Evidence check

26 August 2020

Medium- and long-term health sequelae of COVID-19

Rapid review question

What are the medium- and long-term health sequelae of COVID-19 infection among survivors?

In brief

General health sequelae

- Symptoms commonly reported among recovered COVID-19 patients two to eight weeks after the onset of symptoms (or a positive COVID-19 test) include: fatigue, shortness of breath, muscle or joint pain, chest pain, cough, and insomnia and/or sleep disorders.(1-6)
- A study of 202 confirmed COVID-19 patients with mild symptoms, found altered sense of smell or taste occurred in 18.6% of patients, feelings of being tired in 13.1%, problems breathing in 10.4% and muscle or joint pains in 7.7%.(2) Another study of 143 patients reported fatigue in 53.1%, dyspnea in 43.4%, joint pain in 27.3%, and chest pain 21.7% of patients.(1)
- A study conducted among discharged intensive care unit (ICU) and ward COVID-19 patients found that post-traumatic stress disorder, anxiety and/or depression, voice change, laryngeal sensitivity, new continence problems and dysphagia were commonly reported among recovered patients.(5)

Respiratory health sequelae

- Commonly reported respiratory consequences among COVID-19 patients, two to five weeks after the onset of symptoms or being discharged from the hospital included: abnormal carbon monoxide diffusion capacity, abnormal forced expiratory volume in the first second (FEV1), abnormal forced vital capacity (FVC), abnormal FEV1/FVC, small airway dysfunction, abnormal forced inspiratory volume, abnormal maximal expiratory flow (MEF)25, MEF50, and MEF75,(7) abnormal residual computed tomography (CT) changes including ground-glass opacity and pulmonary fibrosis.(7-11)
- Across studies, 33-81% of patients had reported abnormal pulmonary function.(7, 9, 10)
- Respiratory consequences were worse in patients who had severe COVID-19 symptoms prior to discharge, compared to those with non-severe symptoms.(7, 10)

Cardiovascular health sequelae

- Reported cardiovascular consequences among some recovered COVID-19 patients five to ten weeks after diagnosis included: myocardial injury with either or both non-ischemic heart disease-related and ischemic heart disease-related pathology, presence of high-sensitivity troponin T (hsTnT) and elevated hsTnT, raised myocardial native T1 and T2, having myocardial late gadolinium enhancement and having pericardial enhancement.(12, 13)

- In a study of 100 patients, 78% of patients had abnormal cardiovascular magnetic resonance imaging findings.(13) A study of 29 patients with no previously known cause for elevated hsTnT, 69% had identifiable mechanism of myocardial injury.(12)

Neurological sequelae

- Commonly reported neurological consequences that persisted among some recovered COVID-19 patients three to eight weeks after being diagnosed or being discharged from the hospital included: deterioration in hearing and/or tinnitus, olfactory (sense of smell) dysfunction, gustatory dysfunction. (1, 2, 14-22)
- In small studies, 13% of patients reported a change in their hearing, 11-78% had persistent olfactory dysfunction, and 16% had gustatory dysfunction.(14, 17-19, 21, 22)

Mental health sequelae

- Reported mental health symptoms or conditions among some recovered COVID-19 patients three to four weeks after hospital discharge included: post-traumatic stress disorder, depression, anxiety, obsessive-compulsive symptomatology and insomnia.(23, 24)
- In one study, 55.7% of COVID-19 survivors had at least one form of psychopathological symptom that was in the clinical range.(23) Another found 50 (13.5%) had anxiety, 40(10.8%) had depression, and 23 (6.2%) had comorbid anxiety and depression.(24)

Limitations

The empirical evidence on direct medium- and long-term health sequelae of COVID-19 is limited and still developing. Given the short timeline COVID-19 pandemic, studies included in this evidence check are limited to those that describe symptoms that persist or develop a few weeks or months after recovering from COVID-19 infection.

