COVID-19: updates on follow-up & long-term effects

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* Accolade for city’s specialist post-Covid-19 healthcare services
* Over 2 million adults in England may have had long COVID - Imperial REACT
* COVID and the brain: researchers zero in on how damage occurs
* Health systems should be prepared’: doctors brace for tsunami of long Covid
* Are Latent Viruses Causing Long Covid-19 Symptoms? Patient Groups Push for Testing
* Long covid should be treated as disability, says TUC
* Delta surge ‘could leave hundreds of thousands with long covid’
* Meeting the need of long covid
* We must take long covid into account when easing covid restrictions
* Doctors worry that memory problems after covid-19 may set the stage for Alzheimer's

**national policy & data**

**Title:** LONG COVID: THE NHS PLAN FOR 2021/22

Source: NHS England, 15th June 2021

The Long COVID Plan 21/22 builds on the [five-point plan](https://www.england.nhs.uk/coronavirus/post-covid-syndrome-long-covid/#five-point-plan) which outlines 10 key next steps to be taken to support those suffering from long COVID.
<https://www.england.nhs.uk/coronavirus/publication/long-covid-the-nhs-plan-for-2021-22/>

**Title:** PREVALENCE OF ONGOING SYMPTOMS FOLLOWING CORONAVIRUS (COVID-19) INFECTION IN THE UK: 1 JULY 2021

**Source:** ONS, 1st July 2021

An estimated 962,000 people living in private households in the UK (1.5% of the population) were experiencing self-reported "long COVID" (symptoms persisting for more than four weeks after the first suspected coronavirus (COVID-19) infection that were not explained by something else), as of 6 June 2021; this is down slightly from 1.021 million (1.6%) at 2 May 2021. [Full report](https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/1july2021)

**Title:** NHS ENGLAND PLEDGES £30M FOR GPS TO BOOST LONG COVID DIAGNOSIS AND CARE

Source: GP Online, 15th June 2021

NHS England has promised £30m for general practice to improve diagnosis and care of long COVID as part of a £100m package to boost care for patients with the condition.
<https://www.gponline.com/nhs-england-pledges-30m-gps-boost-long-covid-diagnosis-care/article/1719185>

**publications**

**Title:** COVID-19: PREPARING FOR THE FUTURE LOOKING AHEAD TO WINTER 2021/22 AND BEYOND

Source: The Academy of Medical Sciences, 15th July 2021

Section 4.2 ‘Understanding and Managing Long COVID’ (page 51).
<https://acmedsci.ac.uk/file-download/4747802>

**Title:** SHORT REPORT ON LONG COVID

Source: ONS/ COVID-19 Longitudinal Health and Wellbeing National Core Study, 22 July 2021

This report is provided at the request of SAGE and includes information from ongoing studies investigating long COVID including the COVID-19 Longitudinal Health and Wellbeing National Core Study-CONVALESCENCE Study, REACT-2, PHOSP-COVID, ONS’s COVID-19 Infection Survey (CIS) and the COVID Symptom Study App.

Executive Summary Long COVID symptom prevalence at 12 weeks post SARS-CoV-2 infection is uncertain and estimates vary by study design, ranging from 2.3%-37% in those infected [Medium Confidence]. The proportion reporting symptoms limiting daily living range from 1.2% in young adults, to 4.8% in middle age [High Confidence]. Trends in long COVID lag but map to those for COVID-19 infections [High Confidence]. Fatigue is the most frequently reported persistent long COVID symptom [High Confidence]. No clear individual syndromes have yet been identified [Medium Confidence]. Consistent risk factors across studies include increasing age, female sex, overweight/obesity, pre-existing asthma, pre-pandemic poor physical and mental health, and hospitalisation for initial infection [High Confidence]. Evidence of long COVID prevalence specifically in school-aged children is limited and existing studies are small; published estimates suggest that it does occur but is uncommon, 25 (1.8%) of 1,379 children (all ages) experienced symptoms for ≥56 days [Medium Confidence]. Risk of Long COVID may be reduced in individuals who become infected after double vaccination compared to those not vaccinated; however, published evidence is limited to small observational studies, which may be subject to bias [Medium Confidence]. Rates of medium-long term multi-organ sequelae (respiratory disease, major adverse cardiovascular event, diabetes, renal failure, and liver disease) are elevated in patients hospitalised with COVID-19 compared with matched general population but are similar to those hospitalised with pneumonia; however, estimates of the incidence of post-infection adverse events in non-hospitalised COVID-19 cases are lacking [High Confidence].
<https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1007511/S1327_Short_Long_COVID_report.pdf>

**research papers**

**GENERAL LONG-TERM EFFECTS/FOLLOW-UP**

**Title:** LONG COVID—MECHANISMS, RISK FACTORS, AND MANAGEMENT

Source: BMJ, 22nd July 2021

Since its emergence in Wuhan, China, covid-19 has spread and had a profound effect on the lives and health of people around the globe. As of 4 July 2021, more than 183 million confirmed cases of covid-19 had been recorded worldwide, and 3.97 million deaths. Recent evidence has shown that a range of persistent symptoms can remain long after the acute SARS-CoV-2 infection, and this condition is now coined long covid by recognized research institutes. Studies have shown that long covid can affect the whole spectrum of people with covid-19, from those with very mild acute disease to the most severe forms. Like acute covid-19, long covid can involve multiple organs and can affect many systems including, but not limited to, the respiratory, cardiovascular, neurological, gastrointestinal, and musculoskeletal systems. The symptoms of long covid include fatigue, dyspnea, cardiac abnormalities, cognitive impairment, sleep disturbances, symptoms of post-traumatic stress disorder, muscle pain, concentration problems, and headache. This review summarizes studies of the long term effects of covid-19 in hospitalized and non-hospitalized patients and describes the persistent symptoms they endure. Risk factors for acute covid-19 and long covid and possible therapeutic options are also discussed.
<https://www.bmj.com/content/374/bmj.n1648>

**Title:** Recovery after prolonged ICU treatment in patients with COVID-19

Source: The Lancet Respiratory Medicine, 14th July 2021

This comment piece suggests that the unprecedented volumes of post-ICU patients will require thoughtful system change and the development of a systematised continuum of care. As more data emerge and the features and course of post-COVID-19-associated critical illness become clearer, this continuum of care will need to be refined and optimised to meet the long-term needs of patients and their families. Full detail: [Recovery after prolonged ICU treatment in patients with COVID-19](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600%2821%2900318-0/fulltext)

**Title:** CHARACTERIZING LONG COVID IN AN INTERNATIONAL COHORT: 7 MONTHS OF SYMPTOMS AND THEIR IMPACT

Source: The Lancet eClinicalMedicine, 15th July 21

A significant number of patients with COVID-19 experience prolonged symptoms, known as Long COVID. Few systematic studies have investigated this population, particularly in outpatient settings. Hence, relatively little is known about symptom makeup and severity, expected clinical course, impact on daily functioning, and return to baseline health. Methods: We conducted an online survey of people with suspected and confirmed COVID-19, distributed via COVID-19 support groups (e.g. Body Politic, Long COVID Support Group, Long Haul COVID Fighters) and social media (e.g. Twitter, Facebook). Data were collected from September 6, 2020 to November 25, 2020. We analyzed responses from 3762 participants with confirmed (diagnostic/antibody positive; 1020) or suspected (diagnostic/antibody negative or untested; 2742) COVID-19, from 56 countries, with illness lasting over 28 days and onset prior to June 2020. We estimated the prevalence of 203 symptoms in 10 organ systems and traced 66 symptoms over seven months. We measured the impact on life, work, and return to baseline health.

Findings: For the majority of respondents (>91%), the time to recovery exceeded 35 weeks. During their illness, participants experienced an average of 55.9+/- 25.5 (mean+/-STD) symptoms, across an average of 9.1 organ systems. The most frequent symptoms after month 6 were fatigue, post-exertional malaise, and cognitive dysfunction. Symptoms varied in their prevalence over time, and we identified three symptom clusters, each with a characteristic temporal profile. 85.9% of participants (95% CI, 84.8% to 87.0%) experienced relapses, primarily triggered by exercise, physical or mental activity, and stress. 86.7% (85.6% to 92.5%) of unrecovered respondents were experiencing fatigue at the time of survey, compared to 44.7% (38.5% to 50.5%) of recovered respondents. 1700 respondents (45.2%) required a reduced work schedule compared to pre-illness, and an additional 839 (22.3%) were not working at the time of survey due to illness. Cognitive dysfunction or memory issues were common across all age groups (~88%). Except for loss of smell and taste, the prevalence and trajectory of all symptoms were similar between groups with confirmed and suspected COVID-19. Interpretation: Patients with Long COVID report prolonged, multisystem involvement and significant disability. By seven months, many patients have not yet recovered (mainly from systemic and neurological/cognitive symptoms), have not returned to previous levels of work, and continue to experience significant symptom burden.
[https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00299-6/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370%2821%2900299-6/fulltext)

**Title:** CHARACTERISATION OF IN-HOSPITAL COMPLICATIONS ASSOCIATED WITH COVID-19 USING THE ISARIC WHO CLINICAL CHARACTERISATION PROTOCOL UK: A PROSPECTIVE, MULTICENTRE COHORT STUDY

Source: The Lancet eClinicalMedicine, 17th July 21

COVID-19 is a multisystem disease and patients who survive might have in-hospital complications. These complications are likely to have important short-term and long-term consequences for patients, health-care utilisation, health-care system preparedness, and society amidst the ongoing COVID-19 pandemic. Our aim was to characterise the extent and effect of COVID-19 complications, particularly in those who survive, using the International Severe Acute Respiratory and Emerging Infections Consortium WHO Clinical Characterisation Protocol UK. Methods: We did a prospective, multicentre cohort study in 302 UK health-care facilities. Adult patients aged 19 years or older, with confirmed or highly suspected SARS-CoV-2 infection leading to COVID-19 were included in the study. The primary outcome of this study was the incidence of in-hospital complications, defined as organ-specific diagnoses occurring alone or in addition to any hallmarks of COVID-19 illness. We used multilevel logistic regression and survival models to explore associations between these outcomes and in-hospital complications, age, and pre-existing comorbidities.

Findings: Between Jan 17 and Aug 4, 2020, 80 388 patients were included in the study. Of the patients admitted to hospital for management of COVID-19, 49·7% (36 367 of 73 197) had at least one complication. The mean age of our cohort was 71·1 years (SD 18·7), with 56·0% (41 025 of 73 197) being male and 81·0% (59 289 of 73 197) having at least one comorbidity. Males and those aged older than 60 years were most likely to have a complication (aged ≥60 years: 54·5% [16 579 of 30 416] in males and 48·2% [11 707 of 24 288] in females; aged <60 years: 48·8% [5179 of 10 609] in males and 36·6% [2814 of 7689] in females). Renal (24·3%, 17 752 of 73 197), complex respiratory (18·4%, 13 486 of 73 197), and systemic (16·3%, 11 895 of 73 197) complications were the most frequent. Cardiovascular (12·3%, 8973 of 73 197), neurological (4·3%, 3115 of 73 197), and gastrointestinal or liver (0·8%, 7901 of 73 197) complications were also reported.

