive fatigue (39% prevalence each) and insomnia (24%), with the incidence of insomnia apparently increased at follow-up compared to baseline.

Patients with more severe disease were more symptomatic especially in terms of breathlessness, fatigue, myalgia, and insomnia.

Radiology:

	Total (n=110)	Mild (n = 27)	Moderate (n =65)	Severe (n =18)
Normal	95 (86.4%)	NR	NR	NR
Abnormal	15 (13.6%)	0 (0%)	10 (15.4%)	5 (27.8%)

Pulmonary function testing:

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	Mild (n = 27)	Moderate (n =65)	Severe (n =18)	P-value
O2 Saturations (%)	98.0 (96.5, 99.0)	97.00 (96.0, 98.00)	97.0 (96.0, 98.0)	0.88
Nadir of O2 saturations on STS test	96.0 (95.0, 97.0)	95.0 (93.0, 96.5)	95.0 (91.8, 96.0)	0.75
Respiratory rate	17.0 (14.0, 18.0)	17.0 (14.2, 19.8)	17.0 (16.0, 18.0)	0.95
FVC (L)	3.58 (3.13, 4.31)	3.52 (2.75, 4.36)	3.65 (2.55, 4.14)	0.70
FVC (% predicted)	97 (90, 105)	91 (78, 100)	89 (76, 98)	**0.05**
FEV1 (L)	2.97 (2.56, 3.42)	2.71 (2.12, 3.49)	2.54 (1.88, 3.23)	0.5
FEV1 (% predicted)	94 (82, 101)	90 (78, 100)	89 (73, 101)	0.30
Restrictive pattern	0 (0%)	8 (12%)	3 (17%)	**0.03**
Severe desaturation on STS test	0 (0%)	10 (15%)	5 (28%)	**0.02**

Health-related quality of life

More severe COVID-19 disease at baseline was associated with greater deficiencies. Physical scores such as physical role and the composite physical score were significantly lower in the severe cohort.

Health status (WEMWBS)

	Mild (n = 27)	Moderate (n =65)	Severe (n =18)	
Median score (IQR)	52 (IQR 44-56)	53 (IQR 42-59)	50 (39-58)	Not significant

Blood results

32/35 patients who had deranged liver or renal function on admission had returned to baseline.

Across the cohort, 4 additional patients had significantly abnormal blood results including ongoing lymphopenia (n=2), CRP greater than 10mg/L (n=2). There was no difference between abnormal results and severity of disease.

Summary

Patients with COVID-19 remain highly symptomatic at 8 to 12 weeks, however, clinical abnormalities requiring action are infrequent, especially in those without a supplementary oxygen requirement during their acute illness. This has significant implications for physicians assessing patients with persistent symptoms, suggesting that a more holistic approach focussing on rehabilitation and general wellbeing is paramount.

Comments (e.g. source of funding,	• Single-centre study with relatively small patient numbers so rarer complications from COVID-19 may have been missed

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statistical analysis, any major limitations, or issues with studies)	• Patients were followed up in a manner that might be replicated across may different hospital sites so cross-sectional imaging or full pulmonary function testing was not used routinely • At a time where waiting lists for such investigations are long and departments limited by personal protective equipment requirements, the availability of these tests are limited and should be used only when indicated
Additional references	Part of the DISCOVER study (Diagnostic and Severity markers of COVID-19 to Enable Rapid triage study)

Patient-Led Research Team (Assaf et al, 2020)

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 JIB critical appraisal rating: 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 illness	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

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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 to 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)

Boscolo-Rizzo 2020

Bibliographic reference/s	**Boscolo-Rizzo, Paolo, Borsetto, Daniele, Fabbris, Cristoforo et al. (2020) Evolution of Altered Sense of Smell or Taste in Patients With Mildly Symptomatic COVID-19. JAMA Otolaryngology-Head & Neck Surgery 146(8): 729 to 732**
Questions relevant to?	**Prevalence**
Publication status	Published
Study type	Cross sectional survey
Quality	Low quality evidence JBI checklist rating: High risk of bias

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Objective	The aim of this study was to evaluate the evolution of altered sense of smell or taste and other COVID-19 associated symptoms
Study date	March 19 and March 22
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	Italy
Population (including n)	202 patients who were mildly symptomatic of COVID-19
Time since acute COVID-19 illness	4 weeks from first swab 4 to 12 weeks grouping
Interventions/ Prognostic factors	Not applicable
Baseline characteristics	

Characteristics	N=187
Women	103 (55.1%)
Age, median (range)	56 (20-89)

Inclusion and exclusion criteria

Inclusion criteria:

- Patients were considered mildly symptomatic if they had less severe clinical symptoms with no evidence of pneumonia, not requiring hospitalization, and therefore considered suitable for being treated at home.
- tested positive for SARS-CoV-2 RNA by polymerase chain reaction (PCR) on nasopharyngeal and throat swabs performed according to World Health Organization recommendation

Follow up: Baseline: 5 to 6 days after swab; 4 weeks after swab

Main results

Symptom	Symptomatic at baseline	Symptom evolution in 4 weeks		Onset during follow up
		Recovered	Still present	
Fever	104	99 (95.2%)	5 (4.8%)	3
Dry cough or coughing up mucous	115	70 (60.3%)	46 (39.7%)	8
Blocked nose	70	54 (77.1%)	16 (22.9%)	12
Problems breathing	77	47 (61.0%)	30 (39%)	14
Headache	80	61 (76.3%)	19 (23.7%)	4
Sore throat	59	51 (86.4%)	8 (13.6%)	5
Muscle or joint pains	85	68 (80%)	17 (20%)	13
Chest pain	29	27 (93.1%)	2 (6.9%)	9
Sino nasal pain	31	28 (90.3%)	3 (9.7%)	3
Loss of appetite	101	87 (86.1%)	14 (13.9%)	6
Felt tired	130	101 (86.1%)	29 (13.9%)	0
Diarrhoea	84	74 (88.1%)	10 (11.9%)	1
Nausea	38	37 (97.4%)	1 (2.6%)	1

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Vomiting	12	12 (100%)	0 (0%)	1
Abdominal Pain	23	21 (91.3%)	2 (8.7%)	5
Dizziness	25	22 (88%)	3 (12%)	2
Altered sense of smell or taste	113	55 (48.7%)	58 (51.3%)	11

- During the fourth week after the first swab, the swab test for SARS-CoV-2 was repeated in 163 patients, with 52 (31.9%; 95% CI, 24.8%-39.6%) of them being found to be still positive and 111 (68.1%; 95% CI, 60.4%-75.2%) having no detectable SARS-CoV-2 RNA on PCR results.

The loss of smell or taste is among the most common and persistent symptoms of COVID-19 in patients with mildly symptomatic disease. However, at 4 weeks from the onset, most patients reported a complete resolution or improvement of these symptoms. Ongoing disturbance in smell and taste was not predictive of persistent SARS-CoV-2 infection.

Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	Data were self-reported, based on cross-sectional surveys, and thus may contain suboptimal sensitivity; the sample was relatively small, with patients with more severe disease excluded. Funding not reported
Additional references	N/A

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**
Publication status	Journal pre-proof
Study type	Prospective cohort
Quality	Low quality evidence CASP critical appraisal checklist rating: High risk of bias
Objective	To describe the clinical evolution and predictors of symptom persistence during 2-month follow-up in adults with non-critical COVID-19.
Study date	March 17 to June 3, 2020
COVID-19 prevalence	Not reported

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(high/low) if reported	
Country/ Setting	France
Population (including n)	150 patients with non-critical COVID-19
Time since acute COVID-19 illness	30 to 60 days 4 to 12 weeks grouping
Interventions/ Prognostic factors	None
Baseline characteristics	See results
Inclusion and exclusion criteria	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.
Follow up	30 and 60 days
Main results	**Patient characteristics 30 and 60 days after symptom onset**

		≥1 persisting symptom at 30 or 60 days			
	Total N=150	30 days N =103	P value	60 days N=86	P value
Female	84 (56%)	59 (57.3%)	0.6	48 (55.8%)	0.3
Age (years), mean (SD)	49 (15)		0.06		**0.026**
<30	16 (10.7%)	7 (6.8%)		4 (4.7%)	
30 to 39	32 (21.3%)	21 (20.4%)		19 (22.1%)	
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

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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 [1.2-9.5]	1.8 [0.7-4.7]
Abnormal auscultation	3.3 [1.3-8.0]	2.5 [1.0-6.1]
Hospitalisation	2.8 [1.2-6.2]	2.9 [1.3-6.9]
Dyspnoea	2.4 [1.0-5.3]	1.6 [0.7-3.9]
Flu-like symptoms	1.3 [0.5-3.4]	1.3 [0.5-3.5]

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Diarrhoea	1.2 [0.6-2.7]	1.0[0.5-3.5]
Fever	1.2 [0.6-2.4]	1.1 [0.5-2.2]
Chest pain	1.2 [0.4-3.7]	1.4 [0.4-5.0]
Anosmia/ageusia	0.9 [0.4-1.9]	1.6 [0.8-3.4]
Other respiratory signs	0.6 [0.2-2.3]	0.7 [0.2-2.8]
Female	1.2 [0.6-2.4]	1.5 [0.7-3.1]
Healthcare professional	0.7 [0.3-1.4]	0.8 [0.4-5.0]
1 comorbidity	1.0 [0.5-2.2]	0.8 [0.4-1.8]
2 comorbidities or more	1.5 [0.6-4.1]	1.7 [0.6-4.8]
Age 30 to 39	3.2 [0.9-11.1]	4.2 [1.0-17.8]
Age 40 to 49	13.3 [2.8-64.1]	15.3 [2.8-83.9]
Age 50 to 59	5.2 [1.5-18.3]	4.2 [1.0-17.3]
Age 60 to 69	2.3 [0.6-8.9]	2.9 [0.6-13.3]
Age≥70	2.9 [0.7-11.3]	2.6 [0.5-12.2]

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 40-60 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

Cirulli 2020

Bibliographic reference/s	**Cirulli, Elizabeth T., Barrett, Kelly M. Schiabor, Riffle, Stephen et al. (2020) Long-term COVID-19 symptoms in a large unselected population. medRxiv: 2020100720208702**
Questions relevant to?	**Prevalence, risk factors**
Publication status	Published
Study type	Retrospective cohort (survey administered at periodic intervals)
Quality	Low quality evidence

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	High risk of bias
Objective	To characterise the frequency, duration, and other properties of long-term COVID-19 symptoms
Study date	April 2020 to September 2020
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	USA/community
Population (including n)	General population, regardless of history of COVID-19 infection or test (n=21,359)
Time since acute COVID-19 illness	30 to 90 days 4 to 12 weeks grouping And 12+ weeks grouping
Interventions/ Prognostic factors	None
Baseline characteristics	See results
Inclusion and exclusion criteria	Inclusion criteria: • Adults Exclusion criteria: • Children
Follow up	30,60 and 90 days from symptom onset. Surveys were administered at intervals of 4 to 6 weeks from April to September 2020.
Main results	**Patient characteristics**

Median age (range)	58 (18-89+)
N female (%*)	11,570 (63.6%)
Ancestry N (%*) African East Asian European Latinx South Asian Other / mixed ancestry	 367 (2.0%) 302 (1.7%) 15267 (83.7%) 1658 (9.1%) 121 (0.7%) 520 (2.9%)
N with COVID-19 test (%) Positive (%) Negative (%)	3885 (18.2%) 233 (6.0%) 3652 (94.0%)
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			

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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 17.
- 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 *).