Background

The literature on epidemiology and acute symptoms of COVID-19 is fast developing and growing, however, due to short timeline since the first discovery of the disease, the empirical evidence on the medium- and long-term health sequelae of COVID-19 is limited. Sequelae of COVID-19 are sometimes referred to as ‘long COVID’, referring to ongoing or persistent symptoms that persist beyond the recovery from COVID-19 infection. (Appendix 1)(3, 25)

Methods (Appendix 2)

PubMed and Google searches were conducted on 12 August 2020. Archived records from daily evidence digest were searched on 7 and 12 August 2020 respectively. Only peer-reviewed or pre-peer reviewed literature were included. Studies reporting on indirect health impacts of COVID-19 pandemic, long-term complications due to COVID-19 treatment and hospitalisation, persistent viral shedding and associated symptoms, anecdotal evidence, and hypothesis on potential long-term sequelae of COVID-19 based on review of historical scientific literature were not included.

Results

Table 1 General health sequelae

Source	Summary
Peer reviewed sources	
Persistent symptoms in patients after acute COVID-19 Carfi, et al. 2020 (1)	• 143 COVID-19 survivors who were discharged from an Italian hospital, and were tested negative for COVID-19 at the time of enrolment in the study, were offered comprehensive medical examination and their results were analysed. The average time since the onset of COVID-19 symptoms was 60.3 days (SD 13.6). • 55% had three or more COVID-19 related symptoms, 32% had one or two COVID-19 related symptoms, and only 12.6% did not have any COVID-19 related symptoms. 44% of the patient had a worsened quality of life. • Most commonly reported symptoms were: fatigue (53.1%), dyspnea (43.4%), joint pain (27.3%) and chest pain (21.7%). Other less commonly reported symptoms included: cough, anosmia, sicca syndrome, rhinitis, red eyes, dysgeusia, headache, sputum production, lack of appetite, sore throat, vertigo, myalgia and diarrhea.
Predominance of an altered sense of smell or taste among long-lasting symptoms in patients with mildly symptomatic COVID-19 Boscole-Rizzo, et al. 2020 (2)	• 202 COVID-19 positive adults from Italy with mild symptoms were assessed at baseline for symptoms and followed up at four and eight weeks. • The most common persistent symptoms and their progression from baseline to four and eight weeks were: altered sense of smell or taste (60.1%, 36.6%, 18.6%), feelings of being tired (68.9%, 15.8%, 13.1%), problems breathing (41.5%, 24.0%, 10.4%) muscle or joint pains (45.4%, 16.4%, 7.7%). • Less than 3% of patients, or five or less patients, reported the following symptoms with a declining trend from baseline to four and eight weeks: dry cough (62.8%, 29.0%, 2.7%), headache (42.1%, 12.6%, 2.7%), sore throat (31.1%, 7.1%, 2.7%), chest pain (15.3%, 6.0%, 1.1%), sinonasal pain (16.9%, 2.7%, 1.1%), loss of appetite (54.6%, 10.9%, 2.7%), diarrhoea (45.4%, 6.0%, 1.1%), dizziness (13.7%, 2.7%, 2.7%). • Baseline symptoms such as fever, nausea, vomit, abdominal pain were reported by none of the patients at eight weeks.
Management of post-acute covid-19 in primary care Greenhalgh, et al. 2020 (3)	• Authors define the post-acute COVID-19 as 'extending beyond three weeks from the onset of first symptoms and chronic COVID-19 as extending beyond 12 weeks'. • Based on the COVID symptom study in the United Kingdom, they note that around 10% of people experience ongoing symptoms, such as breathlessness, cough, fatigue, chest pain,