Interpretation: Complications and worse functional outcomes in patients admitted to hospital with COVID-19 are high, even in young, previously healthy individuals. Acute complications are associated with reduced ability to self-care at discharge, with neurological complications being associated with the worst functional outcomes. COVID-19 complications are likely to cause a substantial strain on health and social care in the coming years. These data will help in the design and provision of services aimed at the post-hospitalisation care of patients with COVID-19.
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00799-6/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2821%2900799-6/fulltext)

**Title:** PREVALENCE OF SYMPTOMS MORE THAN SEVEN MONTHS AFTER DIAGNOSIS OF SYMPTOMATIC COVID-19 IN AN OUTPATIENT SETTING

Source: Annals of Internal Medicine, 6th July 21

With millions of SARS-CoV-2 infections worldwide, increasing numbers of patients are coming forward with long-term clinical effects of the disease lasting several weeks to months. Objective: To characterize symptoms 7 to 9 months after diagnosis of COVID-19. Design: Self-reported surveys and semistructured telephone interviews at enrollment and 30 to 45 days and 7 to 9 months from diagnosis. Setting: From 18 March to 15 May 2020, symptomatic persons who tested positive for SARS-CoV-2 at the Geneva University Hospitals were followed by CoviCare, a virtual, clinical, outpatient follow-up program. Persons were contacted again at 30 to 45 days and 7 to 9 months from diagnosis. Participants: Persons who were a part of the CoviCare program from 18 March to 15 May 2020. Measurements: A standardized interview of symptoms consistent with COVID-19, with grading of intensity. Results: Of the 629 participants in the study who completed the baseline interviews, 410 completed follow-up at 7 to 9 months after COVID-19 diagnosis; 39.0% reported residual symptoms. Fatigue (20.7%) was the most common symptom reported, followed by loss of taste or smell (16.8%), dyspnea (11.7%), and headache (10.0%). Limitation: Limitations include generalizability and missing data for 34.8% of participants. Conclusion: Residual symptoms after SARS-CoV-2 infection are common among otherwise young and healthy persons followed in an outpatient setting. These findings contribute to the recognition of long-term effects in a disease mostly counted by its death toll to date by promoting communication on postacute sequelae of SARS-CoV-2 and encouraging physicians to continue long-term monitoring of their patients.
<https://www.acpjournals.org/doi/10.7326/M21-0878>

**Title:** LONG COVID HAS EXPOSED MEDICINE'S BLIND-SPOT

Source: The Lancet, 18th June 21

…For now, the most important thing is to study long COVID with no assumptions and to interrogate potential unique factors about COVID-19 that could explain why these symptoms seem to be triggered with particularly high propensity. The COVID-19 pandemic and the large (and growing) number of patients with long-term symptoms offers an unprecedented window to study these symptoms, their inter-relationships, and their puzzling pathogenesis. Attention is finally being paid to this important topic, and even if this line of research does not lead to definitive answers, we are confident that there will be valuable new insights for this field. We should not care about what ends up being right or more right, wrong or more wrong; we should care about getting closer to reliable, objective markers of these complex symptoms and easing the suffering of these oft-neglected patient populations.
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00333-9/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2821%2900333-9/fulltext)

**Title:** PERSISTENT SYMPTOMS IN ADULT PATIENTS ONE YEAR AFTER COVID-19: A PROSPECTIVE COHORT STUDY

Source: Clinical Infectious Diseases, Jul 2021

BACKGROUND Long COVID is defined as the persistence of symptoms beyond 3 months after SARS-CoV-2 infection. To better understand the long-term course and etiology of symptoms we analyzed a cohort of COVID-19 patients prospectively. METHODS Patients were included at 5 months after acute COVID-19 in this prospective, non-interventional follow-up study. Patients followed until 12 months after COVID-19 symptom onset (n=96, 32.3% hospitalised, 55.2% females) were included in this analysis of symptoms, quality of life (based on a SF-12 survey), laboratory parameters including antinuclear antibodies (ANA), and SARS-CoV-2 antibody levels. RESULTS At month 12, only 22.9% of patients were completely free of symptoms and the most frequent symptoms were reduced exercise capacity (56.3%), fatigue (53.1%), dyspnoea (37.5%), concentration problems (39.6%), problems finding words (32.3%), and sleeping problems (26.0%). Females showed significantly more neurocognitive symptoms than males. ANA titres were ≥1:160 in 43.6% of patients at 12 months post COVID-19 symptom onset, and neurocognitive symptom frequency was significantly higher in the group with an ANA titre ≥1:160 compared to <1:160. Compared to patients without symptoms, patients with at least one long COVID symptom at 12 months did not differ significantly with respect to their SARS-CoV-2-antibody levels, but had a significantly reduced physical and mental life quality compared to patients without symptoms. CONCLUSIONS Neurocognitive long COVID symptoms can persist at least for one year after COVID-19 symptom onset, and reduce life quality significantly. Several neurocognitive symptoms were associated with ANA titre elevations. This may indicate autoimmunity as cofactor in aetiology of long COVID.
<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab611/6315216>

**Title:** Post-covid Syndrome: A Single-Center Questionnaire Study On 1007 Participants Recovered from COVID-19

Source: Journal of Medical Virology | 13th July 2021

Post-recovery manifestations have become another concern in patients who recovered from COVID-19. Numerous reports have shown that COVID-19 has a variety of long-term effects on almost all systems including respiratory, cardiovascular, gastrointestinal, neurological, psychiatric, and dermatological systems. This research aimed to investigate the prevalence and characteristics of the post-covid syndrome among COVID-19 survivors and to determine the factors associated with persistent symptoms. A total of 1007 participants, 39.0% had at least one comorbidity, and 47.5% had persistent symptoms. Fatigue/easy fatigability, myalgia, and loss of weight were the most frequent persistent symptoms (overall 29.3%) and followed by respiratory symptoms (25.4%). A total of 235 participants had visited outpatient clinics due to several reasons during the post-COVID-19 period, 17 of them were hospitalized. Severe acute COVID-19, hospitalization, and presence of comorbidity were independent factors for the development of persistent symptoms.

The authors conclude that fully understanding the spectrum of post-covid syndrome is essential for appropriate management of all its long-term effects. The study once again underlined that the prevalence of post-covid syndrome is higher than expected and concerns many systems, and a multidisciplinary follow-up should be provided to COVID-19 survivors in the post-recovery period.
Full paper: [Post-covid Syndrome: A Single-Center questionnaire study on 1007 participants recovered from COVID-19](https://onlinelibrary.wiley.com/doi/epdf/10.1002/jmv.27198)

**Title:** PERSISTENCE OF SYMPTOMS AFTER IMPROVEMENT OF ACUTE COVID19 INFECTION, A LONGITUDINAL STUDY

Source: Journal of Medical Virology; 25th Jun 2021

**Abstract:** BACKGROUND AND AIMS With increasing the number of COVID-19 infected patients all over the world, a large number of survivors reported changes in their quality of life or experienced re-infection. So, we aimed to detect the percentage, type, and risk factors of persistent symptoms after improvement from acute COVID-19 infection and to detect the percentage of COVID-19 re-infection and degree of severity of the second infection. PATIENTS AND METHODS One hundred seventy-two (59 male, 113 female) patients who were tested positive for SARS-CoV2 were followed up via mobile phone every 2 months for 8 to 10 months. RESULTS After recovery, 105 patients (61%) (30 male, 75 female) reported persistent one or more COVID-19 symptoms. Fatigue, dyspnea, and depression were the most common persistent symptoms representing 37.3%, 22 %, 22% respectively. We found that age was independently related to the persistence of symptoms. During the follow-up, six females (3.5%) had laboratory-confirmed COVID-19 re-infection. Their mean age was 35.7 ± 11 years. The mean interval from the complete recovery of the first infection to the onset of the second one was 53 ± 22.2 days and ranged from 30-90 days. The second infection was mild in severity than the first infection in 83.33% of cases. CONCLUSION There was a high percentage of patients who complained of persistent symptoms after recovery from COVID-19. Fatigue and headache were the most common persistent symptoms. Age was considered a risk factor for persistent symptoms. Re-infection with SARS-CoV2 can occur after recovery.
<https://onlinelibrary.wiley.com/doi/10.1002/jmv.27156>

**Title:** HEALTH-RELATED QUALITY OF LIFE ISSUES, INCLUDING SYMPTOMS, IN PATIENTS WITH ACTIVE COVID-19 OR POST COVID-19; A SYSTEMATIC LITERATURE REVIEW

Source: Quality of Life Research: an International Journal Of Quality Of Life Aspects Of Treatment, Care And Rehabilitation; 19th Jun 2021

PURPOSE This systematic review was performed to identify all relevant health-related quality of life (HRQoL) issues associated with COVID-19.METHODSA systematic literature search was undertaken in April 2020. In four teams of three reviewers each, all abstracts were independently reviewed for inclusion by two reviewers. Using a pre-defined checklist of 93 criteria for each publication, data extraction was performed independently by two reviewers and subsequently compared and discussed. If necessary, a third reviewer resolved any discrepancies. The search was updated in February 2021 to retrieve new publications on HRQoL issues including issues related to the long-term consequences of COVID-19.RESULTSThe search in April 2020 identified 3342 potentially relevant publications, and 339 publications were selected for full-text review and data extraction. We identified 75 distinct symptoms and other HRQoL issues categorized into 12 thematic areas; from general symptoms such as fever, myalgia, and fatigue, to neurological and psychological issues. The updated search revealed three extra issues experienced during active disease and long-term problems with fatigue, psychological issues and impaired cognitive function. CONCLUSION This first comprehensive systematic review provides a detailed overview of the wide range of HRQoL issues experienced by patients with COVID-19 throughout the course of the disease. It demonstrates the devastating impact of the disease and provides critically important information for clinicians, to enable them to better recognize the disease and to provide knowledge important for treatment and follow-up. The results provided the foundation for the international development of a COVID-19 specific patient-reported HRQoL questionnaire.
<https://pubmed.ncbi.nlm.nih.gov/34146226/>

**Title:** ACUTE AND PERSISTENT SYMPTOMS IN NON-HOSPITALIZED PCR-CONFIRMED COVID-19 PATIENTS

Source: Nature Scientific Reports; 23rd Jun 2021; vol. 11 (no. 1)

Reports of persistent symptoms after hospitalization with COVID-19 have raised concern of a “long COVID” syndrome. This study aimed at determining the prevalence of and risk factors for acute and persistent symptoms in non-hospitalized patients with polymerase chain reaction (PCR) confirmed COVID-19. We conducted a cohort study of non-hospitalized participants identified via the Danish Civil Registration System with a SARS-CoV-2-positive PCR-test and available biobank samples. Participants received a digital questionnaire on demographics and COVID-19-related symptoms. Persistent symptoms: symptoms > 4 weeks (in sensitivity analyses > 12 weeks). We included 445 participants, of whom 34% were asymptomatic. Most common acute symptoms were fatigue, headache, and sneezing, while fatigue and reduced smell and taste were most severe. Persistent symptoms, most commonly fatigue and memory and concentration difficulties, were reported by 36% of 198 symptomatic participants with follow-up > 4 weeks. Risk factors for persistent symptoms included female sex (women 44% vs. men 24%, odds ratio 2.7, 95% CI 1.4–5.1, p = 0.003) and BMI (odds ratio 1.1, 95% CI 1.0–1.2, p = 0.001). In conclusion, among non-hospitalized PCR-confirmed COVID-19 patients one third were asymptomatic while one third of symptomatic participants had persistent symptoms illustrating the heterogeneity of disease presentation. These findings should be considered in health care planning and policy making related to COVID-19.
<https://www.nature.com/articles/s41598-021-92045-x>

**Title:** COVID-19: THIRD OF PEOPLE INFECTED HAVE LONG TERM SYMPTOMS

Source: BMJ (Clinical Research); Jun 2021; vol. 373; p. n1626

Around a third of people in England who developed covid-19 went on to experience long term symptoms sometimes called “long covid,” a UK study has found and experts believe that more than two million people could have been affected in this way. Findings from the React-2 (Real-time Assessment of Community Transmission) study from Imperial College London used self-reported data from 508 707 adults aged 18 or older who took part in three rounds of surveys that were carried out between September 2020 and February 2021, in which they were asked about 29 different symptoms. The study, published as a preprint and not yet peer reviewed, found that around a fifth (19.2%) of those surveyed reported having had contracted covid-19 previously, with more than a third (37.7%) reporting at least one persistent symptom and 14.8% experiencing three or more symptoms lasting at least 12 weeks…
<https://www.bmj.com/content/373/bmj.n1626>

**Title:** POST-COVID-19 SYNDROME (LONG HAUL SYNDROME): DESCRIPTION OF A MULTIDISCIPLINARY CLINIC AT MAYO CLINIC AND CHARACTERISTICS OF THE INITIAL PATIENT COHORT

Source: Mayo Clinic Proceedings; Jul 2021; vol. 96 (no. 7); p. 1782-1791

Abstract OBJECTIVE To describe characteristics of a series of patients reporting prolonged symptoms after an infection with coronavirus disease 2019 (COVID-19).PATIENTS AND METHODS This study describes the multidisciplinary COVID-19 Activity Rehabilitation Program, established at Mayo Clinic to evaluate and treat patients with post-COVID syndrome, and reports the clinical characteristics of the first 100 patients receiving evaluation and management during the timeframe of June 1, 2020, and December 31, 2020. RESULTSThe cohort consisted of 100 patients (mean age, 45.4±14.2 years; 68% women; mean body mass index, 30.2 kg/m2; presenting a mean of 93 days after infection). Common preexisting conditions were respiratory (23%) and mental health, including depression and/or anxiety (34%). Most (75%) had not been hospitalized for COVID-19. Common presenting symptoms ware fatigue (80%), respiratory complaints (59%), and neurological complaints (59%) followed by subjective cognitive impairment, sleep disturbance, and mental health symptoms. More than one-third of patients (34%) reported difficulties in performing basic activities of daily living. Only 1 in 3 patients had returned to unrestricted work duty at the time of the analysis. For most patients, laboratory and imaging tests showed no abnormalities or were nondiagnostic despite debilitating symptoms. Most patients required physical therapy, occupational therapy, or brain rehabilitation. Face-to-face and virtual care delivery modalities were feasible. CONCLUSION Most of the patients did not have COVID-19-related symptoms that were severe enough to require hospitalization, were younger than 65 years, and were more likely to be female, and most had no preexisting comorbidities before severe acute respiratory syndrome coronavirus 2 infection. Symptoms including mood disorders, fatigue, and perceived cognitive impairment resulted in severe negative impacts on resumption of functional and occupational activities in patients experiencing prolonged effects.
[https://www.mayoclinicproceedings.org/article/S0025-6196(21)00356-6/fulltext](https://www.mayoclinicproceedings.org/article/S0025-6196%2821%2900356-6/fulltext)