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	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

Daher 2020

Bibliographic reference/s	**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**
Questions relevant to?	**Investigations, prevalence, risk factors**
Publication status	Published
Study type	Cohort (retrospective)
Quality	Low quality evidence CASP critical appraisal rating: High risk of bias
Objective	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
Study date	February to May 2020
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	Germany
Population (including n)	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

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Time since acute COVID-19 illness	Time from discharge to follow up 56 (48 to 71) days 4 to 12 weeks grouping
Investigations	• Pulmonary function tests (PFTs) • Electrocardiography • Transthoracic echocardiography • Whole-body plethysmography • Blood tests • Heath-related quality of life • 6-min walk test
Baseline characteristics	

--	Patients (n=33)
Age (years)	64 ±3
Female	11 (33%)
Comorbidities	--
COPD	3 (9%)
Bronchial asthma	4 (13%)
Hypertension	19 (59%)
Heart failure	3 (9%)
Atrial fibrillation	3 (9%)
Chronic kidney disease	7 (22%)
Coronary artery disease	6 (19%)
Diabetes mellitus	8 (25%)

Inclusion and exclusion criteria	Inclusion criteria • 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
Follow up	6 weeks from discharge
Main results	**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:**

	Admission day (n=33)	Follow up (n=33)
Fever	22 (67%)	1 (3%)
Cough	23 (70%)	11 (33%)
Dyspnoea	16 (48%)	11 (33%)
Fatigue	21 (64%)	15 (45%)
Tiredness	15 (55%)	15 (45%)
Haemoptysis	1 (3%)	0 (%)
Rhinorrhoea	2 (6%)	4 (12%)
Sore throat	8 (24%)	3 (9%)

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Pharyngalgia	4 (12%)	0 (0%)
Angina pectoris	4 (12%)	6 (18%)
Myalgia	12 (42%)	5 (15%)
Headache	7 (21%)	5 (15%)
Cognitive disorders	--	6 (18%)
Loss of smell	8 (24%)	4 (12%)
Loss of taste	9 (27%)	3 (9%)
Diarrhoea	13 (39%)	3 (9%)
Nausea	8 (24%)	2 (6%)
Emesis	2 (6%)	0 (0%)
Stomach pains	7 (21%)	1 (3%)

Pulmonary function parameters and ABGs

--	Follow up (n=33)
TLC, % of predicted	94 (85 to 105)
VC, % of predicted	93 (78 to 101)
RV, % of predicted	112 (98 to 127)
RV/TLC, % of predicted	109 (98 to 126)
FEV1, % of predicted	95 (72 to 103)
FEV1/FVC, %	79 (76 to 85)
R eff, % of predicted	86 (62 to 104)
DLCO, % of predicted	65 (53 to 73)
DLCO/VA, % of predicted	77 (69 to 95)
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 - +1.2)
COHb, vol%	0.9 (0.71)

6-min walk test

--	Follow up (n=33)
Distance, m	380 (180-470)
Distance < predicted value, n	26 (79%)
Distance < LLN, n	15 (45%)
Walk distance - predicted value, m	138 (-37to -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)

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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

Eiros 2020

Bibliographic reference/s	**Eiros, Rocio, Perez Manuel, Barreiro-Perez, Garcia Ana, Martin-Garcia et al. Pericarditis and myocarditis long after SARS-CoV-2 infection: a cross-sectional descriptive study in health-care workers. medrxiv preprint**
Questions relevant to?	**Prevalence, Investigations**

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Publication status	Preprint
Study type	Cross sectional observational cohort
Quality	Low quality evidence JBI critical appraisal checklist rating: Moderate risk of bias
Objective	A cross-sectional study in health-care workers to report evidence of pericarditis and myocarditis after SARS-CoV-2 infection.
Study date	25 May 2020 to 12 June 2020
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	Spain
Population (including n)	139 health-care workers with confirmed past SARS-CoV-2 infection (103 diagnosed by RT-PCR between March 13 and April 25 and 36 by serology April 10 and May 22)
Time since acute COVID-19 illness	Approximately 10 weeks after infection onset 4 to 12 weeks grouping
Investigations	• Complete medical history • Physical examination • Questionnaire • ECG • Blood investigations • CMR
Baseline characteristics	

--	--	Presence of pericardial and myocardial manifestations				--
--	All participants (n=139)	No (n=84)	Pericarditis (n=4)	Myopericarditis (n=15)	Myocarditis (n=36)	P value
Age, median (range)	52 (41–57)	52 (38–57)	45 (34–52)	54 (44–60)	52 (48–57)	0.503
Female sex	100 (72)	56 (67)	3 (75)	12 (80)	29 (81)	0.4
Health care worker category	--	--	--	--	--	0.669
– Medical Staff	35 (25)	22 (26)	1 (25)	6 (40)	6 (17)	--
– Nurse	49 (35)	28 (33)	1 (25)	4 (27)	16 (44)	--
– Other	55 (40)	34 (40)	2 (50)	5 (33)	14 (39)	--
Coexisting conditions	--	--	--	--	--	--

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Obesity	17 (12)	14 (17)	1 (25)	0	2 (6)	0.108
Hypertension	17 (12)	11 (13)	1 (25)	1 (7)	4 (11)	0.679
Diabetes	2 (1)	2 (2)	0	0	0	1
Dyslipidaemia	27 (19)	17 (20)	1 (25)	2 (13)	7 (19)	0.936
Current smoking	6 (4)	4 (5)	0	1 (7)	1 (3)	0.741
Past smoking	70 (50)	43 (51)	0	6 (40)	21 (58)	0.140
Alcohol (≥1 drink per day)	23 (16)	10 (12)	1 (25)	3 (20)	9 (25)	0.217
CVD	8 (6)	5 (6)	0	2 (13)	1 (3)	0.472
Pulmonary disease	8 (6)	5 (6)	0	0	3 (8)	0.805
Sleep apnoea-hypopnea	8 (6)	5 (6)	0	2 (13)	1 (3)	0.472
CKD	5 (4)	2 (2)	0	0	3 (8)	0.319
Cancer	4 (3)	3 (4)	0	0	1 (3)	1

Inclusion and exclusion criteria	Inclusion criteria: • tested positive for SARSCoV-2 by RT-PCR between March 13 and April 25; and 36 health-care workers were diagnosed after testing positive for anti-SARS-CoV-2-IgG antibodies between April 10 and May 22
Follow up	

Main results

--	All participants	Presence of pericardial and myocardial manifestations				P value
--	All participants (n=139)	No (N=84)	Pericarditis (n=4)	Myopericarditis (N=15)	Myocarditis (N=36)	--
Time from onset to exam (weeks)	10.4 (9.3 to 11.0)	10.4 (9.0 to 11.1)	9.0 (6.9 to 13.3)	10.4 (9.9 to 10.9)	10.3 (9.3 to 11.1)	0.841
Symptoms on examination						
No symptoms	48 (34%)	33 (39%)	0	3 (20%)	12 (33%)	0.274
General	--	--	--	--	--	--
Fatigue	37 (27%)	23 (27%)	1 (25%)	4 (27%)	9 (25%)	0.982

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Anosmia	12 (9%)	5 (6%)	1 (25%)	1 (7%)	5 (14%)	0.188
Ageusia	7 (5%)	4 (5%)	1 (25%)	0	2 (6%)	0.307
Headache	7 (5%)	4 (5%)	0	2 (13%)	1 (3%)	0.455
Sore throat	7 (5%)	3 (4%)	0	1 (7%)	3 (8%)	0.515
Abdominal pain	6 (4%)	3 (4%)	0	1 (7%)	2 (6%)	0.625
Memory loss	4 (3%)	2 (2%)	0	0	2 (6%)	0.770
Joint pain	3 (2%)	1 (1%)	0	2 (13%)	0	0.071
Piloerection	2 (1%)	1 (1%)	1 (25%)	0	0	0.068
Cardiac						
Dyspnoea	36 (26%)	20 (24%)	2 (50%)	7 (47%)	7 (19%)	0.115
Chest pain	27 (19%)	8 (9%)	3 (75%)	11 (73%)	5 (14%)	**<0.001**
Chest pain (pericarditis like)	18 (13%)	3 (4%)	3 (75%)	11 (73%)	1 (3%)	**<0.001**
Palpitations	20 (14%)	10 (12%)	2 (50%)	3 (20%)	5 (14%)	0.163
Dizziness	8 (6%)	2 (2%)	1 (25%)	2 (13%)	0	0.071
At least one cardiac symptom	58 (42%)	28 (33%)	4 (100%)	11 (73%)	15 (42%)	**0.002**
Electrocardiographic measures						
Widespread ST elevation	13 (9%)	7 (8%)	0	5 (33%)	1 (3%)	**0.017**
PR depression	33 (24%)	17 (20%)	2 (50%)	8 (53%)	6 (17%)	**0.016**
Laboratory measures						
GFR <60ml/min x 1.73[3]	2 (1%)	0	1 (25%)	0	1 (3%)	**0.033**
CMR imaging measures						
T2-weighted hyperintensity	6 (4%)	0	0	1 (7%)	5 (14%)	**0.006**
Increase of native myocardial	58 (42%)	24 (29%)	0	7 (47%)	27 (75%)	**<0.001**

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T1-relaxation time						
Increase of T1-extracellular volume	52 (37%)	17 (20%)	0	9 (60%)	26 (72%)	**<0.001**
T1-late gadolinium enhancement	10 (7%)	2 (2%)	0	4 (27%)	4 (11%)	**0.008**
Pericardial effusion	42 (30%)	4 (5%)	3 (75%)	15 (100%)	20 (57%)	**<0.001**

- CMR abnormalities were observed in 104 (75%)

Pericarditis and myocarditis with clinical stability are frequent long after SARS-CoV-2 infection, even in presently asymptomatic subjects. These observations will probably apply to the general population infected and may indicate that cardiac sequelae might occur late in association with an altered (delayed) innate and adaptative immune response

Comments (e.g. source of funding, statistical analysis, any major limitations or issues with studies)	Funding: This study was supported by CIBERCV (CB16/11/00374), CIBERONC (CB16/12/00400) and the COV20/00386 grant from the Instituto de Salud Carlos III and FEDER, Ministerio de Ciencia e Innovación, Madrid, Spain. Limitations: • Focused only on HCWs so may have limited generalisability to non-health care settings
Additional references	The study is registered with ClinicalTrials.gov NCT04413071