Source	Summary
Peer reviewed sources	
	thromboembolism, ventricular dysfunction, stroke, seizures, mental health, malnutrition, etc.(26) • They propose strategies to investigate and manage ongoing persistent symptoms of COVID-19. See appendix 2 for the infographics on assessment and management of patients with continuing symptoms.
Long-term patient-reported symptoms of COVID-19: an analysis of social media data Banda, et al. 2020 (4)	• This is an analysis of social media posts on Twitter. Precise hashtags were used to search for Twitter users' posts discussing the long-term symptoms of COVID-19 post-recovery. 2603 tweets were reviewed, and 150 tweets from 107 users were analysed. • Commonly reported persistent symptoms were (in order of most common to less common): malaise and fatigue, dyspnoea, tachycardia or palpitations, chest pain, insomnia or sleep disorders, cough, headache, joint pain, fever and unspecified pain.
Post-discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation Halpin, et al. 2020 (5)	• 100 discharged COVID-19 survivors from the Unites Kingdom were followed up by telephone. The average time since being discharged from the hospital is 48 days (SD: 10.3 days). 32 survivors with a median age of 58.5 (range: 34-84) were ICU patients, and 68 survivors with a median age of 70.5 (range: 20-93) were ward patients. • 72% ICU patients reported symptoms of fatigue, with 12.5% reporting severe fatigue. 60.3% ward patients reported fatigue, with 14.7% reporting severe fatigue. • 65.6% ICU patients reported breathlessness, with 12.5% reporting severe breathlessness. 42.6% ward patients reported breathlessness, with 7.4% reporting severe breathlessness. • 46.9% ICU patients reported post-traumatic stress disorder , with 6.3% reporting severe symptoms, 3.1% reporting thoughts of self-harm, 34.4% reporting a new or worsened concentration problem and 18.8% reporting a new or worsened short-term memory problem. 23.5% ward patients reported post-traumatic stress disorder, with none reporting severe symptoms, 1.5% reporting thoughts of self-harm, 16.2% reporting a new or worsened concentration problem and 17.6% reporting a new or worsened short term memory problem. • Other common persistent symptoms included: worsened anxiety pr depression (ICU: 37.5%, ward 16.2%), worsened pain (ICU:28.1%, ward 14.7%), voice change (ICU: 25%, ward 17.6%), laryngeal sensitivity (ICU: 25%, ward: 11.8%), new continence problems (ICU: 15.6%, ward: 11.7%) and dysphagia (ICU: 12.5%, ward: 5.9%)

Source	Summary
Peer reviewed sources	
	• EQ-5D-l value, which reflects mobility, self-care, usual activities, pain or discomfort and anxiety or depression symptoms, indicated a significant decline in 68.8% in ICU patients and 45.6% in ward patients.
Symptom duration and risk factors for delayed return to usual health among outpatients with COVID-19 in a multistate health care systems network – United States, March–June 2020 Tenforde, et al. 2020 (6)	• 270 confirmed COVID-19 cases were followed up by telephone 14 to 21 days after testing in the United States. The median age was 42.5 years (interquartile range: 31-54). The median time since the testing until the interview date was 16 days (interquartile range: 14-19). • 175 (65%) cases reported returning to their usual health after a median of 7 days (interquartile range: 5-12) since testing. 95 (35%) reported not returning to usual health. • Older age (≥50 vs 18-34) was associated with a higher proportion of people not returning to usual health after 14-21 days since testing positive (47% vs 28%; adjusted odds ratio: 2.29; 95% CI=1.14-4.58). • Having three or more chronic conditions was associated with higher rates of not having returned to usual health compared with people with no chronic conditions (aOR:2.29; 95% CI: 1.07-4.90). • Obesity (body mass index ≥30kg/m^2) was associated with higher rates of not having returned to usual health compared with people with no obesity (aOR:2.31; 95% CI:1.21-4.42). • Reporting a psychiatric condition was associated with higher rates of not having returned to usual health (aOR:2.32; 95% CI:1.17-4.58). • Most common symptoms that persisted were cough (not resolved in 43% of those who had symptoms), fatigue (35%) and shortness of breath (29%).