**Title:** EPIDEMIOLOGY AND ORGAN SPECIFIC SEQUELAE OF POST-ACUTE COVID19: A NARRATIVE REVIEW

Source: The Journal of infection; Jul 2021; vol. 83 (no. 1); p. 1-16

In this review, by addressing separately each body system, we describe the pleiotropic manifestations reported post COVID-19, their putative pathophysiology and risk factors, and attempt to offer guidance regarding work-up, follow-up and management strategies. Long term sequelae involve all systems with a negative impact on mental health, well-being and quality of life, while a subset of patients, report debilitating chronic fatigue, with or without other fluctuating or persistent symptoms, such as pain or cognitive dysfunction. Although the pathogenesis is unclear, residual damage from acute infection, persistent immune activation, mental factors, or unmasking of underlying co-morbidities are considered as drivers. Comparing long COVID with other post viral chronic syndromes may help to contextualize the complex somatic and emotional sequalae of acute COVID-19. The pace of recovery of different aspects of the syndrome remains unclear as the pandemic began only a year ago. Early recognition of long-term effects and thorough follow-up through dedicated multidisciplinary outpatient clinics with a carefully integrated research agenda are essential for treating COVID-19 survivors holistically.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8118709/>

**Title:** ANTIBODY RESPONSE TO SARS-COV-2 IS ASSOCIATED WITH LONG-TERM CLINICAL OUTCOME IN PATIENTS WITH COVID-19: A LONGITUDINAL STUDY

Source: Journal of Clinical Immunology, 17th July 21

The relationship of host immune response and viral replication with health outcomes in patients with COVID-19 remains to be defined. We aimed to characterize the medium and long-term clinical, virological, and serological outcomes after hospitalization for COVID-19, and to identify predictors of long-COVID.
<https://link.springer.com/article/10.1007/s10875-021-01083-7>

**Title:** COVID-19: LONG COVID CASES ARE UNDERREPORTED IN GP RECORDS

Source: BMJ (Clinical research ed.); Jul 2021; vol. 374; p. n1685

GPs may be underreporting long covid say researchers who analysed 58 million patients’ primary care records and found a much lower prevalence than previous survey estimates. An analysis of pseudonymised electronic health records of patients in England found only 40 cases of long covid reported per 100 000 people. This is a much lower prevalence than estimates using questionnaire research methods such as the React-2 study which estimated that around two million people have the condition. The analysis, published in the British Journal of General Practice, also found wide variation in reporting of long covid by GP practice, geographic region, and electronic notes systems doctors used.
<https://www.bmj.com/content/374/bmj.n1685>

**Title:** LONG-TERM CONSEQUENCES IN CRITICALLY ILL COVID-19 PATIENTS: A PROSPECTIVE COHORT STUDY

Source: Acta Anaesthesiologica Scandinavica; Jun 2021

**Abstract:** BACKGROUNDCOVID-19 can cause severe disease with need of treatment in the intensive care unit (ICU) for several weeks. Increased knowledge is needed about the long-term consequences. METHODS This is a single-center prospective follow-up study of COVID-19 patients admitted to the ICU for respiratory organ support between March and July 2020. Patients with invasive ventilation were compared with those with high-flow nasal oxygen (HFNO) or non-invasive ventilation (NIV) regarding functional outcome and health-related qualify of life. The mean follow-up time was 5 months after ICU discharge and included clinical history, three well-validated questionnaires about health-related quality of life and psychological health, pulmonary function test, 6-minute walk test (6MWT) and work ability. Data were analyzed with multivariable general linear and logistic regression models with 95% confidence intervals. RESULTS Among 248 ICU patients, 200 patients survived. Of these, 113 patients came for follow-up. Seventy patients (62%) had received invasive ventilation. Most patients reported impaired health-related quality of life. Approximately one-third suffered from post-traumatic stress, anxiety and depression. Twenty-six percent had reduced total lung capacity, 34% had reduced 6MWT and 50% worked fulltime. The outcomes were similar regardless of ventilatory support, but invasive ventilation was associated with more bodily pain (MSD -19, 95% CI: -32 to -5) and <80% total lung capacity (OR 4.1, 95% CI: 1.3-16.5).CONCLUSION Among survivors of COVID-19 who required respiratory organ support, outcomes 5 months after discharge from ICU were largely similar among those requiring invasive compared to non-invasive ventilation.
<https://onlinelibrary.wiley.com/doi/full/10.1111/aas.13939>

**Title:** LONG-TERM PATIENT-CENTRED FOLLOW-UP IN A PROSPECTIVE COHORT OF PATIENTS WITH COVID-19

Source: Infectious Diseases and Therapy; Jun 2021

**Abstract:** INTRODUCTION To better define COVID-19 long-term impact we prospectively analysed patient-centred outcomes, including general health and symptom duration. METHODS Barthel index (BI), St. George's Respiratory Questionnaire adapted to patients with COVID-19 (aSGRQ) and WHO Clinical Progression Scale (CPS) were measured at enrolment and at 6 weeks from the onset of symptoms. Persistence of most frequently reported symptoms was assessed at 6 weeks and, among symptomatic patients, at 12 weeks from the onset of symptoms. Predictors of impaired general health over time were identified using an ordinal multilevel multivariate model. RESULTS A total of 448 patients (55% men, median age 56 years) were enrolled. WHO-CPS showed mild, moderate and severe disease in 48%, 42% and 10% of patients at admission and mild disease in all patients at follow-up, respectively. BI and aSGRQ were normal in 96% and 93% patients before COVID-19 but only in 47% and 16% at COVID-19 diagnosis and in 87% and 65% at 6-week follow-up. Male gender was identified by all three assessments as a predictor of impaired general health (BI, OR 2.14, p < 0.0001; aSGRQ, OR 0.53, p = 0.003; WHO-CPS, OR 1.56, p = 0.01). Other predictors included age, ICU admission and comorbidities (e.g. cardiovascular disease and cancer) for BI, hospital admission for aSGRQ, age and presence of comorbidities for WHO-CPS. At 6- and 12-week follow-up, 39% and 20% of patients, respectively, were still reporting symptoms. Fatigue and breathlessness were the most frequently reported symptoms. CONCLUSIONS Long-term follow-up facilitates the monitoring of health impairment and symptom persistence and can contribute to plan tailored interventions.
<https://adisjournals.figshare.com/articles/media/Long-Term_Patient-Centred_Follow-up_in_a_Prospective_Cohort_of_COVID-19_Patients/14573679>

**Title:** LONG COVID, OR POST-COVID SYNDROME, AND THE GLOBAL IMPACT ON HEALTH CARE

Source: Medical Science Monitor; 2021; vol. 27; p. e933446

**Abstract:** During 2020, increasing numbers of case reports, case series, and small observational studies reported long-term complications of coronavirus disease 2019 (COVID-19) in patients who had recovered from acute infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Long COVID has a prevalence of between 10-30% in patients with a recent history of SARS-CoV-2 infection. Pulmonary, hematologic, cardiovascular, neuropsychiatric, renal, endocrine, gastrointestinal and hepatobiliary, and dermatologic involvement, and chronic multisystem inflammatory syndrome in children (MIS-C) highlights the requirement for a multidisciplinary approach to the management of patients with long COVID. This Editorial aims to present the current status of long COVID, or post-COVID syndrome, and its global impact on health and the provision of health care.
<https://pubmed.ncbi.nlm.nih.gov/34092779/>

**Title:** ASSESSMENT OF PROLONGED PHYSIOLOGICAL AND BEHAVIORAL CHANGES ASSOCIATED WITH COVID-19 INFECTION

Source: JAMA Network Open. 2021;4(7):e2115959

Long-term COVID symptoms marked by autonomic dysfunction and cardiac damage following COVID-19 infection have been noted for up to 6 months after symptom onset, but to date have not been quantified, to our knowledge. Previous studies have found that wearable data can improve real-time detection of viral illness or discrimination of individuals with COVID-19 vs other viral infections. Wearable devices provide a way to continuously track an individual’s physiological and behavioral metrics beginning when healthy (ie, before infection), during the course of infection, and recovery back to baseline. In this cohort study, we aimed to examine the duration and variation of recovery among COVID-19–positive vs COVID-19–negative participants. Methods: DETECT (Digital Engagement and Tracking for Early Control and Treatment) is a remote, app-based, longitudinal research study enrolling adult participants from all over the US and collecting their wearable data to better understand individual changes associated with viral illness, including COVID-19 … To our knowledge, this is the first study to examine longer duration wearable sensor data. We found a prolonged physiological impact of COVID-19 infection, lasting approximately 2 to 3 months, on average, but with substantial intraindividual variability, which may reflect various levels of autonomic nervous system dysfunction or potentially ongoing inflammation. Transient bradycardia has been noted in a case study approximately 9 to 15 days after symptom onset, which was also seen in our population. Our data suggest that early symptoms and larger initial RHR response to COVID-19 infection may be associated with the physiological length of recovery from this virus.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781687?utm_source=For_The_Media&utm_medium=referral&utm_campaign=ftm_links&utm_term=070721>

**Title:** REFINING "LONG-COVID" BY A PROSPECTIVE MULTIMODAL EVALUATION OF PATIENTS WITH LONG-TERM SYMPTOMS ATTRIBUTED TO SARS-COV-2 INFECTION

Source: Infectious Diseases and Therapy, 10th July 21

In this prospective study, we recruited 30 consecutive patients seeking medical help for persistent symptoms (> 30 days) attributed to COVID-19. All reported a viral illness compatible with COVID-19. The patients underwent a multi-modal evaluation, including clinical, psychologic, virologic and specific immunologic assays and were followed longitudinally. A group of 17 convalescent COVID-19 individuals without persistent symptoms were included as a comparison group…

Half of patients seeking medical help for post-acute COVID-19 syndrome lack SARS-CoV-2 immunity. The presence of SARS-CoV-2 immunity, or not, had no consequence on the clinical or biologic characteristics of post-acute COVID-19 syndrome patients, all of whom reported severe fatigue, altered quality of life and psychologic distress.
<https://pubmed.ncbi.nlm.nih.gov/34245450/>

**Title:** THE PRESENCE OF HEADACHE AT ONSET IN SARS-COV-2 INFECTION IS ASSOCIATED WITH LONG-TERM POST-COVID HEADACHE AND FATIGUE: A CASE-CONTROL STUDY

Source: Cephalalgia: an International Journal of Headache; Jun 2021

**Abstract:** OBJECTIVE To investigate the association of headache during the acute phase of SARS-CoV-2 infection with long-term post-COVID headache and other post-COVID symptoms in hospitalised survivors. METHODS A case-control study including patients hospitalised during the first wave of the pandemic in Spain was conducted. Patients reporting headache as a symptom during the acute phase and age- and sex-matched patients without headache during the acute phase participated. Hospitalisation and clinical data were collected from medical records. Patients were scheduled for a telephone interview 7 months after hospital discharge. Participants were asked about a list of post-COVID symptoms and were also invited to report any additional symptom they might have. Anxiety/depressive symptoms and sleep quality were assessed with the Hospital Anxiety and Depression Scale and the Pittsburgh Sleep Quality Index. RESULTS Overall, 205 patients reporting headache and 410 patients without headache at hospitalisation were assessed 7.3 months (Standard Deviation 0.6) after hospital discharge. Patients with headache at onset presented a higher number of post-COVID symptoms (Incident Rate Ratio: 1.16, 95% CI: 1.03-1.30). Headache at onset was associated with a previous history of migraine (Odd Ratio: 2.90, 95% Confidence Interval: 1.41-5.98) and with the development of persistent tension-type like headache as a new post-COVID symptom (Odd Ratio: 2.65, 95% CI: 1.66-4.24). Fatigue as a long-term symptom was also more prevalent in patients with headache at onset (Odd Ratio: 1.55, 95% CI: 1.07-2.24). No between-group differences in the prevalence of anxiety/depressive symptoms or sleep quality were seen. CONCLUSION Headache in the acute phase of SARS-CoV-2 infection was associated with higher prevalence of headache and fatigue as long-term post-COVID symptoms. Monitoring headache during the acute phase could help to identify patients at risk of developing long-term post-COVID symptoms, including post-COVID headache.
<https://pubmed.ncbi.nlm.nih.gov/34134526/>