Fjaeldstad 2020

Bibliographic reference/s	**Fjaeldstad, Alexander Wieck (2020) Prolonged complaints of chemosensory loss after COVID-19. Danish medical journal 67(8)**
Questions relevant to?	**Prevalence**
Publication status	Published
Study type	Cross sectional
Quality	Low quality evidence JBI critical appraisal checklist rating: High risk of bias
Objective	To map the rate of subjective improvement and recovery of chemosensory function in the weeks following confirmed or suspected COVID-19.
Study date	Data collection started on 22 April and concluded on 4 May
COVID-19 prevalence	Not reported

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Bibliographic reference/s	**Fjaeldstad, Alexander Wieck (2020) Prolonged complaints of chemosensory loss after COVID-19. Danish medical journal 67(8)**
Questions relevant to?	**Prevalence**
Publication status	Published
(high/low) if reported	
Country/ Setting	Denmark
Population (including n)	Non-hospitalised people experiencing a sudden chemosensory loss in 2020 (n=109)
Time since acute COVID-19 illness	--
Interventions/ Prognostic factors	--
Baseline characteristics	Olfactory loss (n=100): Mean age 39.4 years, 79% female, Confirmed COVID-19 (n=42) and unknown COVID-19 (n=58) Gustatory loss (n=104): Mean age 40.3 years, 79% female, Confirmed COVID-19 (n=41) and unknown COVID-19 (n=63)
Inclusion and exclusion criteria	Patients were eligible for participation if they were above 18 years of age and had experienced a sudden chemosensory loss after 27 February 2020.
Follow up	Mean 33.5 days
Main results	• After mean of >30 days after symptom onset, 28% of participants had not yet experienced any improvement of their olfactory function, whereas 44% had fully recovered from their olfactory loss. • Participants who had improved their sense of smell were not significantly younger (mean difference: –3.5 years (95% CI: –9.6 to 2.7), p = 0.2611), and no age difference was found for recovery (mean difference: 0.03 years (95% CI: –4.8 to 4.8), p = 0.9888). • After a mean of >30 days after symptom onset, 20% of participants still had had not experienced any improvement of their gustatory function, whereas 50% had fully recovered from their olfactory loss. • Among participants with olfactory deficits (n = 100), most reported complete olfactory loss (anosmia, n = 82), whereas 15 participants reported a reduction of olfactory intensity (hyposmia). • Among participants with gustatory complains (n = 104), complete taste loss was most common (ageusia, n = 72), whereas 24 participants reported having a reduced taste intensity (hypogeusia). 15 participants complained of distorted taste, among whom 7 also had hypogeusia. No participants complained of phantom taste sensations. • Nine of the 109 participants experienced smell loss as the primary symptom, among whom seven reported a combined smell and taste loss (three had been COVID-19 tested, all of whom were SARS-CoV-2-positive). • Age had no impact on time to recovery.
Comments (e.g. source of funding,	Limitations:

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Bibliographic reference/s	**Fjaeldstad, Alexander Wieck (2020) Prolonged complaints of chemosensory loss after COVID-19. Danish medical journal 67(8)**
Questions relevant to?	**Prevalence**
Publication status	Published
statistical analysis, any major limitations or issues with studies)	• The chemosensory deficits reported in this study are based on subjective assessments. There is a risk of misclassifying the nature of chemosensory deficits when subjective assessments are used. • Not all participants in this study had undergone SARS-CoV-2 testing. However, as indicated in Table 1, participants without confirmed COVID-19 had a similar age and improvement rate as the confirmed COVID-19 participants. • The design of the study carries an inherent risk of recall bias.
Additional references	N/A

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: 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 illness	4 to 12 weeks grouping
Interventions/ Prognostic factors	Not applicable

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Baseline characteristics	--	Whole sample (n=2113)	Hospitalised (n=112)	Non-hospitalised (confirmed COVID-19) (n=345)	Non-hospitalised (symptom-based COVID-19) (n=882)	Non-hospitalised (suspected COVID-19) (n=774)	p value
	Women	1803 (85.3%)	78 (69.6%)	314 (91%)	774 (87.8%)	637 (82.3%)	<0.001
	Age, years	47.0 (39.0 to 54.0)	53.0 (46.3 to 60.0)	47.0 (37.0 to 53.5)	46.0 (38.0 to 53.0)	47.0 (39.0 to 54.0	<0.001
	BMI kgm^{-2}	25.2 (22.6 to 28.8)	26.9 (24.5 to 30.9)	26.0 (23.2 to 29.4)	25.0 (22.3 to 28.7)	24.9 (22.5 to 28.4)	<0.001
	Comorbidities (self-reported)						
	None	1293 (61.2)	51 (45.5)	225 (65.2)	523 (59.3)	494 (63.8)	0.007
	1	541 (25.6)	40 (35.7)	77 (22.3)	240 (27.2)	184 (23.8)	
	≥2	279 (13.2)	21 (18.8)	43 (12.5)	119 (13.5)	96 (12.4)	
	Health status before onset of symptoms (self-reported)						
	Good	1799 (85.1%)	88 (78.6%)	316 (91.6%)	743 (84.6%)	652 (84.2%)	0.011
	Moderate	301 (14.2%)	23 (20.5%)	27 (7.8%)	134 (15.2%)	117 (15.1%)	
	Poor	13 (0.6%)	1 (0.9%)	2 (0.6%)	5 (0.6%)	5 (0.6%)	

Inclusion and exclusion criteria	Exclusion criteria: • Patients admitted to ICU
Follow up	79 days since onset of first symptoms

Main results	Symptoms at follow up	N=2113
	Fatigue	87%
	Dyspnoea	71%
	Headache	38%
	Chest tightness	44%
	Cough	29%
	Muscle pain	26%
	Sore throat	26%
	Increased body temp	22%
	Pain between shoulder blades	33%
	Pain/burning in lungs	24%
	Heart palpitations	32%
	Increased resting HR	28%
	Dizziness	27%

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Burning feeling in trachea	20%
Nose cold	18%
Fever	2%
Ageusia	11%
Diarrhoea	10%
Anosmia	13%
Joint pain	22%
Nausea	12%
Mucus	18%
Sneezing	12%
Hot flushes	13%
Eye problems	12%
Ear pain	8%
Sudden loss of body weight	3%
Vomiting	1%
Red spots on toes/feet	2%
Others	27%

	During infection (n=2113)	At follow up (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.

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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

Halpin 2020

Bibliographic reference/s	**Halpin, Stephen J, McIvor, Claire, Whyatt, Gemma et al. (2020) Post-discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. Journal of medical virology**		
Questions relevant to?	**Prevalence, monitoring**		
Publication status	Published		
Study type	Cross sectional		
Quality	Low quality evidence JBI Critical appraisal checklist rating: High risk of bias		
Objective	To report on the assessment of post discharge symptoms and rehabilitation needs in COVID-19 survivors after hospital discharge		
Study date	May to June 2020		
COVID-19 prevalence (high/low) if reported	High		
Country/ Setting	UK, secondary care		
Population (including n)	hospitalised patients diagnosed with COVID-19 (n=100)		
Time since acute COVID-19 illness	4 to 8 weeks since discharge		
Interventions/ Prognostic factors	None		
Baseline characteristics	--	**Ward no. (%)**	**Intensive care unit patients no. (%)**

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Bibliographic reference/s	**Halpin, Stephen J, McIvor, Claire, Whyatt, Gemma et al. (2020) Post-discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. Journal of medical virology**
Questions relevant to?	**Prevalence, monitoring**
Publication status	Published

Demographic information	--	--
Total no.	68	32
Age, median (range), y	70.5 (20 to 93)	58.5 (34 to 84)
Sex	--	--
Female	33 (48.5)	13 (40.6)
Male	35 (51.5)	19 (59.4)
Ethnicity	--	--
White	54 (79.4)	19 (59.4)
Mixed	1 (1.5)	0
Asian or Asian British	2 (2.9)	8 (25)
Black or Black British	5 (7.4)	3 (9.4)
Other Ethnic groups	0	0
Unknown	6 (8.8)	2 (6.3)
Occupation	--	--
Keyworker	16 (23.5)	14 (20.6)
Works in a health care setting	4 (5.9)	11 (16.2)
Comorbidities	--	---
Body mass index:	--	--
Underweight	2 (2.9)	1 (3.3)
Healthy weight	18 (26.5)	7 (23.3)

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Bibliographic reference/s	Halpin, Stephen J, McIvor, Claire, Whyatt, Gemma et al. (2020) Post-discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. Journal of medical virology
Questions relevant to?	**Prevalence, monitoring**
Publication status	Published

Overweight	25 (36.8)	10 (33.3)
Obese	12 (17.6)	12 (40.0)
Unknown	11 (16.2)	0
Cancer:	--	--
Active	7 (10.3)	0
Active or previous	16 (23.5)	5 (15.6)
Cardiovascular disease:	--	--
Heart failure	5 (7.4)	0
Hyperlipidaemia	2 (2.9)	2 (6.3)
Hypertension	27 (39.7)	14 (43.8)
Ischemic heart disease	9 (13.2)	1 (3.1)
Tachyarrhythmias	9 (13.2)	2 (6.3)
Valvular heart disease	2 (2.9)	1 (3.1)
Venous thromboembolism	4 (5.9)	1 (3.1)
Chronic respiratory disease:		
Asthma	9 (13.2)	4 (12.5)
Chronic obstructive pulmonary disease	6 (8.8)	2 (6.3)
Obstructive sleep apnoea	4 (5.9)	3 (9.4)
Other	3 (4.4)	0
Chronic kidney disease	11 (16.2)	4 (12.5)

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Bibliographic reference/s	**Halpin, Stephen J, McIvor, Claire, Whyatt, Gemma et al. (2020) Post-discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. Journal of medical virology**
Questions relevant to?	**Prevalence, monitoring**
Publication status	Published

Other urological disease	9 (13.2)	4 (12.5)
Endocrine:		
Type 1 diabetes	1 (1.5)	0
Type 2 diabetes	19 (27.9)	9 (28.1)
Prediabetic	5 (7.4)	1 (3.1)
Thyroid disease	2 (2.9)	3 (9.4)
Other	3 (4.4)	0
Gastrointestinal disease	20 (29.4)	5 (15.6)
Gynaecological disease	3 (4.4)	0
Haematological disease (excluding malignancy)	4 (5.9)	6 (18.8)
Immunosuppressed	9 (13.2)	6 (18.8)
Infectious disease	3 (4.4)	3 (9.4)
Mental health condition	14 (20.6)	5 (15.6)
Musculoskeletal disease and rheumatology	--	--
Osteoarthritis	11 (16.2)	2 (6.3)
Rheumatological disease	6 (8.8)	8 (25.0)
Other musculoskeletal disease	12 (17.6)	5 (15.6)
Neurological disease	8 (11.8)	4 (12.5)
Total with ≥3 significant comorbidities	48 (70.6)	18 (56.3)

Inclusion and exclusion criteria	Inclusion criteria for telephone follow-up were: patients diagnosed with COVID-19 by polymerase chain reaction (PCR) test of a nasopharyngeal sample during inpatient hospital admission, 4 weeks, or more since discharge from hospital for

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Bibliographic reference/s	**Halpin, Stephen J, McIvor, Claire, Whyatt, Gemma et al. (2020) Post-discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. Journal of medical virology**
Questions relevant to?	**Prevalence, monitoring**
Publication status	Published
	the index admission, not currently a hospital inpatient, and resident within the Leeds Metropolitan District. Exclusion criteria were if no contact details were available for the patient, under 18 years of age, or if telephone contact was inappropriate due to dementia, learning disability, or other cognitive or communication impairment.
Follow up	4 to 8 weeks since discharge
Main results	Summary: New illness-related fatigue was the most common reported symptom by 72% participants in the ICU group and 60.3% participants in the ward group. The next common symptoms were breathlessness (65.6% in ICU group and 42.6% in ward group) and psychological distress (46.9% in ICU group and 23.5% in ward group). There was a clinically significant drop in EQ5D in 68.8% of participants in the ICU group and in 45.6% of participants in the ward group. Sixty percent of the ICU group and 15% of the ward group remained off-sick from work at the point of follow-up.