Table 2 Respiratory system sequelae

Source	Summary
Peer reviewed sources	
Abnormal pulmonary function in COVID-19 patients at time of hospital discharge Mo, et al. 2020 (8)	• Spirometry and pulmonary diffusion capacity tests were performed with a total of 104 discharged cases of COVID-19 with mild to severe symptoms. Cases who had critical symptoms were not included. The intervals between the onset of symptoms and the tests were 20±6 days for mild cases, 29±8 days for pneumonia cases and 34±7 days for severe pneumonia cases. • 51 (47.2%) cases were found to have abnormal carbon monoxide diffusion capacity. 27 (25%) had abnormal total lung capacity. 15 (13.6%) had abnormal FEV1. 10 (9.1%) had abnormal FVC. Five (4.5%) had abnormal FEV1/FVC. 8 (7.3%) had small airway function. • This letter to the editors concludes that COVID-19 survivors, especially those presented with pneumonia, may need to be routinely followed-up with pulmonary function tests.
Pulmonary function of patients with 2019 novel coronavirus induced pneumonia: a retrospective cohort study Lv, et al. 2020 (7) (preprint)	• A retrospective, observational, single-centre study from China. • 137 discharged COVID-19-induced pneumonia cases underwent pulmonary ventilation function tests two weeks after being discharged. Mean age was 47 years (SD:13). • 81% of all patients had a forced inspiratory volume <80% of the predicted value and the figure was 88.9% for cases who had severe COVID-19 symptoms prior to discharge and 79.1% for non-severe cases. 24.1% of all patients had an FVC<80% of the predicted value and the figure was 55.6% for severe cases and 16.4% for non-severe cases. The inspiratory volume and FVC values were reduced more significantly in severe cases than non-severe cases. • In the severe-case group, the proportion of those with maximal expiratory flow (MEF)25, MEF50, and MEF75 < 70% were 55.6%, 40.7%, and 25.9%, respectively. In the non-severe-case group, the proportion of those with MEF25, MEF50, and MEF75 < 70% were 57.3%, 30%, and 13.6%, respectively. • This study's findings suggest the manifestation of restrictive ventilation disorder and small airway obstruction in patients recovered from COVID-19 induced pneumonia.

Source	Summary
Peer reviewed sources	
Anormal pulmonary function and residual CT abnormalities in rehabilitating COVID-19 patients after discharge You, et al. 2020 (9)	• 18 COVID-19 patients discharged from a hospital in China underwent pulmonary function tests. 12 had moderate COVID-19 symptoms, five severe symptoms and one had critical symptoms. Mean age was 50.7 years (SD: 12.1). Mean time between hospital discharge and test was 40 days (SD: 11.6) for non-severe cases and 34.7 days (SD: 16.5) for severe cases. • At the time of lung function test, five (41.7%) non-severe cases and two (33.3%) severe cases had abnormal lung function. • Among 12 non-severe cases, three (25.0%), one (8.3%) and five (41.7%) had obstructive ventilation impairment, restrictive ventilatory impairment, and small airway dysfunction, respectively. Among the six severe cases, two (33.3%) and one (16.7%) had a restrictive ventilatory impairment and small airway dysfunction, respectively. • Computed tomography (CT) scan revealed 15 (83.3%) cases had abnormal CT changes, with 11 (61.1%) having ground-glass opacity and four (22.2%) having pulmonary fibrosis.
Prediction of the development of pulmonary fibrosis using serial thin-section CT and Clinical features in patients discharged after treatment for COVID-19 pneumonia Yu, et al. 2020 (11)	• Clinical records of 32 discharged COVID-19 patients from a hospital in China, who underwent at least two thin-section chest CT scans during the hospital stay and at least one follow-up CT scan after discharge, were reviewed and analysed. The average days since discharge to the latest scan was 9.0 • 14 patients had evidence of fibrosis on the latest follow-up scan, which was conducted median 9.0 (interquartile range: 7.0-11.0) days after discharge. 18 patients had no evidence of fibrosis on the latest follow-up scan, which was conducted an average of median 9.0 (interquartile range: 7.8-11.3) days after discharge. • Cases with fibrosis were significantly older than the cases without fibrosis (median age: 54.0 years vs. 37.0 years; p=0.008), had significantly longer hospital stay (19.5 days vs 10.0 days; p=0.001) and had significantly higher inflammatory indicators.
Impact of coronavirus disease 2019 on pulmonary function in early convalescence phase Huang, et al. 2020 (10)	• 57 COVID-19 cases from a hospital in China underwent pulmonary function tests 30 days after being discharged. 40 had non-severe symptom and 17 had severe symptoms. • 43 (54.3%) had abnormal pulmonary function test findings. The proportion of cases with values less than 80% of predicted values for the following assessment measures were as following: carbon monoxide diffusion capacity(52.6%), Maximum static inspiratory pressures (PImax) (49.1%), (FEV1/FVC ratio (43.8%), Maximum static expiratory pressures (PEmax) (22.8%), total lung capacity (12.3%), FVC (10.5%), FEV1 (8.7%). • Compared to non-severe cases, severe cases had a higher incidence of abnormal diffusion capacity or DLCO impairment