**Title:** CAUSATION OR CONFOUNDING: WHY CONTROLS ARE CRITICAL FOR CHARACTERIZING LONG COVID

Source: Nature Medicine, 17th June 2021

…Studies of long COVID thus far—nearly all from high-income countries—have been difficult to interpret or compare (Fig.1), not only because of the lack of a consistent case definition but also because of systematic selection bias of cases, often without appropriate controls. Unsurprisingly, hospitalized patients with COVID-19, especially those who require prolonged intensive care, have reported very high rates of persistent symptoms, even though the vast majority of the more than 136 million cases worldwide occurred in healthy working-age, non-hospitalized adults, with mild to moderate self-limited illness. Meanwhile, community-based studies have raised questions about the representativeness of cases compared with the general population, especially those using online recruitment, with many studies relying on self-reported symptoms and without laboratory-confirmed diagnosis of SARS-CoV-2 infection. Selection bias becomes even more pronounced when people are recruited through online support groups, where very high rates of often nonspecific long-term symptoms have been reported, even in children. These biases are further compounded in systematic reviews of published studies, with estimates of up to 80% (95% confidence interval, 65–92%) of patients with COVID-19 reported to have one or more long-term symptoms after acute infection.
<https://www.nature.com/articles/s41591-021-01402-w>

**Title:** PROMIS SCALES FOR ASSESSMENT OF THE IMPACT OF POST-COVID SYNDROME: A CROSS SECTIONAL STUDY

Source: Infectious Diseases and Therapy, 10th July 21

[**This article is a preprint and has not been peer-reviewed. It reports new medical research that has yet to be evaluated and so should not be used to guide clinical practice.**](https://www.medrxiv.org/content/what-unrefereed-preprint)
The post-COVID syndrome is estimated to occur in up to 10% of patients who have had COVID-19. This condition manifests as lingering symptoms which persist for weeks to months after resolution of the acute illness. The syndrome is poorly understood and efforts are just beginning to appropriately characterize the symptoms expressed by this population. We present a population of patients with persistent symptoms as measured by a select number of PROMIS surveys (i.e. fatigue, sleep, pain, physical functioning, and social roles). We believe this to be the first use of the PROMIS survey data collected in this population and one of the first to attempt to measure social dysfunction secondary to the post-COVID syndrome. Our patient population is notably younger (30.9% were between 40-59 years of age), with a majority being female (60.5%). They also reported deficits in social roles (34.5%), and greater fatigue (14.7%), and pain (15.9%); along with a variety of disease severity ranging from asymptomatic to requiring admission. Despite this increased heterogeneity of population, the symptomatology of the post-COVID syndrome is preserved. These findings differ significantly from previously published data that demonstrated that outpatients can have duration of post-COVID syndrome similar to those who were hospitalized.
<https://www.medrxiv.org/content/10.1101/2021.05.25.21257817v1.full>

**Title:** LONG-COVID FOLLOWING MILD SARS COV-2 INFECTION: CHARACTERISTIC T CELL ALTERATIONS AND RESPONSE TO ANTIHISTAMINES

**Source:** MedRxiv Preprint Server, 7th June 2021

[**This article is a preprint and has not been peer-reviewed. It reports new medical research that has yet to be evaluated and so should not be used to guide clinical practice.**](https://www.medrxiv.org/content/what-unrefereed-preprint)

Long-COVID is characterised by the emergence of multiple debilitating symptoms following SARS CoV2 infection. Its aetiology is unclear, and it often follows a mild acute illness. Anecdotal reports of gradual clinical responses to histamine receptor antagonists (HRA) suggest a histamine-dependent mechanism distinct from anaphylaxis. Histamine is a paracrine regulator of T-cells: although T-cell perturbations are reported in acute COVID-19, the T-cell landscape in recovered patients and its relationship to long-COVID remains under-explored. Objective To survey T-cell populations in patients recovered from mild COVID-19, comparing those with long-COVID and asymptomatic individuals, and to analyse these data in light of symptoms and response to HRA. Design Prospective observational cohort study. Setting Single-site outpatient clinic. Participants 65 (87 to 408 days post mild COVID-19). None had sought treatment for acute COVID-19. 16 recovered uneventfully (asymptomatic group), 49 presented with long-COVID (symptomatic group), of whom 25 received HRA. Measurements Structured long-COVID symptom questionnaire; quantification of T-cell subsets using a standard diagnostic assay. Results HRA significantly reduced mean symptom burden. T-cell profiles distinguished asymptomatic and long-COVID groups, but did not predict response to HRA. Long-COVID patients had reduced CD4+ and CD8+ effector memory (EM) cells and increased PD-1 expression on central memory (CM) cells. Asymptomatic controls had reduced CD8+ EM cells and increased CD28 expression on CM cells. Conclusion HRA reduce long-COVID symptoms. T-cell perturbations persist for up to 400 days following mild acute COVID-19 irrespective of long-COVID symptoms.
<https://www.medrxiv.org/content/10.1101/2021.06.06.21258272v1>

**RESPIRATORY MEDICINE**

**Title:** EIGHT MONTHS FOLLOW-UP STUDY ON PULMONARY FUNCTION, LUNG RADIOGRAPHIC, AND RELATED PHYSIOLOGICAL CHARACTERISTICS IN COVID-19 SURVIVORS

**Source**: Nature Scientific Reports; 8th Jul 2021; vol. 11 (no. 1); p. 13854

**Abstract:** To describe the long-term health outcomes of patients with COVID-19 and investigate the potential risk factors. Clinical data during hospitalization and at a mean (SD) day of 249 (15) days after discharge from 40 survivors with confirmed COVID-19 (including 25 severe cases) were collected and analyzed retrospectively. At follow-up, severe cases had higher incidences of persistent symptoms, DLCO impairment, and higher abnormal CT score as compared with mild cases. CT score at follow-up was positively correlated with age, LDH level, cumulative days of oxygen treatment, total dosage of glucocorticoids used, and CT peak score during hospitalization. DLCO% at follow-up was negatively correlated with cumulative days of oxygen treatment during hospitalization. DLCO/VA% at follow-up was positively correlated with BMI, and TNF-α level. Among the three groups categorized as survivors with normal DLCO, abnormal DLCO but normal DLCO/VA, and abnormal DLCO and DLCO/VA, survivors with abnormal DLCO and DLCO/VA had the lowest serum IL-2R, IL-8, and TNF-α level, while the survivors with abnormal DLCO but normal DLCO/VA had the highest levels of inflammatory cytokines during hospitalization. Altogether, COVID-19 had a greater long-term impact on the lung physiology of severe cases. The long-term radiological abnormality maybe relate to old age and the severity of COVID-19. Either absent or excess of inflammation during COVID-19 course would lead to the impairment of pulmonary diffusion function.
<https://www.nature.com/articles/s41598-021-93191-y>

**CARDIOLOGY**

**Title:** CARDIAC SEQUELAE AFTER COVID-19 RECOVERY: A SYSTEMATIC REVIEW

Source: Clinical microbiology and infection; 23rd Jun 2021

Background: Coronavirus disease 2019 (COVID-19) has been implicated in a wide spectrum of cardiac manifestations following the acute phase of the disease. Objectives: To assess the range of cardiac sequelae after COVID-19 recovery. Results: Thirty-five studies (fifteen prospective cohort, seven case reports, five cross-sectional, four case series, three retrospective cohort and one ambidirectional cohort) evaluating cardiac sequelae in 52 609 patients were included. Twenty-nine studies used objective cardiac assessments, mostly cardiac magnetic resonance imaging (CMR) in 16 studies, echocardiography in 15, electrocardiography (ECG) in 16 and cardiac biomarkers in 18. Most studies had a fair risk of bias. The median time from diagnosis/recovery to cardiac assessment was 48 days (1-180 days). Common short-term cardiac abnormalities (<3 months) included increased T1 (proportion: 30%), T2 (16%), pericardial effusion (15%) and late gadolinium enhancement (11%) on CMR, with symptoms such as chest pain (25%) and dyspnoea (36%). In the medium term (3-6 months), common changes included reduced left ventricular global longitudinal strain (30%) and late gadolinium enhancement (10%) on CMR, diastolic dysfunction (40%) on echocardiography and elevated N-terminal proB-type natriuretic peptide (18%). In addition, COVID-19 survivors had higher risk (risk ratio 3; 95% CI 2.7-3.2) of developing heart failure, arrythmias and myocardial infarction. Conclusions: COVID-19 appears to be associated with persistent/de novo cardiac injury after recovery, particularly subclinical myocardial injury in the earlier phase and diastolic dysfunction later. Larger well-designed and controlled studies with baseline assessments are needed to better measure the extent of cardiac injury and its clinical impact.
<https://pubmed.ncbi.nlm.nih.gov/34171458/>

**Title:** LONG TERM EFFECTS OF MILD SEVERITY COVID 19 ON RIGHT VENTRICULAR FUNCTIONS

Source: Clinical Microbiology and Infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases; Jun 2021

BACKGROUND Coronavirus disease 2019 (COVID-19) has been implicated in a wide spectrum of cardiac manifestations following the acute phase of the disease. OBJECTIVES To assess the range of cardiac sequelae after COVID-19 recovery. DATA SOURCES PubMed, Embase, Scopus (inception through 17 February 2021), and Google scholar (2019 through 17 February 2021).STUDY ELIGIBILITY CRITERIA Prospective and retrospective studies, case reports and case series. PARTICIPANTS Adult patients assessed for cardiac manifestations after COVID-19 recovery. EXPOSURE Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection diagnosed by polymerase chain reaction (PCR).RESULTS Thirty-five studies (fifteen prospective cohort, seven case reports, five cross-sectional, four case series, three retrospective cohort and one ambidirectional cohort) evaluating cardiac sequelae in 52609 patients were included. Twenty-nine studies utilized objective cardiac assessments, mostly cardiac magnetic resonance imaging (CMR) in sixteen studies, echocardiography in fifteen, electrocardiography (ECG) in sixteen and cardiac biomarkers in eighteen. Most studies had a fair risk of bias. The median time from diagnosis/recovery to cardiac assessment was 48 days (1-180). Common short-term cardiac abnormalities (<3 months) included increased T1 (proportion: 30%), T2 (16%), pericardial effusion (15%) and late gadolinium enhancement (LGE, 11%) on CMR, with symptoms such as chest pain (25%) and dyspnea (36%). In the medium term (3-6 months), common changes included reduced left ventricular global longitudinal strain (30%) and LGE (10%) on CMR, diastolic dysfunction (40%) on echocardiography and elevated NT-proBNP (18%). In addition, COVID-19 survivors had higher risk (RR = 3; 95% CI: 2.7-3.2) of developing heart failure, arrythmias and myocardial infarction.CONCLUSIONSCOVID-19 appears to be associated with persistent/de novo cardiac injury after recovery, particularly subclinical myocardial injury in the earlier phase and diastolic dysfunction later. Larger well-designed and controlled studies with baseline assessments are needed to better measure the extent of cardiac injury and its clinical impact.
<https://pubmed.ncbi.nlm.nih.gov/34171458/>

**Title:** CARDIAC INVOLVEMENT IN CONSECUTIVE UNSELECTED HOSPITALIZED COVID-19 POPULATION: IN-HOSPITAL EVALUATION AND ONE-YEAR FOLLOW-UP