Prevalence of reported problems after COVID-19 inpatients discharged from hospital:

Domain	Ward patients (68)		ICU patients (32)	
	Number	%	Number	%
Fatigue				
Any new fatigue	41	60.3	23	72.0
Mild (0 to 3)	17	25.0	6	18.8
Moderate (4 to 6)	14	20.6	13	40.6
Severe (7-10)	10	14.7	4	12.5
Breathlessness				
Any new or worsened breathlessness[a]	29	42.6	21	65.6
Mild (increased by 1-3/10)	14	20.6	10	31.3
Moderate (increased by 4-6/10)	10	14.7	7	21.9
Severe (increased by 7-10/10)	5	7.4	4	12.5
Increased at rest	13	19.1	9	28.1

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Bibliographic reference/s	Halpin, Stephen J, McIvor, Claire, Whyatt, Gemma et al. (2020) Post-discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. Journal of medical virology
Questions relevant to?	**Prevalence, monitoring**
Publication status	Published

Increased on dressing	18 (/66)b	27.3	10	31.3	
Increased on stairs	24 (/57)b	42.1	21	65.6	
Neuropsychological					
Any PTSD symptoms related to illness	16	23.5	15	46.9	
Mild symptoms	12	17.6	9	28.1	
Moderate symptoms	4	5.9	4	12.5	
Severe symptoms	0	0.0	2	6.3	
Thoughts of self-harm	1	1.5	1	3.1	
New or worsened concentration problem	11	16.2	11	34.4	
New or worsened short-term memory problem	12	17.6	6	18.8	
Speech and swallow					
Swallow problem	4	5.9	4	12.5	
Laryngeal sensitivity	9	11.8	8	25.0	
Voice change	12	17.6	8	25.0	
Communication difficulty	4	5.9	2	6.3	
SLT referral criteria met (impact rating of 1 or more in any SLT domain)	14	20.6	9	28.1	
Nutrition					
Concern about weight/nutrition	10	14.7	2	6.3	
Appetite problem severity 2 or more	6	8.8	2	6.3	
Dietetics referral criteria met (either of the above criteria)	12	17.6	4	12.5	

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Bibliographic reference/s	Halpin, Stephen J, McIvor, Claire, Whyatt, Gemma et al. (2020) Post-discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. Journal of medical virology				
Questions relevant to?	**Prevalence, monitoring**				
Publication status	Published				
	Continence				
	New bowel control problem	2	2.9	1	3.1
	New bladder control problem	6	8.8	4	12.5
	EQ-5D-5L				
	Mean EQ-5D-5L index value on day of screen	0.724		0.693	
	Mean change	−0.061		−0.155	
	Decreased by at least 0.05 (MCIDc)	31	45.6	22	68.8
	Worsened mobility	21	30.9	16	50
	Worsened self-care	12	17.6	4	12.5
	Worsened usual activities	25	36.8	19	29.4
	Worsened pain/discomfort	10	14.7	9	28.1
	Worsened anxiety/depression	11	16.2	12	37.5
	Perceived health (self-rated 0-100 scale)				
	Mean change	−5.8		−12.53	
	Decrease by more than 7 points (MCIDc)	22	32.4	17	53.1
	Health service contact				
	Represented to hospital	8	11.8	4	12.5
	Used other health services	42	61.8	21	65.6
	Vocation change since COVID-19 illness	*n* = 20d		*n* = 20d	

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Bibliographic reference/s	**Halpin, Stephen J, McIvor, Claire, Whyatt, Gemma et al. (2020) Post-discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. Journal of medical virology**
Questions relevant to?	**Prevalence, monitoring**
Publication status	Published

Returned to same level of employment	14	70.0	2	10.0
Previously full time, now part-time	0	0.0	2	10.0
Off sick	3	15.0	12	60.0
Furloughed	2	10.0	4	20.0
Newly retired	1	5.0	0	0.0

Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	**Limitations** The method of selecting ICU patients was not reported clearly. The authors reported that participants who received treatment on the ICU were expected to present as a distinct group with more severe needs, therefore, as many as possible of this group were included in follow-up. Participants who had received ward-based care were then selected randomly from the list and until a total of 100 participants had been successfully followed up. The MDT made use of telephone calls as a method of contact, which allowed for data collection during a restrictive lockdown period; however, this created limitations on being able to contact certain participants, such as those with dementia, learning difficulties, non-English speakers. Selected participants were those who had been diagnosed with a positive PCR swab result of COVID-19 while as an inpatient within LTHT; however, patients who had a negative swab result but who were likely to have COVID-19 based on clinicoradiological criteria were not included in this study. This study does not include COVID-19 survivors who were not hospitalised. It is likely that non-hospitalised COVID-19 survivors will have different rehabilitation needs.
Additional references	N/A

Kamal 2020

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

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Study type	Cross-sectional
Quality	Low quality evidence JBI critical appraisal rating: 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 illness	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 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-

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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%

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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

Landi 2020

Bibliographic reference/s	**Landi, Francesco, Carfi, Angelo, Benvenuto, Francesca et al. (2020) Predictive Factors for a New Positive Nasopharyngeal Swab Among Patients Recovered From COVID-19. American journal of preventive medicine**
Questions relevant to?	**Risk factors, prevalence**
Publication status	Published
Study type	Prospective cohort
Quality	Low quality evidence CASP critical appraisal checklist rating: Moderate risk of bias
Objective	To identify the potential risk factors associated with a new positive nasopharyngeal swab RTPCR test (after 2 negative tests) in a large sample of patients who recovered from COVID-19
Study date	April 21 and May 21, 2020
COVID-19 prevalence	Not reported

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(high/low) if reported	
Country/ Setting	Italy
Population (including n)	131 recovered from COVID-19
Time since acute COVID-19 illness	Around 8 weeks 4 to 12 weeks grouping
Interventions/ Prognostic factors	Not applicable
Baseline characteristics	

Characteristics	Total (N=131)	Negative test (n=109)	Positive test (n=22)	P value
Age (years)	55.8 ± 14.8	55.7 ± 14.7	56.4 ± 15.7	0.84
Sex, female	51 (38.9)	41 (37.6)	10 (45.4)	0.41
Education, years	14.4 ± 7.8	14.9 ± 8.2	12.4 ± 4.3	0.21
Smoking habit	11 (8.3)	9 (8.2)	2 (9.0)	0.33
Influenza vaccination	23 (17.5)	17 (15.5)	6 (27.2)	0.20
Hypertension	38 (29.0)	32 (29.3)	6 (27.2)	0.53
Heart failure	8 (6.1)	6 (5.5)	2 (9.0)	0.40
Diabetes	7 (5.3)	5 (4.5)	2 (9.0)	0.33
Renal failure	4 (3.0)	3 (2.7)	1 (4.5)	0.52
COPD	12 (9.1)	10 (9.1)	2 (9.0)	0.67
BMI (kg/m^2)	26.2 ± 4.2	25.9 ± 4.3	27.6 ± 3.2	0.10
Days from COVID-19 onset	55.8 ± 10.8	56.5 ± 11.1	52.6 ± 8.8	0.26
Days from first positive test	47.1 ± 10.6	47.4 ± 10.8	45.5 ± 9.3	0.46
Needed oxygen support	66 (50.3)	55 (50.4)	11 (50.0)	0.57

Inclusion and exclusion criteria	Inclusion criteria: 1. Fever-free without fever-reducing medications for 3 consecutive days 2. Improvement of any symptoms related to COVID-19 including reduced coughing and shortness of breath 3. ≥7 days since the onset of the first symptom related to COVID-19 4. Testing negative for the SARS-CoV-2 virus twice (at least 24 hours apart) with nucleic acid RT-PCR
Follow up	Approx 8 weeks from COVID-19 onset A new RT-PCR test was repeated at the time of post-acute care admission
Main results	Symptoms reported at follow up

Characteristics	Total (N=131)	Negative test (n=109)	Positive test (n=22)	P value
Cough	22 (16.7)	16 (14.6)	6 (27.2)	0.13
Fatigue	67 (51.1)	56 (51.3)	11 (50.0)	0.54
Diarrhoea	5 (3.8)	4 (3.6)	1 (4.5)	0.60
Headache	14 (10.6)	11 (10.0)	3 (13.6)	0.42

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Smell disorders	18 (13.7)	16 (14.6)	2 (9.0)	0.38
Dysgeusia	15 (11.4)	11 (10.0)	4 (18.1)	0.22
Red eyes	21 (16.0)	16 (14.6)	5 (22.7)	0.42
Joint pain	33 (25.1)	28 (25.6)	5 (22.7)	0.51
Short of breath	58 (44.2)	50 (45.8)	8 (36.3)	0.28
Loss of appetite	13 (9.9)	11 (10.0)	2 (9.0)	0.62
Sore throat	9 (6.8)	5 (4.5)	4 (18.1)	**0.04**
Rhinitis	19 (14.5)	13 (11.9)	6 (27.2)	**0.05**

Adjusted Association (PR and 95% CI) Between Potential Risk Factors and the Positive RT-PCR for SARS-CoV-2 Test

Characteristic	Adjusted, PR (95% CI)
Age, years	0.99 (0.96, 102)
Sex (female)	0.85 (0.31, 2.38)
Cough	1.93 (0.54, 6.80)
Sore throat	6.50 (1.38, 30.6)
Rhinitis	3.72 (1.10, 12.5)
BMI	1.10 (0.99, 1.23)