Source	Summary
Peer reviewed sources	
	(75.6% vs 42.5%, p<0.05) and more severe reduction in total lung capacity and 6 min walk distance (6MWD). • Six (10.5%) reported symptoms of cough, four (7.0%) had shortness of breath and three (5.3%) had occasional wheezing. • CT scan revealed 31 (54.4%), including 16 severe cases and 15 non-severe cases, had residual abnormalities, with most of whom having patchy ground glass opacity with periphery distribution and four (all severe cases) with pulmonary fibrosis. Severe cases had significantly higher CT score than the non-severe cases (3.94 [SD: 2.23] vs 0.83 [SD: 1.39], p<0.01). • Severe cases had significantly shorter 6 min walking distance than non-severe cases (517.43 m [SD: 44.55 m]; 573.52 m [SD: 38.38 m], p=0.012) and only reaching 88.4% of the predicted values.

Table 3 Cardiovascular sequelae

Source	Summary
Peer reviewed sources	
COVID-19: myocardial injury in survivors Knight, et al. 2020 (12)	• Records of 828 hospitalised COVID-19 patients discharged (alive or dead) from the Royal Free London NHS Foundation Trust until 30 April 2020 were reviewed. • 51 patients, who were discharged alive, had elevated hsTnT (>14ng/L), had no known cardiac pathology likely to cause scar, were aged under 80 years old and were medically eligible, were offered cardiovascular magnetic resonance scan. • 29 patients with unexplained elevated hsTnT and with an interval of 46 days (SD:15) since the COVID-19 symptoms onset and 37 days (SD: 10) since diagnosis were included in the analysis. • 20 (69%) patients had residual lung parenchymal changes, four (14%) had pleural effusions, two (7%) had pericardial effusions, one had left ventricular dysfunction and one had severe biventricular dysfunction. • Late gadolinium enhancement test revealed 20 (69%) patients had identifiable mechanism of myocardial injury, including 11 (38%) non-ischemic heart disease related, five (17%) ischemic heart disease-related, four (14%) with dual ischemic and non-ischemic pathology.
Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from coronavirus disease 2019 (COVID-19) Puntmann, et al. 2020 (13)	• Clinical records of 100 COVID-19 recovered patients from Germany were reviewed. The records included cardiac blood markers and cardiovascular magnetic resonance imaging. Median age was 49 years (interquartile range: 45-53). The median time between the diagnosis of COVID-19 and cardiovascular magnetic resonance imaging was 71 days (interquartile range: 64-92). • At the time of cardiovascular magnetic resonance imaging, 71 (71%) patients had hsTnT 3 pg/mL or greater and five (5%) had elevated hsTnT (13.9 pg/mL or greater). 78 (78%) had abnormal cardiovascular magnetic resonance findings, with 73 (73%) having raised myocardial native T1, 60 (60%) having raised myocardial native T2, 32 (32%) having myocardial late gadolinium enhancement and 22 (22%) having pericardial enhancement. • When compared with 50 age-matched and sex-matched healthy controls and 57 risk factor-matched controls, COVID-19 recovered patients had significantly lower left ventricular ejection fraction, higher left ventricle volumes, higher left ventricle mass, and raised native T1 and T2.