**Source**: International Journal of Cardiology; 3rd Jul 2021

BACKGROUND Cardiovascular disease (CVD) can occur in COVID-19 and has impact on clinical course. Data on CVD prevalence in hospitalized COVID-19 patients and sequelae in survivors is limited. Aim of this prospective study carried out on consecutive unselected COVID-19 population, was to assess: 1) CVD occurrence among hospitalized COVID-19 patients, 2) persistence or new onset of CVD at one-month and one-year follow-up. METHODS Over 30 days n = 152 COVID-19 patients underwent cardiovascular evaluation. Standard electrocardiogram (ECG), Troponin and echocardiography were integrated by further tests when indicated. Medical history, arterial blood gas, blood tests, chest computed tomography and treatment were recorded. CVD was defined as the occurrence of a new condition during the hospitalization for COVID-19. Survivors attended a one-month follow-up visit and a one-year telephone follow-up. RESULTS Forty-two patients (28%) experienced a wide spectrum of CVD with acute myocarditis being the most frequent. Death occurred in 32 patients (21%) and more frequently in patients who developed CVD (p = 0.032). After adjustment for confounders, CVD was independently associated with death occurrence. At one-month follow-up visit, 7 patients (9%) presented persistent or delayed CVD. At one-year telephone follow-up, 57 patients (48%) reported persistent symptoms .CONCLUSION Cardiovascular evaluation in COVID-19 patients is crucial since the occurrence of CVD in hospitalized COVID-19 patients is common (28%), requires specific treatment and increases the risk of in-hospital mortality. Persistence or delayed presentation of CVD at 1-month (9%) and persistent symptoms at 1-year follow-up (48%) suggest the need for monitoring COVID-19 survivors.
<https://pubmed.ncbi.nlm.nih.gov/34224766/>

**Title:** LATE PHASE OF COVID-19 PANDEMIC IN GENERAL CARDIOLOGY. A POSITION PAPER OF THE ESC COUNCIL FOR CARDIOLOGY PRACTICE

**Source**: International Journal of Cardiology; 3rd Jul 2021

**Source:** ESC Heart Failure; Jun 2021

Cardiovascular (CV) engagement in coronavirus disease 2019 (COVID-19) is a huge determinant of prognosis during the acute phase of the disease. However, little is known about the potential chronic implications of the late phase of COVID-19 and about the appropriate approach to these patients. Heart failure, type 1 and type 2 myocardial infarction, arrhythmias, myocarditis, pulmonary fibrosis, and thrombosis have been shown to be related to severe acute respiratory syndrome coronavirus 2 infection, and a 'long COVID-19' illness has been recognized with fatigue, chest pain, and dyspnoea among the most frequent symptoms reported after discharge from hospital. This paper focuses on some open questions that cardiologists are going to face during the next months in a general cardiology outpatient clinic, in particular how to evaluate a 'post-COVID' patient during follow-up of CV complications of the acute phase and how to manage new CV symptoms that could be the consequence, at least in part, of heart/vessels and/or lung involvement of the previous virus infection. Present symptoms and signs, history of previous CV disease (both preceding COVID-19 and occurring during viral infection), and specific laboratory and imaging measurements during the acute phase may be of interest in focusing on how to approach the clinical evaluation of a post-COVID patient and how to integrate in our standard of care the new information on COVID-19, possibly in a multidisciplinary view. Dealing with the increased COVID-associated CV risk burden and becoming acquainted with potential new e-cardiology approaches aimed at integrating the cardiology practice are relevant new challenges brought by severe acute respiratory syndrome coronavirus 2 infection and its sequelae.
<https://onlinelibrary.wiley.com/doi/full/10.1002/ehf2.13466>

**Title:** CARDIOVASCULAR INVOLVEMENT IN COVID-19: WHAT SEQUELAE SHOULD WE EXPECT?

**Source**: Cardiology and Therapy; Jun 2021

Several forms of cardiovascular involvement have been described in patients with Coronavirus disease 19 (COVID-19): myocardial injury, acute coronary syndrome, acute heart failure, myocarditis, pericardial diseases, arrhythmias, takotsubo syndrome, and arterial and venous atherothrombotic and thromboembolic events. Data on long-term outcome of these patients are still sparse, and the type and real incidence of cardiovascular sequelae are poorly known. It is plausible that myocardial injury may be the initiator of an inflammatory cascade, edema, and subsequent fibrosis, but also a consequence of systemic inflammation. The extent and distribution of ongoing inflammation may be the basis for ventricular dysfunction and malignant arrhythmias. Indeed, preliminary observational findings seem to emphasize the importance of close monitoring of COVID-19 patients with myocardial injury after discharge. Residual subclinical disease may be effectively investigated by using second-level imaging modalities such as cardiac magnetic resonance, which allows better characterization of the type and extension of myocardial damage, as well as of the ongoing inflammation after the acute phase. In patients with venous thromboembolism, a very common complication of COVID-19, the type and the duration of anticoagulation therapy after the acute phase should be tailored to the patient and based on the estimation of the individual thromboembolic and hemorrhagic risk. Large randomized clinical trials are ongoing to address this clinical question. Whether the severity of cardiovascular involvement, the type of treatments adopted during the acute phase, and the hemodynamic response, may influence the long-term outcome of patients recovered from COVID-19 is unknown. An etiological diagnosis of myocardial injury during the hospitalization is the first step for an appropriate follow-up in these patients. After discharge, the screening for residual left and right ventricular dysfunction, arrhythmias, residual thrombosis, and myocardial scar should be considered on a case-by-case basis, whereas an active clinical surveillance is mandatory in any patient.

<https://pubmed.ncbi.nlm.nih.gov/34191268/>

**Title:** CORONAVIRUS DISEASE 2019 AND CARDIOVASCULAR COMPLICATIONS: FOCUSED CLINICAL REVIEW

**Source**: Journal of Hypertension; Jul 2021; vol. 39 (no. 7); p. 1282-1292

**T**he coronavirus disease 2019 (COVID-19) may cause not only an acute respiratory distress syndrome (ARDS) but also multiple organ damage and failure requiring intensive care and leading to death. Male sex, advanced age, chronic lung disease, chronic kidney disease and cardiovascular disease, such as hypertension, diabetes and obesity have been identified as risk factors for the COVID-19 severity. Presumably, as these three cardiovascular risk factors are associated with a high prevalence of multiorgan damage. In the present focused clinical review, we will discuss the cardiovascular complications of COVID-19 including acute cardiovascular syndrome (acute cardiac injury/COVID cardiomyopathy, thromboembolic complications and arrhythmias) and post-COVID-19 sequelae. Preliminary data shows that the cause of acute cardiovascular syndrome may be multifactorial and involve direct viral invasion of the heart and vascular system, as well as through the immune and inflammation-mediated systemic cytokine storm. COVID-19 survivors may also show persistently elevated blood pressure and sinus tachycardia at rest. Furthermore, poor diabetic control, persistent renal damage and cerebral sequelae, such as persistent cognitive and neuropsychiatric alterations are also frequently reported. A particular attention should be paid towards cardiovascular protection in COVID-19 patients who develop acute cardiovascular syndromes during hospitalization, and/or permanent/semipermanent sequelae after recovery from COVID-19. These conditions may require careful clinical assessment, treatment and close follow-up to avoid short-term and long-term complications.
<https://pubmed.ncbi.nlm.nih.gov/33687179/>

**Title:** RISK STRATIFICATION OF CARDIAC SEQUELAE DETECTED USING CARDIAC MAGNETIC RESONANCE IN LATE CONVALESCENCE AT THE SIX-MONTH FOLLOW-UP OF RECOVERED COVID-19 PATIENTS

Source: The Journal of Infection; Jul 2021; vol. 83 (no. 1); p. 119-145

…Whether COVID-19 has a continuous influence on the cardiovascular system in late convalescence is unknown. Therefore, we used traditional CMR sequences to evaluate cardiac abnormalities in late convalescence comprehensively, including cardiac function, myocardial deformation, and myocardial tissue characteristics, and explore its related risk factors. … In this recovered COVID-19 cohort, we screened for cardiac sequela in the late convalescence using CMR. We found that cardiac involvement, including RV systolic dysfunction, segmental LV deformation decrease, myocardial edema and fibrosis were not uncommon even after six months of recovery. Findings in our study was consistent with and a supplement to previous researches in early convalescence.Abnormal findings in COVID-19 survivors after 110 days and 6 months imply continuous inflammation, which may be the reason for the lasting cardiac involvement in our patients.[1](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8054525/#bib0001) , [2](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8054525/#bib0002) What's more, our study also identified that elevated LDH, the presence of echocardiographic abnormalities, the presence of cardiac abnormalities at admission, and the severity of COVID-19 were risk factors for cardiac sequelae in COVID-19 survivors in the late convalescent stage. This was consistent with previous study that focused on risk stratification of cardiac involvement in COVID-19 patients during hospitalization.[10](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8054525/#bib0010) This implies that physicians should pay more attention to these high risk patients during follow-up, and CMR could be performed to screen out cardiovascular involvement in late convalescence.
<https://pubmed.ncbi.nlm.nih.gov/33887285/>

**NEUROLOGY & MENTAL HEALTH**

**Title:** A SYSTEMATIC REVIEW OF NEUROPSYCHOLOGICAL AND PSYCHIATRIC SEQUALAE OF COVID-19: IMPLICATIONS FOR TREATMENT

Source: Current Opinion in Psychiatry, 1st July 21

Purpose of review: COVID-19 impacts multiple organ systems and is associated with high rates of morbidity and mortality. Pathogenesis of viral infection, co-morbidities, medical treatments, and psychosocial factors may contribute to COVID-19 related neuropsychological and psychiatric sequelae. This systematic review aims to synthesize available literature on psychiatric and cognitive characteristics of community-dwelling survivors of COVID-19 infection.

Recent findings: Thirty-three studies met inclusion/exclusion criteria for review. Emerging findings link COVID-19 to cognitive deficits, particularly attention, executive function, and memory. Psychiatric symptoms occur at high rates in COVID-19 survivors, including anxiety, depression, fatigue, sleep disruption, and to a lesser extent posttraumatic stress. Symptoms appear to endure, and severity of acute illness is not directly predictive of severity of cognitive or mental health issues. The course of cognitive and psychiatric sequelae is limited by lack of longitudinal data at this time. Although heterogeneity of study design and sociocultural differences limit definitive conclusions, emerging risk factors for psychiatric symptoms include female sex, perceived stigma related to COVID-19, infection of a family member, social isolation, and prior psychiatry history.

Summary: The extant literature elucidates treatment targets for cognitive and psychosocial interventions. Research using longitudinal, prospective study designs is needed to characterize cognitive and psychiatric functioning of COVID-19 survivors over the course of illness and across illness severity. Emphasis on delineating the unique contributions of premorbid functioning, viral infection, co-morbidities, treatments, and psychosocial factors to cognitive and psychiatric sequelae of COVID-19 is warranted.
<https://pubmed.ncbi.nlm.nih.gov/34016818/>

**Title:** COGNITIVE DEFICITS IN PEOPLE WHO HAVE RECOVERED FROM COVID-19

Source: Lancet eClinical Medicine, 22 July 2021

There is growing concern about possible cognitive consequences of COVID-19, with reports of ‘Long COVID’ symptoms persisting into the chronic phase and case studies revealing neurological problems in severely affected patients. However, there is little information regarding the nature and broader prevalence of cognitive problems post-infection or across the full spread of disease severity. Methods. We sought to confirm whether there was an association between cross-sectional cognitive performance data from 81,337 participants who between January and December 2020 undertook a clinically validated web-optimized assessment as part of the Great British Intelligence Test, and questionnaire items capturing self-report of suspected and confirmed COVID-19 infection and respiratory symptoms. Findings. People who had recovered from COVID-19, including those no longer reporting symptoms, exhibited significant cognitive deficits versus controls when controlling for age, gender, education level, income, racial-ethnic group, pre-existing medical disorders, tiredness, depression and anxiety. The deficits were of substantial effect size for people who had been hospitalised (N = 192), but also for non-hospitalised cases who had biological confirmation of COVID-19 infection (N = 326). Analysing markers of premorbid intelligence did not support these differences being present prior to infection. Finer grained analysis of performance across sub-tests supported the hypothesis that COVID-19 has a multi-domain impact on human cognition. Interpretation. These results accord with reports of ‘Long Covid’ cognitive symptoms that persist into the early-chronic phase. They should act as a clarion call for further research with longitudinal and neuroimaging cohorts to plot recovery trajectories and identify the biological basis of cognitive deficits in SARS-COV-2 survivors.
[https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00324-2/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370%2821%2900324-2/fulltext)

**Title:** SELF-REPORTED MEMORY PROBLEMS 8 MONTHS AFTER COVID-19 INFECTION

Source: JAMA, 29th July 2021

This cohort study was approved by the Regional Research Ethics Committee according to the Declaration of Helsinki. Eligible participants provided informed consent by signing an online electronic consent form and completing an online baseline questionnaire and follow-up questionnaires. This study used the Strengthening the Reporting of Observational Studies in Epidemiology ([STROBE](http://www.equator-network.org/reporting-guidelines/strobe/)) reporting guideline. … We examined the prevalence of self-reported memory problems in a large group of COVID-19 patients who were not hospitalized and had a relatively mild disease. Eight months after the positive SARS-CoV-2 test, the prevalence of memory problems in this group was higher than in the control group with a negative test or in the untested control population.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2782531>

**Title:** PSYCHOLOGICAL BURDEN IN PATIENTS WITH COVID-19 AND THEIR RELATIVES 90 DAYS AFTER HOSPITALIZATION: A PROSPECTIVE OBSERVATIONAL COHORT STUDY

Source: Journal of Psychosomatic Research, August 21

One fifth of each patients and relatives showed psychological distress after 90 days. Illness-related, psychosocial, and hospital-related factors were associated with outcomes. Several associated factors may be modifiable and could enhance mental health.
<https://www.sciencedirect.com/science/article/pii/S0022399921001719>

**Title:** A PROSPECTIVE STUDY OF LONG-TERM OUTCOMES AMONG HOSPITALIZED COVID-19 PATIENTS WITH AND WITHOUT NEUROLOGICAL COMPLICATIONS

Source: Journal of the Neurological Sciences, 15th July 21

Background: Little is known regarding long-term outcomes of patients hospitalized with COVID-19. Methods: We conducted a prospective study of 6-month outcomes of hospitalized COVID-19 patients. Patients with new neurological complications during hospitalization who survived were propensity score-matched to COVID-19 survivors without neurological complications hospitalized during the same period. The primary 6-month outcome was multivariable ordinal analysis of the modified Rankin Scale(mRS) comparing patients with or without neurological complications. Secondary outcomes included: activities of daily living (ADLs;Barthel Index), telephone Montreal Cognitive Assessment and Neuro-QoL batteries for anxiety, depression, fatigue and sleep.