This study is the first to provide a given rate of patients (16.7%) who test positive on RT-PCR test for SARS-CoV-2 nucleic acid after recovering from COVID-19. These findings suggest that a significant proportion of patients who have recovered from COVID-19 still could be potential carriers of the virus

Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	Limitations: • Lack of information on symptom history before acute COVID-19 infection • Lack of details on symptom severity • Single study-centre study with a small number of patients without a control group Funding not reported
Additional references	N/A

Mazza 2020

Bibliographic reference/s	**Mazza, Mario Gennaro, De Lorenzo, Rebecca, Conte, Caterina et al. (2020) Anxiety and depression in COVID-19 survivors: Role of inflammatory and clinical predictors. Brain, behavior, and immunity 89: 594-600**
Questions relevant to?	**Investigations, prevalence**
Publication status	Published

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Study type	Cross sectional
Quality	Low quality evidence JBI critical appraisal checklist rating: High risk of bias
Objective	To investigate the psychopathological impact of COVID-19 in survivors at one month follow up, also considering the effect of possible risk factors
Study date	April 6 to June 9, 2020
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	Italy
Population (including n)	402 patients surviving COVID-19 who had previously been hospitalised
Time since acute COVID-19 illness	4 weeks 4 to 12 weeks grouping
Investigations	Psychiatric assessments Inflammatory biomarkers
Baseline characteristics	Male 265/402 (65.9%) Mean age 57.8 years, range (18-87 years)
Inclusion and exclusion criteria	Exclusion criteria: • Patients under 18 years
Follow up	Psychiatric assessment was performed 31.29 ± 15.7 days after discharge, or 28.56 ± 11.73 days after ED
Main results	Psychiatric symptoms by gender

--	Females (n=137)	Males (n=265)	P value
Age	55.90 ± 14.69	58.79 ± 12.49	
Follow-up oxygen saturation level	97.87 ± 1.27	97.84 ± 1.38	0.868
IES-R (n = 368, 91.5%)	34.24 ± 16.58	18.30 ± 16.58	<0.001
PCL-5 (n = 341, 84.8%)	22.63 ± 12.39	10.29 ± 12.39	<0.001
ZSDS (n = 368, 91.5%)	51.20 ± 9.26	40.61 ± 9.26	<0.001
BDI-13 (n = 372, 91.5%)	5.08 ± 3.48	2.32 ± 3.48	<0.001
STAI-state (n = 341, 84.8%)	44.51 ± 9.55	34.84 ± 9.55	<0.001
STAI-trait (n = 352, 87.6%)	41.23 ± 9.52	33.21 ± 9.52	<0.001
MOS (n = 328, 87.6%)	23.46 ± 5.00	19.08 ± 5.00	<0.001
WHIIRS (n = 367, 91.3%)	9.25 ± 4.62	6.18 ± 4.62	<0.001

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OCI (n = 360, 89.5%)	14.44 ± 9.40	10.41 ± 9.40	<0.001

Psychiatric symptoms by psychiatric history

	Positive psychiatric history (n=106)	Negative psychiatric history (n=296)	P value
Males	52 (19.7%)	212 (80.3%)	< 0.001
Age	55.45 ± 12.47	58.61 ± 13.56	0.036
Follow-up oxygen saturation level	97.98 ± 1.16	97.80 ± 1.40	0.313
IES-R (n = 368, 91.5%)	35.76 ± 22.15	19.34 ± 17.16	< 0.001
PCL-5 (n = 341, 84.8%)	23.30 ± 18.89	10.99 ± 12.93	< 0.001
ZSDS (n = 368, 91.5%)	50.24 ± 13.09	42.00 ± 9.83	< 0.001
BDI-13 (n = 372, 91.5%)	5.58 ± 5.87	2.41 ± 3.29	< 0.001
STAI-state (n = 341, 84.8%)	44.61 ± 12.44	35.74 ± 9.48	< 0.001
STAI-trait (n = 352, 87.6%)	41.88 ± 12.07	33.78 ± 9.23	< 0.001
MOS (n = 328, 87.6%)	22.53 ± 6.68	19.78 ± 5.23	< 0.001
WHIIRS (n = 367, 91.3%)	9.07 ± 5.29	6.57 ± 4.76	< 0.001
OCI (n = 360, 89.5%)	15.94 ± 11.55	10.28 ± 9.17	< 0.001

Psychiatric symptoms by COVID-19 management setting

	Managed at home (n=102)	Admitted (n=300)	P value
Males	45 (17%)	220 (83%)	< 0.001
Age	50.82 ± 14.43	60.18 ± 12.07	< 0.001
Follow-up oxygen saturation level	98.24 ± 1.40	97.73 ± 1.31	0.005
IES-R (n = 368, 91.5%)	26.81 ± 20.35	22.83 ± 19.85	0.098
PCL-5 (n = 341, 84.8%)	16.90 ± 15.91	13.74 ± 15.78	0.117
ZSDS (n = 368, 91.5%)	45.78 ± 11.04	43.71 ± 11.50	0.128
BDI-13 (n = 372, 91.5%)	4.04 ± 4.62	3.03 ± 4.30	0.055

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STAI-state (n = 341, 84.8%)	40.37 ± 11.69	37.44 ± 10.80	0.033
STAI-trait (n = 352, 87.6%)	37.99 ± 10.48	35.25 ± 10.70	0.032
MOS (n = 328, 87.6%)	22.18 ± 6.16	20.03 ± 5.60	0.003
WHIIRS (n = 367, 91.3%)	7.81 ± 5.44	7.05 ± 4.87	0.210
OCI (n = 360, 89.5%)	12.55 ± 10.34	11.56 ± 10.12	0.417

- A significant proportion of patients self-rated symptoms in the pathological range: overall, 55.7% scored in the clinical range in at least one psychopathological dimension, 36.8% in two, 20.6% in three, and 10% in four.
- Severity of depression also included suicide ideation and planning, with 2.9% scoring 1 (suicidal ideation) at the BDI suicide item, 0.8% scoring 2 and 0.8% scoring 3 (suicidal planning)
- Females, patients with a positive previous psychiatric diagnosis, and patients who were managed at home showed an increased score on most measures.
- Considering the previous need for psychiatric interventions, prior of COVID-19, 36 patients had been diagnosed with major depressive disorder, 28 with generalized anxiety disorder, 20 with panic attack disorder, 5 with bipolar disorder, 5 with social phobia, 3 with eating disorders, and 4 with other disorders. These patients suffered a more significant impact on mental health, as rated on most measures.

Summary

COVID-19 survivors presented a high prevalence of emergent psychiatric sequelae, with 55% of the sample presenting a pathological score for at least one disorder.

Higher than average incidence of PTSD, major depression, and anxiety, all high-burden non-communicable conditions associated with years of life lived with disability, is expected in survivors.

Considering the alarming impact of COVID-19 infection on mental health, we now suggest assessing psychopathology of COVID-19 survivors, to diagnose and treat emergent psychiatric conditions, monitoring their changes over time, with the aim of reducing the disease burden, which is expected to be very high in patients with psychiatric conditions.

Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	Limitations: The main limitation of the present study is its cross-sectional nature that does not allow interpretation for causality
Additional references	N/A

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Paderno 2020

Bibliographic reference/s	**Paderno, Alberto, Mattavelli, Davide, Rampinelli, Vittorio et al. (2020) Olfactory and Gustatory Outcomes in COVID-19: A Prospective Evaluation in Nonhospitalized Subjects. Otolaryngology--Head and Neck Surgery: Official Journal of American Academy of Otolaryngology-Head and Neck Surgery: 194599820939538**
Questions relevant to?	**Prevalence**
Publication status	Published
Study type	Prospective cohort study
Quality	Low quality evidence CASP critical appraisal checklist rating: High risk of bias
Objective	To prospectively assess the rate and timing of recovery of olfactory (OD) and gustatory (GD) dysfunction in patients affected by COVID-19.
Study date	April 27 to May 5, 2020
COVID-19 prevalence (high/low) if reported	High
Country/ Setting	Italy
Population (including n)	home-quarantined SARS-CoV-2–positive patients (n=151)
Time since acute COVID-19 illness	The mean lag time between the first symptom onset and T0 survey was 22 days
Interventions/ Prognostic factors	None
Baseline characteristics	

--	n (%)
Mean age, y (range)	45 (18-70)
Gender, n (%)	--
Male	56 (37)
Female	95 (63)
Main comorbidities, n (%)	--
Obesity	4 (3)
Hypertension	20 (13)
Asthma or allergic rhinitis	19 (13)
Cardiopathy	3 (2)
Diabetes	3 (2)
Immune disorders	3 (2)
Pneumopathy	2 (1)
Nephropathy	0 (0)

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Number of comorbidities, n (%)	--
0	105 (70)
1	30 (20)
2	11 (7)
3	5 (3)
Smoking history, n (%)	--
Current smoker	12 (8)
Former smoker	26 (17)
Non-smoker	113 (75)

Inclusion and exclusion criteria	Inclusion criteria: • signed written informed consent, • male or female >18 years of age, • willing and able to participate in the study, • positive nasal-pharyngeal swab for SARS-CoV-2 (reverse transcriptase polymerase chain reaction), and • overall clinical status not requiring hospitalization. Exclusion criteria: • legal incapacity or limited legal capacity. • medical or psychological condition or situation which in the opinion of the investigator would not permit the patient to complete the questionnaire or sign informed consent, and • pre-existing chronic anosmia and/or ageusia.
Follow up	45 days since symptom onset
Main results	A total of 151 patients were included in the final prospective cohort. OD and/or GD were observed in 126 (83%) and 135 (89%) subjects, respectively. A total of 20 (16%) subjects reported ongoing olfactory dysfunction (OD) at the end of the follow-up (mean time from onset, 37 days), of which 16 (80%) reported partial improvement. Late complete recovery was associated with total OD at presentation (P < .001) and female gender (P = .02). Association with nasal congestion was not statistically significant at univariate analysis (P = .1). A total of 16 (12%) subjects reported ongoing gustatory dysfunction (GD) at the end of the follow-up (mean time from onset, 33 days), of which 11 (69%) reported partial improvement. Late complete recovery was associated with total GD at presentation (P =.006), female gender (P = .013), and presence of nasal congestion (P = .046). Three (2%) patients previously reporting complete resolution of symptoms referred a subsequent recurrence of OD (1%; n = 2) and/or GD (1%; n = 2) at a

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	mean of 19 days after resolution of the previous episode. These alterations were still ongoing at the time of the evaluation without other symptoms related to COVID-19.
Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	**Limitations** While the response rate was greater than 70%, the influence of selection bias should not be overlooked. Symptomatic patients are significantly more likely to respond to follow-up surveys, and this could lead to an overestimation of disease prevalence. The study cohort was recruited at T0 by means of a cross-sectional survey. Therefore, symptom evaluation is partially retrospective (i.e., before T0) and partially prospective (i.e. after T0). For this reason, a recall bias could affect the precision of data collection. Although therapies that could potentially influence OD and GD were ruled out at T0, specific evaluation of empiric treatments for OD and GD was not performed during the follow-up. The entire analysis was based on subjective questionnaires.
Additional references	N/A