Table 4 Neurological sequelae

Source	Summary
Peer reviewed sources	
Persistent self-reported changes in hearing and tinnitus in post-hospitalisation COVID-19 cases Munro, et al. 2020 (14)	• 121 adult COVID-19 patients were reviewed eight weeks after being discharged from a United Kingdom hospital and were asked about the changes in their hearing and/or tinnitus. • 16 (13.1%) patients, or nearly 1 in 10 patients, reported a change in their hearing and/or tinnitus, including eight cases of deterioration in hearing and eight cases of tinnitus.
Clinical characteristics associated with persistent olfactory and taste alterations in COVID-19: A preliminary report on 121 patients Lovato, et al. 2020 (22)	• 121 mild-to-moderate COVID-19 cases from Italy with olfactory and/or taste dysfunction at the time of being tested positive were surveyed at least one month after. Mean age 446.7 and mean time since being diagnosed was 38.2 days (SD: 3). • 26 (21.5%) had persistent olfactory and/or taste dysfunction. • Univariate analysis revealed that not having fever symptoms or having olfactory and/or taste dysfunction symptoms before general symptoms were significantly related with having persistent olfactory and/or taste dysfunction.
Persistent psychotic symptoms following COVID-19 disease Lim, et al. 2020 (27)	• This case report study from the United Kingdom reports on a COVID-19 case who had persistent and florid psychotic symptoms for about 40 days after initially developing delirium. No abnormalities were detected on diagnostic tests, such as magnetic resonance imaging of the brain, electroencephalogram, cerebrospinal fluid examinations and extensive autoimmune panel. • Persistent psychotic symptoms included: delusion, complex visual and auditory hallucinations, Capgras phenomenon in the absence of hypoxia but elevated tumor necrosis factor alpha.
Prolonged complaints of chemosensory loss after COVID-19 Fjaeldstad 2020 (16)	• 109 confirmed and non-confirmed COVID-19 cases from Denmark with olfactory and/or gustatory loss symptoms were surveyed after a mean time of >30 days after developing sudden chemosensory loss. Mean age was 39.4 years. • For 100 cases with olfactory loss, only 44 (44%) made a full recovery and 28 (28%) had symptoms unchanged. • For 104 cases with taste loss, only 52 (50%) made a full recovery and 21 (20%) had symptoms unchanged.

Source	Summary
Peer reviewed sources	
Olfactory dysfunction in recovered coronavirus disease 2019 (COVID-19) patients Li, et al. 2020 (17)	• 145 COVID-19 patients were followed up after being discharged from a hospital in China. Mean age was 49 (range: 13-80). • Two to four weeks after discharge, 16 (11%) patients had ongoing dysosmia. The mean time since the onset of symptoms were 62 (range: 25-95).
Persistent smell loss following undetectable SARS-CoV-2 Yan, et al. 2020 (18)	• 23 confirmed COVID-19 cases from the Unites States with symptoms of chemosensory loss were followed up after having two consecutive negative test results. • After a mean time of 25.6 days since the initial positive result and 9.4 days since the negative results, 18 (78%) cases reported experiencing persistent olfactory dysfunction.
Olfactory and gustatory outcomes in COVID-19: a prospective evaluation in nonhospitalised subjects Paderno, et al. 2020 (19)	• 151 confirmed COVID-19 cases who were not hospitalised from Italy were administered a questionnaire at baseline and follow-up with a focus on olfactory dysfunction and gustatory dysfunction. • The mean time between the onset of olfactory dysfunction symptoms and follow-up survey was 37 days (SD: 9). At follow-up, 20 (16%) cases reported ongoing olfactory dysfunction, with 16 of them reporting partial improvement. Late recovery was associated with presentation of total olfactory dysfunction (as opposed to partial olfactory dysfunction) ($p<0.001$) and female gender ($p=0.1$). • The mean time between the onset of gustatory dysfunction symptoms and follow-up was 33 days (SD: 15). At follow-up,16 (12%) cases reported ongoing symptoms, with 11 reporting partial improvement. Late recovery was associated with presentation of total gustatory dysfunction ($p=0.006$) and female gender ($p=0.0.13$) • Three cases reported a recurrence of olfactory dysfunction (n=2) and gustatory dysfunction (n=2) after a previous complete resolution of symptoms. The mean time between the resolution of the previous episode of symptoms and recurrence was 19 days (SD: 5).
Olfactory and gustatory dysfunctions in 100 patients hospitalised for COVID-19: sex differences and recovery time in real-life Meini, et al. 2020 (20)	• 100 hospitalised COVID-19 patients from Italy were followed up a month after being discharged. Mean age was 65 years (SD: 15). • Among 42 patients who experienced chemosensory dysfunction, 83% reported complete or near complete recovery at one-month follow-up. The mean duration of olfactory dysfunction and gustatory dysfunction was 18 and 16 days, respectively. Females had significantly longer recovery duration than males (26 vs 14 days, $p=0.009$). • Four patients reported a partial recovery from gustatory dysfunction, with a mean time since the onset of 32 days. Among them, two had