Results: Of 606 COVID-19 patients with neurological complications, 395 survived hospitalization and were matched to 395 controls; N = 196 neurological patients and N = 186 controls completed follow-up. Overall, 346/382 (91%) patients had at least one abnormal outcome: 56% had limited ADLs, 50% impaired cognition, 47% could not return to work and 62% scored worse than average on ≥1 Neuro-QoL scale (worse anxiety 46%, sleep 38%, fatigue 36%, and depression 25%). In multivariable analysis, patients with neurological complications had worse 6-month mRS (median 4 vs. 3 among controls, adjusted OR 1.98, 95%CI 1.23-3.48, P = 0.02), worse ADLs (aOR 0.38, 95%CI 0.29-0.74, P = 0.01) and were less likely to return to work than controls (41% versus 64%, P = 0.04). Cognitive and Neuro-QOL metrics were similar between groups. Conclusions: Abnormalities in functional outcomes, ADLs, anxiety, depression and sleep occurred in over 90% of patients 6-months after hospitalization for COVID-19. In multivariable analysis, patients with neurological complications during index hospitalization had significantly worse 6-month functional outcomes than those without.
<https://pubmed.ncbi.nlm.nih.gov/34000678/>

**Title:** EMERGING COVID-19 NEUROLOGICAL MANIFESTATIONS: PRESENT OUTLOOK AND POTENTIAL NEUROLOGICAL CHALLENGES IN COVID-19 PANDEMIC

Source: Molecular Neurobiology; Jun 2021

The unremitting coronavirus disease 2019 (COVID-19) pandemic caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) marked a year-long phase of public health adversaries and has severely compromised healthcare globally. Early evidence of COVID-19 noted its impact on the pulmonary and cardiovascular functions, while multiple studies in recent time shed light on its substantial neurological complications, though a comprehensive understanding of the cause(s), the mechanism(s), and their neuropathological outcomes is scarce. In the present review, we conferred evidence of neurological complications in COVID-19 patients and shed light on the SARS-CoV-2 infection routes including the hematogenous, direct/neuronal, lymphatic tissue or cerebrospinal fluid, or infiltration through infected immune cells, while the underlying mechanism of SARS-CoV-2 invasion to the central nervous system (CNS) was also discussed. In an up-to-date manner, we further reviewed the impact of COVID-19 in developing diverse neurologic manifestations associated with CNS, peripheral nervous system (PNS), skeletal muscle, and also pre-existing neurological diseases, including Alzheimer's disease, Parkinson's disease, multiple sclerosis, epilepsy, and myasthenia gravis. Furthermore, we discussed the involvement of key factors including age, sex, comorbidity, and disease severity in exacerbating the neurologic manifestations in COVID-19 patients. An outlook of present therapeutic strategies and state of existing challenges in COVID-19 management was also accessed. Conclusively, the present report provides a comprehensive review of COVID-19-related neurological complications and emphasizes the need for their early clinical management in the ongoing COVID-19 pandemic.
<https://pubmed.ncbi.nlm.nih.gov/34169443/>

**Title:** BRAIN IMAGING BEFORE AND AFTER COVID-19 IN UK BIOBANK

Source: MedRXiv Preprint Server, 15th June 21

[**This article is a preprint and has not been peer-reviewed. It reports new medical research that has yet to be evaluated and so should not be used to guide clinical practice.**](https://www.medrxiv.org/content/what-unrefereed-preprint)

There is strong evidence for brain-related pathologies in COVID-19, some of which could be a consequence of viral neurotropism. The vast majority of brain imaging studies so far have focused on qualitative, gross pathology of moderate to severe cases, often carried out on hospitalised patients. It remains unknown however whether the impact of COVID-19 can be detected in milder cases, in a quantitative and automated manner, and whether this can reveal a possible mechanism for the spread of the disease. UK Biobank scanned over 40,000 participants before the start of the COVID-19 pandemic, making it possible to invite back in 2021 hundreds of previously-imaged participants for a second imaging visit. Here, we studied the effects of the disease in the brain using multimodal data from 782 participants from the UK Biobank COVID-19 re-imaging study, with 394 participants having tested positive for SARS-CoV-2 infection between their two scans. We used structural and functional brain scans from before and after infection, to compare longitudinal brain changes between these 394 COVID-19 patients and 388 controls who were matched for age, sex, ethnicity and interval between scans. We identified significant effects of COVID-19 in the brain with a loss of grey matter in the left parahippocampal gyrus, the left lateral orbitofrontal cortex and the left insula. When looking over the entire cortical surface, these results extended to the anterior cingulate cortex, supramarginal gyrus and temporal pole. We further compared COVID-19 patients who had been hospitalised (n=15) with those who had not (n=379), and while results were not significant, we found comparatively similar findings to the COVID-19 vs control group comparison, with, in addition, a greater loss of grey matter in the cingulate cortex, central nucleus of the amygdala and hippocampal cornu ammonis (all |Z|>3). Our findings thus consistently relate to loss of grey matter in limbic cortical areas directly linked to the primary olfactory and gustatory system. Unlike in post hoc disease studies, the availability of pre-infection imaging data helps avoid the danger of pre-existing risk factors or clinical conditions being mis-interpreted as disease effects. Since a possible entry point of the virus to the central nervous system might be via the olfactory mucosa and the olfactory bulb, these brain imaging results might be the in vivo hallmark of the spread of the disease (or the virus itself) via olfactory and gustatory pathways.
<https://www.medrxiv.org/content/10.1101/2021.06.11.21258690v1>

**Title:** FOCAL SEIZURES WITH IMPAIRED AWARENESS AS LONG-TERM NEUROLOGICAL COMPLICATION OF COVID-19: A CASE REPORT

Source: Neurological Sciences: official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology; Jul 2021

Abstract We report here the first case of a young individual otherwise healthy, who presented with frequent focal seizures with impaired awareness as a possible long-term complication of severe acute respiratory syndrome coronavirus-2 infection. Seizures were documented by electroencephalography and responded clinically and neuro-physiologically to antiseizure therapy. The patient underwent an extensive investigation including cerebrospinal fluid examination, conventional and quantitative brain magnetic resonance imaging, and 18-FDG positron emission tomography. Beyond the clinical interest, this case contributes to clarify the possible pathways by which SARS-CoV-2 may enter the central nervous system and cause long-term neurological complications.
<https://pubmed.ncbi.nlm.nih.gov/33864172/>

**Title:** PERSISTENT COGNITIVE IMPAIRMENT ASSOCIATED WITH CEREBROSPINAL FLUID ANTI-SARS-COV-2 ANTIBODIES SIX MONTHS AFTER MILD COVID-19

Source: Neurological Research and Practice; Jun 2021; vol. 3 (no. 1); p. 34

**Abstract:** Neurological long-term sequelae are increasingly considered an important challenge in the recent COVID-19 pandemic. However, most evidence for neurological symptoms after SARS-CoV-2 infection and central nervous system invasion of the virus stems from individuals severely affected in the acute phase of the disease. Here, we report long-lasting cognitive impairment along with persistent cerebrospinal fluid anti-SARS-CoV-2 antibodies in a female patient with unremarkable standard examination 6 months after mild COVID-19, supporting the implementation of neuropsychological testing and specific cerebrospinal fluid investigation also in patients with a relatively mild acute disease phase.
<https://neurolrespract.biomedcentral.com/articles/10.1186/s42466-021-00135-y>

**Title:** NEUROLOGICAL INVOLVEMENT OF COVID-19: FROM NEUROINVASION AND NEUROIMMUNE CROSSTALK TO LONG-TERM CONSEQUENCES

Source: Reviews in the Neurosciences; Jun 2021; vol. 32 (no. 4); p. 427-442

**Abstract:** As the coronavirus disease 2019 (COVID-19) pandemic continues to be a multidimensional threat to humanity, more evidence of neurological involvement associated with it has emerged. Neuroimmune interaction may prove to be important not only in the pathogenesis of neurological manifestations but also to prevent systemic hyperinflammation. In this review, we summarize reports of COVID-19 cases with neurological involvement, followed by discussion of possible routes of entry, immune responses against coronavirus infection in the central nervous system and mechanisms of nerve degeneration due to viral infection and immune responses. Possible mechanisms for neuroprotection and virus-associated neurological consequences are also discussed.
<https://pubmed.ncbi.nlm.nih.gov/33550780/>

**Title:** THE NEUROLOGICAL MANIFESTATIONS OF POST-ACUTE SEQUELAE OF SARS-COV-2 INFECTION

Source: Current Neurology and Neuroscience Reports; 28th Jun 2021; vol. 21 (no. 9); p. 44

**Abstract:** PURPOSE OF REVIEW Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a global health challenge. This review aims to summarize the incidence, risk factors, possible pathophysiology, and proposed management of neurological manifestations of post-acute sequelae of SARS-CoV-2 infection (PASC) or neuro-PASC based on the published literature. RECENT FINDINGS The National Institutes of Health has noted that PASC is a multi-organ disorder ranging from mild symptoms to an incapacitating state that can last for weeks or longer following recovery from initial infection with SARS-CoV-2. Various pathophysiological mechanisms have been proposed as the culprit for the development of PASC. These include, but are not limited to, direct or indirect invasion of the virus into the brain, immune dysregulation, hormonal disturbances, elevated cytokine levels due to immune reaction leading to chronic inflammation, direct tissue damage to other organs, and persistent low-grade infection. A multidisciplinary approach for the treatment of neuro-PASC will be required to diagnose and address these symptoms. Tailored rehabilitation and novel cognitive therapy protocols are as important as pharmacological treatments to treat neuro-PASC effectively. With recognizing the growing numbers of COVID-19 patients suffering from neuro-PASC, there is an urgent need to identify affected individuals early to provide the most appropriate and efficient treatments. Awareness among the general population and health care professionals about PASC is rising, and more efforts are needed to understand and treat this new emerging challenge. In this review, we summarize the relevant scientific literature about neuro-PASC.
<https://pubmed.ncbi.nlm.nih.gov/34181102/>

**RHEUMATOLOGY**

**Title:** POSTDISCHARGE RHEUMATIC AND MUSCULOSKELETAL SYMPTOMS FOLLOWING HOSPITALIZATION FOR COVID-19: PROSPECTIVE FOLLOW-UP BY PHONE INTERVIEWS