Poyraz 2020

Bibliographic reference/s	**Poyraz, B., Poyraz, C. et al (2020): Psychiatric morbidity and protracted symptoms in recovered COVID-19 patients. medRxiv preprint doi: https://doi.org/10.1101/2020.10.07.20208249**
Questions relevant to?	**Symptoms and prevalence, Risk factors**
Publication status	Preprint
Study type	Cross-sectional survey study
Quality	Low quality evidence JBI Critical appraisal rating: High risk of bias
Objective	To investigate psychiatric symptomatology and protracted symptoms in recently recovered COVID-19 patients.
Study date	March 15 and May 15, 2020
COVID-19 prevalence (high/low) if reported	Not stated
Country/ Setting	Turkey: tertiary hospital of Cerrahpaşa Medical Faculty, Istanbul
Population (including n)	Adult patients who had received care between March 15 and May 15, 2020 (n=284 – N.B. 1,200 patients contacted: response rate ~23%)
Time since acute COVID-19 illness	Patients meeting WHO criteria for discontinuation of quarantine (no fever in three consecutive days and 14 days after significant clinical improvement) Time between the diagnosis of COVID-19 infection and the survey response was 48.7 days (SD = 20.4; range = 14-116 days).
Interventions/ Prognostic factors	None

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Baseline characteristics	Mean age 39.7 (SD=12.7), females 49.8% Majority of subjects: • 28 to 57 years of age (69.4%) • married (65%) • employed (68.3%) • had a university or higher education (50%) • had a child less than 18 years of • age (65.3%) • had a household size of 3 or 4 individuals (54.3%). Ninety-two patients (34.2%) had one or more chronic medical disease(s). Among these, hypertension (10.4%), diabetes mellitus (8.6%), cardiac diseases (9.7%), pulmonary diseases (8.2%), and cancer (3%) were the most common diagnoses.
Inclusion and exclusion criteria	Patients meeting WHO criteria for discontinuation of quarantine (no fever in three consecutive days and 14 days after significant clinical improvement), identified from hospital records. Also volunteering post-acute COVID-19 outpatients followed by the infectious disease department of the above hospital.
Follow up	None
Main results	"One hundred and eighteen patients (44.3%) reported one or more potential symptom(s) that persisted after the acute symptoms subsided. Overall, they reported a median of one potential symptom (range=0-8) that persisted, with fatigue (40%), muscle aches (22%), alteration of taste (18%), headache (17%), alteration of smell (17%), difficulty in concentration (15%), daytime sleepiness (10%), light-headedness (7%), and numbness and tingling sensations on the skin (6%), being the symptoms that persisted. Other protracted symptoms reported by subjects were dyspnoea (4%), chest pain (3%), and cough (2%)." "Of the 202 working subjects, 19 subjects (9.4%) reported that they were still on temporary disability leave, and 28 subjects (13.8%) reported that they lost their jobs or were put on temporary leave by the employer during the lockdown. Twenty-seven subjects (13.3%) started working from home or paid infrequent office visits lately, and 128 subjects (63.3%) did not report a significant change in their work routine. A chi-square test showed that PTSD severity in the working subjects did not differ significantly by the state of having lost a job or being on temporary leave by the employer (X2 (2, N = 202) = 0.618, p=0.91). On the other hand, PTSD severity differed by the state of being on temporary disability leave (X2 (2, N = 202) = 6.57, p=0.03), and a significantly higher number of subjects with moderate-to-severe PTSD symptoms (20% of them) was still on temporary disability leave."
Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	Note that the focus of this study was more on the links between PTSD and persistent symptoms following COVID infection as well as risk factors for developing PTSD - rather than on the symptoms themselves; however, the study may be useful in identifying prevalence of various symptoms post-COVID. Authors: questioned on a checklist whether the potential symptoms of interest persisted after the acute infectious symptoms subsided. These symptoms included the alteration of smell and taste, headache, fatigue, daytime sleepiness, muscle aches, light-headedness, difficulty in concentration, and numbness and tingling sensations on the skin. Authors: "Patients with COVID-19 are prone to substantial psychological distress after the infection. PTSD symptoms and comorbid depression, as well as anxiety, and impaired sleep comprise a substantial part of the distress described by these individuals. Various personal (i.e. gender and prior trauma history) and psychosocial factors (i.e., perceived stigmatization and a personal

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	view on seriousness of the threat posed by the COVID-19 pandemic) are likely to mediate the mental health effects in the context of COVID-19. The protracted symptoms are also frequent in this period, and these symptoms are related to the posttraumatic psychiatric morbidity."
Additional references	N/A

Taquet 2020

Bibliographic reference/s	**Taquet, M., Luciano, S. et al (2020): Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62 354 COVID-19 cases in the USA. Lancet Psychiatry 2020. Published Online November 9, 2020 https://doi.org/10.1016/ S2215-0366(20)30462-4**
Questions relevant to?	**Prevalence**
Publication status	Preprint
Study type	Retrospective cohort
Quality	Low quality evidence CASP critical appraisal checklist rating: Moderate risk of bias
Objective	To assess psychiatric sequelae and antecedents to COVID-19
Study date	People with a diagnosis of COVID-19 from January 20 2020 onward
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	USA
Population (including n)	Data from TriNetX analytics network (global federated healthcare research network), anonymised HER data from 54 healthcare organisations in the USA. Totalling 69.8 million patients 62,354 diagnosis of COVID-19. Subset of 44,779 had no prior psychiatric illness and who had not died were used as the COVID-19 cohort.
Time since acute COVID-19 illness	14 to 90 days 4 to 12-week group
Interventions/ Prognostic factors	Groups with COVID matched to cohorts who had been diagnosed with other health events (influenza, another respiratory tract infection, skin infection, cholelithiasis, urolithiasis fracture of a large bone).
Baseline characteristics	Mean (SD) age 49.3 (19.7); 55.3% female;
Inclusion and exclusion criteria	COVID-19 diagnosis People with previous psychiatric illness excluded.
Follow up	Incidence of a first psychiatric over a period of 14 to 90 days after a diagnosis of COVID-19
Main results	A diagnosis of COVID-19 led to significantly more first diagnoses of psychiatric illness (HR 1.58 to 2.24, all P values <0.0001). At 90 days the estimated probability of having been diagnosed with a new onset psychiatric illness following COVID-19 was 5.8% (95%CI 5.2, 6.4). The most frequent diagnosis was anxiety disorder (HRs 1.59 – 2.62), with a probability of outcome within 90 days of 4.7% (95%CI 4.2, 5.3). The most

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	common disorders seen were adjustment disorder, generalised anxiety disorder and to a lesser extent PTSD There was a low probability of being newly diagnosed with a psychotic disorder on 14- 90 days post COVID-19 (HR 0.1 95%CI 0.08, 0.2) Insomnia: 1.9 (1.6, 2.2). About 60% of insomnia diagnoses were not accompanied by a concurrent diagnosis of an anxiety disorder Dementia: increased probability of diagnosis, among patients over 65 years the risk was 1.6% (95%CI 1.2, 2.1) with HR between 1.89 and 3.18. Increased risk of sequalae remained unchanged when cohorts limited to patients with known race (HR between 1.52 and 2.19), and patients with confirmed COVID (HR between 1.63 and 2.28) Patients with COVID-19 requiring inpatient admission were more at risk of psychiatric sequelae than patients not needing an admission (HR 1.40 95%CI 1.06, 1.85) When limiting cohorts to people not requiring inpatient admission, large differences in psychiatric sequelae remain between COVID-19 and other cohorts (HR 1,54 2.23 all p<0.0001).
Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	Primary aim of the study was to see whether psychiatric illness was an antecedent for COVID-19 illness
Additional references	N/A

Vaira 2020

Bibliographic reference/s	**Vaira, L.A., Hopkins, C. et al (2020): Smell and taste recovery in coronavirus disease 2019 patients: a 60-day objective and prospective study. J Laryngol Otol 2020;1 to 7. https://doi.org/ 10.1017/S0022215120001826**
Questions relevant to?	**Signs and symptoms** **Prevalence**
Publication status	Published
Study type	Prospective cohort
Quality	Low quality evidence CASP critical appraisal rating: 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

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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 illness	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 chemo sensitive 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	N/A

Valiente-De Santis 2020

Bibliographic reference/s	**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**
Questions relevant to?	**Risk factors, prevelance, investigations**
Publication status	Preprint
Study type	Prospective cohort
Quality	Low quality evidence CASP critical appraisal rating: High risk of bias

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Objective	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.
Study date	14 March to 15 April
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	Spain
Population (including n)	108 patients with previous acute SARS-CoV-2 infection contacted by telephone
Time since acute COVID-19 illness	12 weeks after acute phase (4 to 12 weeks grouping)
Investigations	• Blood test • Chest radiograph • Chest CT • Spirometry • Serological test
Baseline characteristics	During acute episode

Characteristic	Total (N=108)	Symptomatic (n=82)	Asymptomatic (n=26)	P value
Age > 65 years	29 (26.9%)	17 (20.7%)	12 (46.2%)	0.011
Female	60 (55.6%)	47 (57.3%)	13 (50%)	NS
Male	48 (44.4%)	35 (42.7%)	12 (50%)	
Healthcare worker	30 (27.8)	28 (34.1)	2 (7.7)	0.009
Mild acute symptoms	64 (59.3)	48 (58.5)	16 (61.5)	NS
Severe acute symptoms	44 (40.7)	34 (41.5)	10 (38.5)	
ICU during acute episode,	4 (3.7)	3 (3.7)	1 (3.8)	NS

Inclusion and exclusion criteria	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)
Follow up	12 weeks
Main results	Symptoms 12 weeks after the acute episode

Symptom	N= 82 (75.9%)
Dyspnoea	60 (55.6)
Asthenia	48 (44.9)
Cough	28 (25.9)
Chest pain	28 (25.9)
Palpitations	24 (22.2)
Headache	10 (9.3)

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Anosmia	10 (9.3)
Dysgeusia	5 (5.6)
Fever	4 (3.7)
Chills	4 (3.7)
Arthomyalgia	3 (2.8)
Hair loss	3 (2.8)
Diarrhoea	2 (1.9)
Anxiety	7 (6.4)
Sadness	7 (6.4)
Insomnia	2 (1.9)
Loss of memory	2 (1.9)
Difficulty concentrating	2 (1.9)

Main results of the laboratory studies

Parameters	
Leukopenia (leukocytes <4000)	6 (5.8)
Lymphopenia (lymphocytes <900)	7 (6.8)
CD4/CD8 ratio <1	6 (5.8)
D-dimer >500 ng/mL	32 (31.3)
LDH > 246 U/L	7 (6.8)
CRP >2.9 mg/dL	25 (24.5)
Ferritin >252 ng/mL	9 (8.8)
IL-6 >40 pg/mL	4 (3.9)
IgM <40 mg/dL	6 (5.8)
IgG <600 mg/dL	11 (10.7)

Chest radiograph at 12 weeks

--	N = 89 (82.4%)
Normal	56 (62.9%)
Favourable evolution	24 (26.0%)
Persistent or worsened	9 (10.1%)

Chest CT scan

--	N = 37 (41.5%)
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.