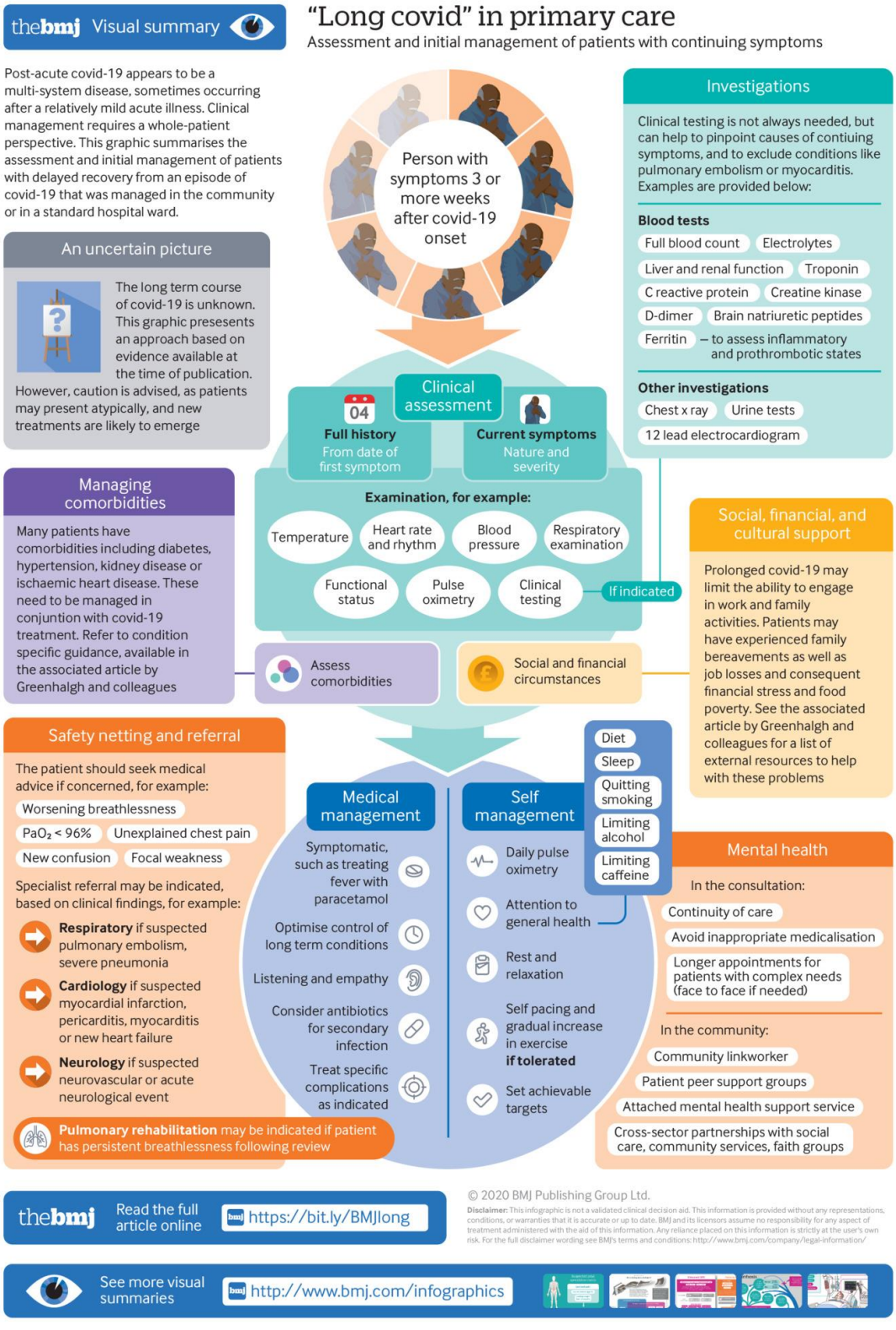
Source	Summary
Peer reviewed sources	
	olfactory dysfunction. Three patients reported no improvement after a mean time of 27 days and had both ageusia and anosmia.
Persisting olfactory dysfunction in patients after recovering from COVID-19 Otte, et al. 2020 (21)	• 50 COVID-19 patients from Germany underwent olfactory testing at least three weeks after the recovery from the infection. Mean age was 43.2 years (range: 23-69). • At the time of olfactory testing, among 47 patients who experienced a sudden loss of smell, 38% still had ongoing symptoms and 61.7% had completely recovered. • Sniffing test results revealed that 26 (52%), 23 (46%) and 1 (1.9%) patients were hyposmic (mean threshold, discrimination, and identification: 26.86), normosmic (mean threshold, discrimination, and identification: 34.23) and anosmic (mean threshold, discrimination, and identification: 11), respectively. • Among 23 normosmic patients, only seven (30.43%) reported subjective persistent olfactory symptoms, while the other 16 (69.57%) did not report persistent symptoms. • Among 26 hyposmic patients, only 13 (50%) reported subjective persistent olfactory symptoms, while the other 13 (50%) did not report persistent symptoms.