Source: Rheumatology International; Jul 2021; vol. 41 (no. 7); p. 1263-1271

Abstract To describe the rheumatic and musculoskeletal symptoms at hospitalization as well as their persistence/ severity after discharge with coronavirus disease 2019 (COVID-19) and to identify whether age, sex, body mass index (BMI), and length of hospital stay are associated with persistence of these symptoms. In this single-center cohort study, comprising 300 participants, two phone interviews were conducted (2-week and 1-month after hospitalization) and symptoms were queried with a standardized form. This form included musculoskeletal symptoms and other COVID-19 symptoms. Considering all symptoms (musculoskeletal and other), 100.0%, 86.7%, and 72.0% of patients reported one or more symptoms, at hospitalization, 2-week, and 1-month, respectively. Considering only musculoskeletal symptoms, 92.3%, 72.7%, and 56.3% of patients reported any musculoskeletal symptom at hospitalization, 2-week, and 1-month, respectively. The musculoskeletal symptoms were fatigue (44.3% of patients reported), back pain (22.7%), arthralgia (22.0%), myalgia (21.0%), low back pain (16.3%), and neck pain (10.3%); the other symptoms were shortness of breath (26.3%), loss of taste (15.0%), cough (14.0%), loss of smell (12.3%), loss of appetite (10.3%), headache (8.7%), sore throat (3.0%), diarrhea (1.3%), dizziness (1.3%), and fever (0.3%) at 1-month. Increasing BMI was associated with higher odds of persistence of fatigue (OR: 1.08, 1.03 to 1.13), myalgia (OR: 1.08, 1.01 to 1.14), and arthralgia (OR: 1.07, 1.02 to 1.14, p = 0.012) at 1-month. Nearly three-quarters reported one or more symptoms, with more than half of patients reported any musculoskeletal symptom at 1 month. The most common musculoskeletal symptom was fatigue, followed by back pain, arthralgia, myalgia, low back pain, and neck pain. The persistence of fatigue, myalgia, and arthralgia was related to BMI. The study results increase our understanding of the spectrum of COVID-19, which, in turn, may lead to more efficient and better care for COVID-19 survivors.
<https://pubmed.ncbi.nlm.nih.gov/33978818/>

**Title:** COVID-19 AND THE CLINICAL COURSE OF RHEUMATIC MANIFESTATIONS

Source: Rheumatology International; Jul 2021; vol. 41 (no. 7); p. 1263-1271

 **Abstract:** The manifestations of COVID-19 have been evolving over time. Various post-COVID-19 syndromes are being recognised. Various viruses have been implicated in the pathogenesis of autoimmune diseases, and we expect a similar outcome with the severe acute respiratory syndrome-associated coronavirus-2 (SARS-CoV-2). The SARS-CoV-2 virus penetrates various tissues and organs and has a predisposition to lead to endotheliitis that may cause vascular manifestations including thrombosis. SARS-CoV-2 has been shown to activate Toll-like receptors and the complement system. It perpetuates NETosis and leads to autoantibody formation. These predispose to systemic autoimmunity. Both reactive arthritis and connective tissue disorders such as lupus and inflammatory myositis have been reported after COVID-19. Other reported autoimmune disorders include haemolytic anaemia, immune thrombocytopenia, cutaneous vasculitis, and Guillain Barré-like acute demyelinating disorders. The multi-system inflammatory syndrome in children and its adult counterpart are another post-COVID-19 entity that presents as an admixture of Kawasaki disease and staphylococcal toxic shock syndrome. Patients with preexisting rheumatic diseases may flare during the SARS-CoV-2 infection. They may develop novel autoimmune features also. The immune-suppressants used during the acute COVID-19 illness may confound the outcomes whereas comorbidities present in patients with rheumatic diseases may mask them. There is an urgent need to follow-up patients recovering from COVID and monitor autoantibody production in the context of rheumatic manifestations. Key Points • COVID-19 is associated with both innate and acquired immune reactions and production of various autoantibodies. • Various immune-mediated manifestations such as arthritis, myositis, haemolytic anaemia, thrombocytopenia, and acute demyelination may develop after COVID-19. • Longitudinal cohort data are warranted to describe, predict, and test prevent various rheumatic manifestations in post-COVID-19 subjects.
<https://pubmed.ncbi.nlm.nih.gov/33733315/>

**DERMATOLOGY**

**Title:** FOLLOW-UP OF DERMATOLOGICAL MANIFESTATIONS IN NON-CRITICAL HOSPITALIZED PATIENTS WITH COVID-19 PNEUMONIA AND THEIR PROGNOSTIC CORRELATION WITH DISEASE SEVERITY

Source: Journal of the European Academy of Dermatology and Venereology: JEADV; Jul 2021; vol. 35 (no. 7); p. e421

…In our centre, we performed a case-control study involving 97 hospitalized patients in non-critical care areas. We did a complete dermatological physical examination and measured biochemical inflammatory markers to all patients with a positive molecular test for SARS-CoV-2. Afterwards, we analysed our variables to correlate cutaneous manifestations with PaO2/FiO2 (P/F) ratio and biochemical inflammatory markers to determine prognosis and disease severity of COVID-19 infection.
<https://onlinelibrary.wiley.com/doi/10.1111/jdv.17236>

**HAEMATOLOGY**

**Title:** COVID-19-ASSOCIATED COAGULOPATHY AND ANTITHROMBOTIC AGENTS-LESSONS AFTER 1 YEAR

Source: The Lancet. Haematology; Jul 2021; vol. 8 (no. 7); p. e524

 **Abstract:** COVID-19 is associated with a high incidence of thrombotic complications, which can be explained by the complex and unique interplay between coronaviruses and endothelial cells, the local and systemic inflammatory response, and the coagulation system. Empirically, an intensified dose of thrombosis prophylaxis is being used in patients admitted to hospital with COVID-19 and several guidelines on this topic have been published, although the insufficiency of high quality and direct evidence has led to weak recommendations. In this Viewpoint we summarise the pathophysiology of COVID-19 coagulopathy in the context of patients who are ambulant, admitted to hospital, and critically ill or non-critically ill, and those post-discharge from hospital. We also review data from randomised controlled trials in the past year of antithrombotic therapy in patients who are critically ill. These data provide the first high-quality evidence on optimal use of antithrombotic therapy in patients with COVID-19. Pharmacological thromboprophylaxis is not routinely recommended for patients who are ambulant and post-discharge. A first ever trial in non-critically ill patients who were admitted to hospital has shown that a therapeutic dose of low-molecular-weight heparin might improve clinical outcomes in this population. In critically ill patients, this same treatment does not improve outcomes and prophylactic dose anticoagulant thromboprophylaxis is recommended. In the upcoming months we expect numerous data from the ongoing antithrombotic COVID-19 studies to guide clinicians at different stages of the disease.
[https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(21)00105-8/fulltext](https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026%2821%2900105-8/fulltext)

**Title:** CRITICAL ISCHAEMIA OF THE HAND AND UPPER LIMB IN A PATIENT WITH LONG COVID-19 INFECTION

Source: The Journal of Hand Surgery, European volume; Jul 2021; vol. 46 (no. 6); p. 684-686

We report the case of a 31-year-old, right-hand dominant female, who presented with critical ischaemia of the dominant hand following iatrogenic injury to the ulna artery at the wrist, during attempted venepuncture to monitor renal function (after a recent kidney infection). Past medical history included a clinical history of COVID-19 infection 5 months previously and occasional chronic pyelonephritis over 8 years. The patient was taking the combined oral contraceptive pill and her body mass index (BMI) was 25.7 … Five months prior to presentation, the patient had contracted COVID-19 infection. Although patients were not being routinely tested at this stage, she developed symptoms of ageusia, fever, cough, shortness of breath and fatigue persisting for a period of 5 weeks and requiring overnight hospital admission for low oxygen saturations. The haematology opinion is that previous COVID-19 infection and the longstanding effects of COVID-19 was likely a significant causative factor in the highly unusual hypercoagulable state, with predisposition to arterial thrombotic sequence that would not have normally arisen from a needle puncture.
<https://journals.sagepub.com/doi/full/10.1177/17531934211014358>

**ENT**

**Title:** INTERVENTIONS FOR THE TREATMENT OF PERSISTENT POST‐COVID‐19 OLFACTORY DYSFUNCTION

**Source:** Cochrane Systematic Review, 22 July 2021

Objectives: To assess the effects (benefits and harms) of interventions that have been used, or proposed, to treat persisting olfactory dysfunction due to COVID‐19 infection. A secondary objective is to keep the evidence up‐to‐date, using a living systematic review approach. … Authors' conclusions: There is very limited evidence available on the efficacy and harms of treatments for persistent olfactory dysfunction following COVID‐19 infection. However, we have identified other ongoing trials in this area. As this is a living systematic review we will update the data regularly, as new results become available. For this (first) version of the living review we identified only one study with a small sample size, which assessed systemic steroids and nasal irrigation (intranasal steroid/mucolytic/decongestant). However, the evidence regarding the benefits and harms from this intervention to treat persistent post‐COVID‐19 olfactory dysfunction is very uncertain.
<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013876.pub2/full>

**Title:** COMPARISON OF SELF-REPORTED SYMPTOMS AND PSYCHOPHYSICAL TESTS IN CORONAVIRUS DISEASE 2019 (COVID-19) SUBJECTS EXPERIENCING LONG-TERM OLFACTORY DYSFUNCTION: A 6-MONTH FOLLOW-UP STUDY

**Source:** International Forum of Allergy & Rhinology, 20th June 2021

Since the novel severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) emerged in Wuhan, China, coronavirus disease 2019 (COVID-19) has rapidly spread worldwide leading to the current pandemic. Olfactory and taste dysfunction (OD, TD) have been included among the most frequent reported symptoms, with a prevalence reported to be 47.85%. Studies published on COVID-19–related OD have mainly assessed smell loss using patient-reported outcome measures (PROMs) such as the visual analogue scale (VAS) and the 22-item Sino-Nasal Outcome Test (SNOT-22). However, self-reported OD poorly correlates with olfactory tests such as Sniffin’ Sticks (S'S). The aim of this study is to provide a prospective long-term assessment of COVID-19–related OD using PROMs and S'S and to investigate their correlation. … In conclusion, when assessing olfactory performance in patients with COVID-19–related OD we discourage the sole use of PROMs and recommend the use of psychophysical tests with additional subtest analysis. We also showed that in COVID-19–related OD, threshold is the most affected S'S subtest, suggesting an end-organ failure pathogenesis.
<https://onlinelibrary.wiley.com/doi/full/10.1002/alr.22828>

**Title:** EIGHT-MONTH FOLLOW-UP OF OLFACTORY AND GUSTATORY DYSFUNCTIONS IN RECOVERED COVID-19 PATIENTS

**Source:** American Journal of Otolaryngology; 2021; vol. 42 (no. 4); p. 103065

**Abstract:** PURPOSE To investigate the recovery of loss of smell and taste among recovered COVID-19 patients. MATERIALS AND METHODS This cross-sectional follow-up study is a sequel to a study by Biadsee et al. Among the previous study population of 128 non-hospitalized patients, positive for COVID-19 by reverse transcription-polymerase chain reaction (RT-PCR), 97 patients participated in a survey designed for this study. Information and data regarding loss of smell and taste, rate of recovery, xerostomia, and additional symptoms; (Cough, Myalgia, Weakness, Rhinorrhea, Nasal congestion) were collected. RESULTS A total of 43 men and 54 women were included. Mean age was 37.5 years (range 19-74). Mean follow-up was 229 days (range 191-253). Sixty-five patients reported gustatory dysfunction during the disease of which 61.5% reported full recovery, 38.5% partial recovery. Of 65 patients who reported olfactory impairment during the disease, 52% had full recovery and 48% reported partial recovery of olfactory function. Complete recovery of olfactory function was positively associated with full recovery of gustatory function (p = 0.01). Gender did not significantly affect the recovery of OD and GD (p = 0.45, p = 0.90, respectively). Patients who experienced olfactory dysfunction as an initial symptom had lower rates of olfactory complete recovery (p = 0.043).CONCLUSION After a mean follow-up of 229 days, complete recovery of smell and taste functions occurred in 52% and 61.5%, respectively. However, dysfunction persisted in 48%-38.5% of patients.
<https://pubmed.ncbi.nlm.nih.gov/33894627/>

**Title:** OROPHARYNGEAL DYSPHAGIA AFTER HOSPITALIZATION FOR COVID-19 DISEASE: OUR SCREENING RESULTS

**Source:** Dysphagia  24th June 2021

As the pathophysiology of COVID-19 emerges, the aim of our study was to describe the prevalence of oropharyngeal dysphagia after COVID-19 disease. From March to July 2020 we enrolled patients recovered from SARS-CoV-2 infection who had been previously hospitalized for the disease. They were screened for dysphagia by mean of the Eating Assessment Tool-10 (EAT-10). The cases with EAT-10 score > 3 were graded for the aspiration risk by applying the Gugging Swallowing Screen (GUSS) and were submitted to the Swal-QoL questionnaire. The cases with a GUSS score > 19 were subjected to FEES. 8/117 (7%) patients had positive screening result. 4/8 (50%) revealed an abnormal health related quality of life in oropharyngeal dysphagia with a mean Swal-QoL score of 69.73. The most affected domain was the “time of meals” (mean score 65) following by the “sleep” (mean score 66) and “eating desire” (mean score 72). 1/8 cases showed increased risk for aspiration and did not showed endoscopic signs of oropharyngeal dysphagia. Our results showed that the prevalence of upper dysphagia after hospitalization for SARS-CoV-2 is not anecdotal and that probably this long-lasting sequela has a psychogenic etiology.
<https://link.springer.com/article/10.1007/s00455-021-10325-0>