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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
Health-care 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 patents with COVID is usual 12 weeks after the acute episode, especially in patients <65 years and healthcare workers. All our patients had 28 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

Weerahandi 2020

Bibliographic reference/s	**Weerahandi, H., Hochman, K. et al (2020): Post-discharge health status and symptoms in patients with severe COVID-19. medRxiv preprint doi: https://doi.org/10.1101/2020.08.11.20172742**
Questions relevant to?	**Symptoms and prevalence**
Publication status	Preprint
Study type	Observational cohort (prospective) [Unclear how prospective it actually was]

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Quality	Low quality evidence CASP critical appraisal rating: High risk of bias
Objective	To understand recovery from severe COVID-19: characterising overall health, physical health and mental health of patients one month after discharge
Study date	14/11/20
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	'Single health system': NYU Langone Health
Population (including n)	Patients recovering from severe COVID (n=161 – of which 152 completed survey)
Time since acute COVID-19 illness	30 to 40 days after discharge (median 37 days – range 30 to 43 days)
Interventions/ Prognostic factors	Not evident
Baseline characteristics	Median age 62 years (IQR 50-67); 57 (37%) female. Ethnicity: White 71 (44%) Hispanic 35 (22%) Other/Multiracial 14 (9%) Asian 16 (10%) Black 18 (11%) Unknown 7 (4%) Comorbidities: Any chronic condition 134 (83%) Chronic kidney disease 13 (8%) Cancer 12 (7%) Coronary artery disease 15 (9%) Diabetes 59 (37%) Heart failure 8 (5%) Hyperlipidaemia 75 (47%) Hypertension 97 (60%) Asthma or chronic obstructive pulmonary disorder 39 (24%) BMI: <25kg/m2 23 (14%) 25 to <30 kg/m2 49 (30%) 30 to <40 kg/m2 66 (41%) >=40 kg/m2 22 (14%) Unknown 1 (1%) Smoking status: Never 94 (58%) Former 45 (28%) Current 4 (3%) Unknown 18 (11%)
Inclusion and exclusion criteria	**Inclusion:** 18 years and older who required at least 6 litres of oxygen at any point during a hospitalization for laboratory-confirmed COVID-19, who were

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	discharged alive to either home or a facility after April 15, 2020, and were still alive at the time of study contact. **Exclusion:** Patients with communication impairment or baseline dementia - determined by chart review or if upon consent for this study, the patient was unable to articulate the purpose of this study and what would be required of them to participate. Patients discharged to hospice, patients who resided in long-term care prehospitalization, patients fully dependent in activities of daily living pre-hospitalization, and patients that opted out of research.
Follow up	No follow-up after initial survey ~1 month following discharge after acute illness
Main results	Dyspnoea outcomes (see table 2 also): 113/152 (74%) participants reported shortness of breath within the prior week (median score 3 out of 10 [IQR 0-5]), vs. 47/152 (31%) pre-COVID-19 infection (0, IQR 0-1), p<0.001. For those that did have shortness of breath prior to COVID-19, intensity, frequency, and duration of the shortness of breath worsened after COVID-19. More patients reported feeling short of breath "quite a bit" and "very much" in the past 7 days (18 [11.8%]) compared to before COVID-19 infection (4 [2.6%], p=0.028). Global (overall), physical and mental health (see table 2 also): PROMIS® Global Health-10 instrument scores indicated worse general health after COVID-19 illness (3 out of 5, IQR 2-4) compared to baseline (4, IQR 3-5). Before COVID-19, participants' summary t-scores in both the physical health and mental health domains were slightly above the United States mean of 50 (54.3, standard deviation 9.3; 54.3 SD 7.8, respectively). One month after COVID-19 infection, both scores were significantly lower (physical health: 43.8, SD 9.3; mental health 47.3, SD 9.3; p<0.001 for both). For the physical health score, this represents a decline of more than a full standard deviation. Patients also reported worsened ability to carry out social activities after COVID-19 (p<0.001).
Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	Authors' conclusions: "Survivors of severe COVID-19 experience shortness of breath and worsened physical and mental health more than a month after hospital discharge. Whether these harms will persist is presently unknown."
Additional references	N/A

Xiong 2020

Bibliographic reference/s	**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**
Questions relevant to?	**Prevalence, risk factors**

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Publication status	Preprint
Study type	Retrospective cohort
Quality	Low quality evidence CASP critical appraisal rating: High risk of bias
Objective	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
Study date	Up to 1 March 2020
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	China
Population (including n)	538 COVID-19 survivors who were discharged from hospital prior to March 1 2020 and 184 controls COVID-free volunteers living in Wuhan
Time since acute COVID-19 illness	3 months 4 to 12 weeks grouping
Interventions/ Prognostic factors	Not applicable
Baseline characteristics	

Characteristic	COVID-19 survivors (n=538)	Comparison group (n=184)	P value
Sex	--	--	0.12
Male	245 (45.5%)	96 (52.2%)	---
Female	293 (54.5%)	88 (47.8%)	--
Median age (IQR)	52.0 (41-62)	--	--
Age group	--	--	0.19
20-40 years	117 (21.7)	51 (27.7)	--
41-60 years	250 (46.5)	84 (45.7)	--
61-80 years	171 (31.8)	49 (26.6)	--
Comorbidity	177 (32.9)	63 (34.2)	0.74
Hypertension	82 (15.2)	32 (17.4)	0.49
Diabetes	40 (7.4)	16 (8.7)	0.58
Chronic obstructive lung disease	22 (4.1)	6 (3.3)	0.62
Coronary heart disease	18 (3.3)	9 (4.9)	0.34
Chronic kidney disease	12 (2.2)	3 (1.6)	0.77
Carcinoma	5 (0.9)	3 (1.6)	0.43
Other	32 (5.9)	7 (3.8)	0.27

Inclusion and exclusion criteria	Inclusion criteria: • diagnosed with COVID-19 according to World Health Organization interim guidance and

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	• 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
Follow up	3 months
Main results	Characteristics and prevalence of residual or new symptoms

Characteristic	COVID-19 survivors (n=538)	Comparison group (n=184)	P value
General symptoms	267 (49.6)	22 (12.0)	<0.01
– Physical decline/fatigue	152 (28.3)	17 (9.2)	<0.01
– Sweating	127 (23.6)	3 (1.6)	<0.01
– Myalgia	24 (4.5)	0 (0.0)	<0.01
– Arthralgia	41 (7.6)	0 (0.0)	<0.01
– Chills	25 (4.6)	0 (0.0)	<0.01
– Limb oedema	14 (2.6)	0 (0.0)	0.03
– Dizziness	14 (2.6)	3 (1.6)	0.58
Respiratory symptoms	210 (39)	11 (6.0)	<0.01
– Post activity polypnoea	115 (21.4)	10 (5.4)	<0.01
– Non-motor polypnoea	25 (4.7)	0 (0.0)	<0.01
– Chest distress	76 (14.1)	0 (0.0)	<0.01
– Chest pain	66 (12.3)	0 (0.0)	<0.01
– Cough	38 (7.1)	1 (0.5)	<0.01
– Sputum	16 (3)	1 (0.5)	0.09
– Throat pain	17 (3.2)	0 (0.0)	<0.01
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

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– 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

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%)	--

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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

Review question 2 (12 week-plus period)

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 rating: 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

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	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 illness	Around 3 to 5 months 12+ weeks grouping
Investigations	• Symptom assessment • Multi-organ MRI • Blood investigations for inflammatory markers
Baseline characteristics	

--	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)

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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)

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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 (50-55%)	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 (800-865ms)	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)	

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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 (800-865ms)	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 (5-10%)	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

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Additional references	Ongoing study (https://clinicaltrials.gov/ct2/show/NCT04369807

Klein 2020

Bibliographic reference/s	**Klein, Hadar, Asseo, Kim, Karni, Noam et al. Onset, duration, and persistence of taste and smell changes and other COVID-19 symptoms: longitudinal study in Israeli patients. medrxiv preprint**
Questions relevant to?	**Prevalence**
Publication status	Preprint
Study type	Longitudinal study
Quality	Very low-quality evidence JBI critical appraisal rating: High risk of bias
Objective	Longitudinal characterization of symptoms, to aid with screening and disease management
Study date	April 2020 to October 2020
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	Israel
Population (including n)	112 Israeli residents aged ≥18 years with positive COVID-19 RT-PCR results, who were recruited via social media (Twitter and Facebook) and word of mouth for phone interviews The questionnaire had five parts: 1) General information (e.g., age, gender); 2) Medical history (e.g., medical conditions, chronic medications use); 3) Current illness (e.g. 23 physical signs and symptoms, RT-PCR swab test results and dates, subjective recovery feeling); 4 and 5) Smell and taste: Participants were instructed to rate their sense of smell/taste before, during and after their illness, on a scale from 1 to 10 (1 corresponding to “no sense of smell” and 10 to excellent sense of smell). Data was kept in Compusense Cloud online software
Time since acute COVID-19 illness	6 months 12+ weeks grouping
Interventions/ Prognostic factors	Not applicable
Baseline characteristics	Median age 35 ±12 years 72/112 (64.3%) male 106/112 (94.6%) were ambulatory patients 6/112 (5.4%) were hospitalized (received respiratory support during their hospitalization and / or were hospitalized in the intensive care unit)
Inclusion and exclusion criteria	Exclusion criteria: • severely ill patients • and non-Israeli residents

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Follow up	6 weeks to 6 months
Main results	At 6 month follow up: • 51/112 (46%) still reported unresolved symptoms • Fatigue: 23/112 (20.5%) • Smell change: 15/112 (13.4%) • Breath difficulty: 10/112 (8.9%) • Taste change: 8/112 (7.1%) • Memory disorders 6/112 (5.4%) • Muscle aches 8/112 (7.14%) • Headaches 4/112 (3.57%) • Hair loss 3/112 (2.68%) Fatigue, breath difficulty, memory disorders and hair loss, were not typically reported during the 6-weeks follow-ups (thus "new symptoms"), while other symptoms such as muscle aches, headache and chemosensory changes usually carried over from previous interviews. **Summary** Chemosensory changes and cough persisted after negative RT-PCR in a quarter of the patients. Almost half of the patients reported at least one unresolved symptom at six-months follow up, mainly fatigue, smell changes and breath difficulty. Our findings highlight the prevalence of long-lasting effects of COVID-19
Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	Limitations: • Did not include severely ill patients, and therefore is relevant for light to moderately ill patients only • No objective testing was performed, and the information was self-reported by the participants • Retrospective data collection method used in this study may have caused recall bias Funding: MYN is supported by Israel Science Foundation (ISF) grant #1129/19. HK is a recipient 8 of the Uri Zehavi Scholarship. This work was supported in part by Edmond de 9 Rothschild foundation
Additional references	N/A