Table 5 Mental health sequelae

Source	Summary
Peer reviewed sources	
Anxiety and depression in COVID-19 survivors: Role of inflammatory and clinical predictors Mazza, et al. 2020 (23)	• 402 discharged COVID-19 survivors from a hospital in Italy were screened for psychiatric symptoms at one-month follow up. Mean age was 58, with ages ranging from 18 to 87. • 55.7% of COVID-19 survivors had at least one form of psychopathological symptom that was in the clinical range. More specifically, 28% had post-traumatic stress disorder, 31% had depression, 42% had anxiety, 20% had obsessive-compulsive symptomatology and 40% had insomnia. • Females had significantly higher values on the all psychopathological measures than males, indicating that they suffered more severe symptoms.
Mental health status and related influencing factors of COVID-19 survivors in Wuhan, China Wu, et al. 2020 (24)	• 370 confirmed and discharged COVID-19 cases from Wuhan, China were followed up after a mean time of 22 days (interquartile range: 20-30). Mean age was 50.5 (SD: 13.1) years. • 50 (13.5%) had anxiety, 40 (10.8%) had depression, and 23 (6.2%) had comorbid anxiety and depression. • Anxiety was significantly associated with post-discharge respiratory symptoms, worries about recurrence, and worries about passing the virus to others. • Depression was significantly associated with female gender, post-discharge respiratory symptoms, worries about recurrence and infecting others, or home quarantine lifestyle.

Appendix 1

'Long covid' in primary care: Assessment and initial management of patients with continuing symptoms.(3)



Appendix 2

PubMed search terms

(2019-nCoV[title/abstract] or nCoV*[title/abstract] or covid-19[title/abstract] or covid19[title/abstract] OR "covid 19"[title/abstract] OR "coronavirus"[MeSH Terms] OR "coronavirus"[title/abstract] OR sars-cov-2[title/abstract] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept]) AND ("long term"[title] OR "long-term"[title] OR "sequelae"[title] OR "persistent"[title] OR "permanent"[title] OR "lasting"[title] OR "long-lasting"[title] OR "survivor*"[title] OR "prolong*"[title] OR "disability"[title] OR "aftereffect*"[title] OR "post-acute covid-19"[title/abstract] OR "long-covid"[title/abstract]) AND (2019/12/1:2019/12/31[Date - Publication] OR 2020/1/1:2020/12/31[Date - Publication])

Google search

- “Long term sequelae” and “COVID-19”
- “long term consequences” and “COVID-19”
- “long covid”
- “persistent OR permanent OR ongoing OR lasting symptoms” and “COVID-19”

Statistics glossary

aOR adjusted odds ratio

CI confidence interval

SD standard deviation

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15. . !!! INVALID CITATION !!! {Lovato, 2020 #3;Fjaeldstad, 2020 #4;Li, 2020 #34;Yan, 2020 #5;Paderno, 2020 #29;Meini, 2020 #35;Otte, 2020 #37;Carfì, 2020 #1}.
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