Tomasoni 2020

Bibliographic reference/s	**Tomasoni, Daniele, Bai, Francesca, Castoldi, Roberto et al. Anxiety and depression symptoms after virological clearance of COVID-19: A cross-sectional study in Milan, Italy. Journal of Medical Virology na(na)**
Questions relevant to?	**Prevalence**
Publication status	Published

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Study type	Cross sectional
Quality	Low quality evidence JBI Critical appraisal checklist: High risk of bias
Objective	Not reported
Study date	April to June 2020.
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	Italy
Population (including n)	105 patients clinically and virologically recovered from COVID-19.
Time since acute COVID-19 illness	> 3 months 12+ weeks grouping
Interventions/ Prognostic factors	Not applicable
Baseline characteristics	See results
Inclusion and exclusion criteria	Clinical recovery was defined as absence of fever for 48 to 72 hours and normal oxygen saturation on ambient air with concomitant hospital discharge. Virological clearance was defined as presence of two consecutive negative nasopharyngeal swabs taken 24 to 48 hours apart, at least 14 days after clinical recovery
Follow up	3 months from virological clearance
Main results	

	Study population (n=105)	Normal HADS – A/D (n=70)	Pathological HADS-A/D (n=30)	P value
Age, years	55 (43-65)	55 (42-64)	55 (45.5-66)	0.976
Male	77 (73.3%)	55 (78.6%)	19 (63.3%)	0.111
Charlson comorbidity score	1 (0 to 2.5)	1 (0 to 3)	1 (0 to 2)	0.798
Time since virological clearance, days	46 (43 to 48)	46 (43 to 48)	46 (44 to 49)	0.317
Symptoms at follow up:				
Persistence	55 (52.4%)	30 (42.9%)	23 (76.7%)	0.002
Anosmia	--	--	--	---
No, ever	44 (41.9%)	30 (42.9%)	13 (43.3%)	--
Ongoing	6 (5.7%)	4 (5.7%)	2 (6.7%)	--
Resolved	51 (48.6%)	34 (48.6%)	15 (50%)	--
Unknown	4 (3.8%)	2 (2.9%)	0	--
Dysgeusia	--	--	--	0.697
No, ever	39 (37.1%)	25 (35.7%)	13 (43.3%)	--
Ongoing	6 (5.7%)	4 (5.7%)	1 (3.3%)	--
Resolved	57 (54.3%)	39 (55.7%)	16 (53.3%)	--
Unknown	3 (2.9%)	2 (2.9%	0	--

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Gastro-intestinal symptoms	--	--	--	0.02
No, ever	62 (59%)	49 (70%)	13 (43.3%)	--
Ongoing	1 (1%)	0	1 (3.3%)	--
Resolved	37 (35.2%)	21 (30%)	16 (53.3%)	--
Unknown	5 (4.8%)	0	0	--
Fever	--	--	--	0.26
No, ever	8 (7.6%)	7 (10%)	1 (3.3%)	--
Ongoing	0	0	0	--
Resolved	92 (87.6%)	63 (90%)	29 (96.7%)	--
Unknown	5 (4.8%)	0	0	--
Burning pain	--	--	--	0.091
No, ever	69 (65.7%)	52 (74.3%)	17 (56.7%)	--
Ongoing	11 (10.5%)	5 (7.1%)	6 (20%)	--
Resolved	19 (18.1%)	13 (18.6%)	6 (20%)	--
Unknown	6 (5.7%)	0	1 (3.3%)	--
Dyspnoea	--	--	--	0.034
No, ever	30 (28.6%)	19 (27.1%)	6 (20%)	--
Ongoing	7 (6.7%)	13 (18.6%)	14 (46.7%)	--
Resolved	62 (59%)	37 (52.9%)	10 (33.3%)	--
Unknown	6 (5.7%)	1 (1.4%)	0	--
Asthenia	--	--	--	0.044
No, ever	29 (27.6%)	24 (34.3%)	5 (16.7%)	--
Ongoing	33 (31.4%)	18 (25.7%)	15 (50%)	--
Resolved	38 (36.2%)	28 (40%)	10 (33.3%)	--
Unknown	5 (4.8%)	0	0	--
Cognitive deficits (memory disorder)	--	--	--	0.002
No, ever	75 (71.4%)	60 (87.5%)	15 (50%)	--
Ongoing	18 (17.1%)	7 (10%	11 (36.7%)	--
Resolved	4 (3.8%)	2 (2.9%)	2 (6.7%)	--
Unknown	8 (7.6%)	1 (1.4%)	2 (6.7%)	--

Summary

A considerable proportion of patients with COVID-19 still experienced psychological distress and ongoing physical symptoms after hospital discharge, underlining the complexity of patients with COVID-19 management even after clinical and virological recovery, and the need of long-term follow-up within multidisciplinary teams.

Comments (e.g. source of funding, statistical analysis, any major limitations,	Limitations: • only patients with confirmed virological recovery were included in the study • sample size is limited

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or issues with studies)	• baseline (pre-COVID-19) psychological evaluation of the study population was not available, so that no causality hypothesis among anxiety or depression and persistence of physical symptoms can be speculated • data concerning SARS-CoV-2 infection and outcome in other family members, as well as level of education, a factor known to be positively correlated to anxiety levels, were not available.
Additional references	N/A

Real world data studies

Banda 2020

Bibliographic reference/s	**Banda, Juan M., Singh, Gurdas Viguruji, Alser, Osaid et al. (2020) Long-term patient-reported symptoms of COVID-19: an analysis of social media data. medRxiv: 2020072920164418**
Questions relevant to?	**Prevalence**
Publication status	Preprint
Study type	Real world data study
Quality	--
Objective	To present a preliminary characterization of post-COVID-19 symptoms using social media data from Twitter
Study date	21/05/2020 to 10/07/2020
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	Not reported
Population (including n)/ data source	150 tweets from 107 users in the largest publicly available COVID-19 Twitter chatter dataset.
Time since acute COVID-19 illness	Not reported
Interventions/ Prognostic factors	Not applicable
Baseline characteristics	Not reported
Inclusion and exclusion criteria	Inclusion criteria: • Precise hashtags (#longcovid and #chroniccovid) to select tweets relevant to discussions related to the post-COVID experiences of Twitter users. • English language Exclusion criteria: • Retweets that did not have user comments

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	• Any tweets from accounts with unusually high tweeting activity (possible bots) or that only shared other tweets
Follow up	Not reported
Main results	A total of 192 reports including 34 distinct ICD-10 codes were identified. The 10 most commonly mentioned symptoms were: malaise and fatigue (62%), dyspnoea (19%), tachycardia/palpitations (13%), chest pain (13%), insomnia/sleep disorders (10%), cough (9%), headache (7%), and joint pain, fever, and unspecified pain by 6% each. Less common symptoms included ear-nose-throat (tinnitus, anosmia, chronic sinusitis, parageusia, aphonia), neuro-psychological (amnesia, neuralgia/neuropathy, dysautonomia, visual disturbance, cognitive impairment, and disorientation), myalgia, and skin pruritus/rash. An average of 1.79 codes were reported per person, and 1.28 codes per tweet.
Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	Methods: Tweets were annotated using the Social Media Mining Toolkit, Spacy NER annotator and a dictionary created from the Observational Health Data Sciences and Informatics (OHDSI) vocabulary, which allows the annotated terms to tie into clinical conditions and observations. Two clinicians manually reviewed these tweets to identify patients with COVID-19 and their self-reported symptoms, and to attribute ICD-10 codes to them. A third clinician reviewed all decisions and resolved disagreements. Number of symptoms per tweet and person, and frequency (%) of symptoms reported of the total were reported. Limitations: Data obtained from social media and symptoms are self-reported without clinical assessment.
Additional references	N/A

Singh 2020

Bibliographic reference/s	**Singh, Shubh Mohan and Reddy, Chaitanya (2020) An Analysis of Self-reported Longcovid Symptoms on Twitter. medRxiv: 2020081420175059**
Questions relevant to?	**Prevalence**
Publication status	Preprint
Study type	Real world data study
Quality	
Objective	This study attempted to analyse symptoms reported by users on twitter self-identifying as long-COVID
Study date	20 July 2020 to 29tJuly 2020
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	Not reported
Population (including n)	165 tweets from 89 users were included in the final analysis

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Time since acute COVID-19 illness	Not reported
Interventions/ Prognostic factors	Not applicable
Baseline characteristics	Not reported
Inclusion and exclusion criteria	Tweets that were not in English, or by users who did not identify themselves as having long-COVID symptoms or having symptoms due to another disorder such as Lyme disease or chronic fatigue syndrome/myalgic encephalomyelitis, tweets about long-COVID in general but not experienced symptoms excluded.
Follow up	Not reported
Main results	Order Symptoms Prevalence (%) [Symptoms with >1 mention in tweets] 1. Fatigue 42 (47.19) 2. Shortness of breath 23 (25.84) 3. Brainfog 15 (16.85) 4. Exercise intolerance 13 (14.60) 5. Pain in the whole body 9 (10.11) 6. Altered smell 7 (7.86) 7. Headache 7 (7.86) 8. Tachycardia 6 (6.74) 9. Altered taste 6 (6.74) 10. Pain chest 5 (5.61) 11. Dizziness 3 (3.37) 12. Pain abdomen 3 (3.37) 13. Fever 3 (3.37) 14. Nausea 3 (3.37) 15. Cough 3 (3.37) There was no association between nature and number of symptoms reported and the duration of illness. 29 users mentioned the course of their symptoms. The most pattern described was one of episodes or relapses (n=16), followed by a continuous course (n=9), of which some described fluctuations in the course of symptoms (n=3) and 4 users described continuous symptoms with added on symptoms during exacerbations. The common precipitating factors for exacerbations were physical activity (n=3), trauma (n=1) and heat (n=1). 53 users (59.55%) reported more than one symptom
Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	Methods: Tweets were collected using the rtweet package in RStudio software from the twitter public streaming application programming interface. Limitations: There are various limitations in non-experimental twitter derived data including patchy incomplete data, the self-selection of users, lack of objective validations of reported symptoms, inexact reporting of variables such as sociodemographic data and non-exact definitions of symptomatology. T There is also the possibility of relevant data being missed or being available on other social media platforms. In addition, there was no information regarding the symptom severity of initial disease and treatment details
Additional references	N/A

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Appendix 7 Excluded studies

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

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