**Title:** QUANTITATIVE EVALUATION AND PROGRESS OF OLFACTORY DYSFUNCTION IN COVID-19

**Source:** Eur Arch Otorhinolaryngol, 2021 Jul;278(7):2363-2369

**Abstract:** PURPOSE Since many different rates have been reported in the literature and the studies conducted are mostly based on the patient anamnesis, it was aimed to analyze the olfactory dysfunction in Coronavirus Disease 2019 (COVID-19) quantitatively and to reveal its progress by time. METHODS Patients who described new-onset olfactory dysfunction, who were treated in the COVID-19 departments of our hospital and whose PCR tests demonstrated SARS-CoV-2 presence were included in the study and they were investigated prospectively. Clinical information of all the patients was taken and the levels of olfactory function were detected using the Brief Smell Identification Test (BSIT). Scores equal to or below 8 are considered as olfactory dysfunction. Patients who were followed up for 3 months were re-evaluated with the BSIT test at the end of the third month and the progression of the symptom was investigated. RESULTS The mean BSIT test score of the 42 patients (23 female patients, 19 male patients, mean age: 41.2 ± 14.6) was 5.2 ± 2.2. There was severe olfactory dysfunction in 16.7% of the patients (0-2 points), moderate olfactory dysfunction in 31% (3-5 points), and mild olfactory dysfunction in 52.4% (6-8 points). After a follow-up for 3 months, full recovery was observed in 36 patients (85.7%) and the mean test score rose to 9.9 ± 1.8. Although olfactory dysfunction persisted in 6 patients, an elevation in test scores was noted. Olfactory dysfunction was the first symptom in 17 patients (40%) and the other symptoms occurred after 2 days (1-6) on average. CONCLUSION We investigated olfactory dysfunction caused by COVID-19 using BSIT, and found a high rate of moderate-mild level symptoms with a high level of recovery in the 3-month follow-up. The finding revealing that olfactory dysfunction was the first symptom in 40% of the patients suggests the importance of inquiry on olfactory functions for the early diagnosis of the disease.
<https://pubmed.ncbi.nlm.nih.gov/33385250/>

**ENDOCRINOLOGY**

**Title:** MALE PITUITARY-GONADAL AXIS DYSFUNCTION IN POST-ACUTE COVID-19 SYNDROME. PREVALENCE AND ASSOCIATED FACTORS: A MEDITERRANEAN CASE SERIES

Source: Clinical Endocrinology, 23rd June 2021

Severe acute respiratory syndrome coronavirus 2 through angiotensin-converting enzyme 2 receptor can harm testes function. The objectives were to analyse the prevalence of low serum testosterone (LT) and impaired fertility potential (Leydig and Sertoli cells dysfunction, respectively) in coronavirus disease 2019 (COVID-19) male survivors and to evaluate acute infection-related associated factors. Also, we explore its association with post-acute COVID-19 syndrome (PCS) and quality of life (QOL). … Prevalence of male LT and impaired fertility potential in COVID-19 survivors is high in the medium term. Traditional risk factors and severity markers for COVID-19 could be predictive.
<https://onlinelibrary.wiley.com/doi/10.1111/cen.14537>

**PAEDIATRICS**

**Title:** LONG-TERM SYMPTOMS AFTER SARS-COV-2 INFECTION IN CHILDREN AND ADOLESCENTS

**Source:** JAMA, 15th July 2021

This study found a low prevalence of symptoms compatible with long COVID in a randomly selected cohort of children assessed 6 months after serologic testing. Although long COVID exists in children, estimates of the prevalence of persisting symptoms based on scarce literature range from 0% to 27%.1 Initial SARS-CoV-2 infection severity, different methodological approaches (clinical assessment vs self-report), definition of cases (diagnosed vs suspected), variable follow-up times, and prevalence of preexisting clinical conditions likely contribute to the variability in prevalence estimates. This study reports the distribution of symptoms compatible with long COVID on a population level; it did not capture severe SARS-CoV-2 infections because they are rare in children. A strength of this study is the population-based seronegative control group. Limitations include the relatively small number of seropositive children, lack of information on the exact time of SARS-CoV-2 infection, possible misclassification of some children with false seropositive results, potential recall bias, parental report of child’s symptoms, lack of information on symptom severity, and noncompletion of the questionnaire. Also, systematic differences existed between children included vs not included in the analysis, possibly affecting the representativeness of the sample.
<https://jamanetwork.com/journals/jama/fullarticle/2782164>

**Title:** ILLNESS DURATION AND SYMPTOM PROFILE IN SYMPTOMATIC UK SCHOOL-AGED CHILDREN TESTED FOR SARS-COV-2

**Source:** The Lancet Child & Adolescent Health, 3rd August 2021

In this prospective cohort study, data from UK school-aged children (age 5–17 years) were reported by an adult proxy. Participants were voluntary, and used a mobile application (app) launched jointly by Zoe Limited and King's College London. Illness duration and symptom prevalence, duration, and burden were analysed for children testing positive for SARS-CoV-2 for whom illness duration could be determined, and were assessed overall and for younger (age 5–11 years) and older (age 12–17 years) groups. Children with longer than 1 week between symptomatic reports on the app were excluded from analysis. Data from symptomatic children testing negative for SARS-CoV-2, matched 1:1 for age, gender, and week of testing, were also assessed. …

Although COVID-19 in children is usually of short duration with low symptom burden, some children with COVID-19 experience prolonged illness duration. Reassuringly, symptom burden in these children did not increase with time, and most recovered by day 56. Some children who tested negative for SARS-CoV-2 also had persistent and burdensome illness. A holistic approach for all children with persistent illness during the pandemic is appropriate.
[https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(21)00198-X/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642%2821%2900198-X/fulltext)

**Title:** HIDE AND SEEK IN A PANDEMIC: REVIEW OF SARS-COV-2 INFECTION AND SEQUELAE IN CHILDREN

**Source:** Experimental Physiology, 9th July 2021

Here we describe the current literature relating to COVID-19 infection in children and the associated inflammatory condition, Paediatric Multi-inflammatory Syndrome Temporally Associated with SARS-CoV-2 (PIMS-TS). What advances does it highlight? Children with SARS-CoV-2 infection have a distinct clinical phenotype when compared to adults. This may relate to relative differences in their adaptive immunity and in the degree and distribution of expression of the SARS-CoV-2 receptor (angiotensin-converting enzyme 2). There are several similarities between PIMS-TS, Kawasaki disease shock syndrome and other known inflammatory disorders such as macrophage activation syndrome. Few data are available to date regarding vaccination responses of children against COVID-19.
<https://pubmed.ncbi.nlm.nih.gov/34242467/>

**Title:** POST-ACUTE SEQUELAE OF SARS-COV-2 INFECTION (PASC): PERIPHERAL, AUTONOMIC, AND CENTRAL NERVOUS SYSTEM FEATURES IN A CHILD

**Source:** Neurological Sciences: official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology; Jul 2021

This paper describes the detailed evaluation and treatment of an adolescent with PASC manifesting progressive post-infectious central, peripheral, and autonomic nervous system (CNS, PNS, and ANS).
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8272686/>

**Title:** CLINICAL FEATURES AND FOLLOW-UP OF PEDIATRIC PATIENTS HOSPITALIZED FOR COVID-19

**Source:** Pediatric Pulmonology; Jul 2021; vol. 56 (no. 7); p. 1967-1975

This report summarizes the clinical features and 1-month follow-up observations for pediatric patients who were hospitalized with coronavirus disease 2019 (COVID-19) in Wuhan Women and Children's Hospital. METHODS The 1-month follow-up data included clinical manifestations and results from serum severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) IgG and IgM tests, reverse-transcription polymerase chain reaction (RT-PCR) for SARS-CoV-2, lung computed tomography (CT) scans, and laboratory tests. RESULTS Between January 20 and March 15, 2020, 127 patients aged 0-15 years were hospitalized for COVID-19 treatment, including 3 severe cases and 124 mild or moderate cases. The main therapies included inhalation of aerosolized interferon-α (122/127) and additional antiviral drugs (28/127). Among the 81 patients who had pneumonia at admission, 35 with right lobe pneumonia had the longest hospital stay (mean 14.5 ± 7 days); 17 with left lobe pneumonia had the highest creatine kinase (154 ± 106 U/L) and creatine kinase myocardial band (CK-MB, 43 ± 48 U/L) levels; and 29 with bilateral pneumonia had the highest white blood cell counts (8.3 ± 4 × 109 /L). Among the 46 patients who were successfully followed up 1 month after discharge, two notable findings were right lobe pneumonia in 22% (95% confidence interval [CI]: 11%-37%) of patients and persistently elevated serum creatine kinase and CK-MB levels. The median duration of elevated CK-MB was 45 days. The mean concentrations of serum SARS-CoV-2 IgG and IgM in 41 patients were 8.0 ± 7.5 and 98 ± 40 ng/ ml, respectively. At follow-up, four patients retested positive for SARS-CoV-2.CONCLUSIONSThe involvement of different lung lobes in patients with COVID-19 was associated with variations in the persistence of pneumonia and elevation of CK-MB levels and body temperature.
<https://pubmed.ncbi.nlm.nih.gov/33852775/>

**Title:** 6-MONTH MULTIDISCIPLINARY FOLLOW-UP AND OUTCOMES OF PATIENTS WITH PAEDIATRIC INFLAMMATORY MULTISYSTEM SYNDROME (PIMS-TS) AT A UK TERTIARY PAEDIATRIC HOSPITAL: A RETROSPECTIVE COHORT STUDY

**Source:** The Lancet. Child & adolescent health; Jul 2021; vol. 5 (no. 7); p. 473-482

Paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) is a new, rare, post-infectious complication of SARS-CoV-2 infection in children. We aimed to describe the 6-month outcomes of PIMS-TS. Methods. This retrospective cohort study comprised children (aged <18 years) who fulfilled the UK Royal College of Paediatrics and Child Health (RCPCH) diagnostic criteria for PIMS-TS and were admitted to Great Ormond Street Hospital (London, UK) between April 4 and Sept 1, 2020. Patients were followed up by a multidisciplinary team of specialists at 6 weeks and 6 months after admission. Biochemical and functional outcomes were analysed. Findings. 46 children were included in this study. The median age at presentation was 10·2 years (IQR 8·8–13·3), 30 (65%) patients were male and 16 (35%) were female, 37 (80%) were from minority ethnic groups, and eight (17%) had pre-existing comorbidities. All patients had elevated markers of systemic inflammation at baseline. None of the patients died. By 6 months, systemic inflammation was resolved in all but one patient. 38 (90%) of 42 patients who had positive SARS-CoV-2 IgG antibodies within 6 weeks of admission remained seropositive at 6 months. Echocardiograms were normal in 44 (96%) of 46 patients by 6 months, and gastrointestinal symptoms that were reported in 45 (98%) of 46 patients at onset were present in six (13%) of 46 patients at 6 months. Renal, haematological, and otolaryngological findings largely resolved by 6 months. Although minor abnormalities were identified on neurological examination in 24 (52%) of 46 patients at 6 weeks and in 18 (39%) of 46 at 6 months, we found minimal functional impairment at 6 months (median Expanded Disability Status Scale score 0 [IQR 0–1]). Median manual muscle test-8 scores improved from 53 (IQR 43–64) during hospital admission to 80 (IQR 68–80) at 6 months, but 18 (45%) of 40 patients showed 6-min walk test results below the third centile for their age or sex at 6 months. PedsQL responses revealed severe emotional difficulties at 6 months (seven [18%] of 38 by parental report and eight [22%] of 38 by self report). 45 (98%) of 46 patients were back in full-time education (virtually or face to face) by 6 months. Interpretation. Despite initial severe illness, few organ-specific sequelae were observed at 6 months. Ongoing concerns requiring physical re-conditioning and mental health support remained, and physiotherapy assessments revealed persisting poor exercise tolerance. Longer-term follow-up will help define the extended natural history of PIMS-TS.
[https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(21)00138-3/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642%2821%2900138-3/fulltext)

**Title:** RISK FACTORS FOR LONG COVID IN PREVIOUSLY HOSPITALISED CHILDREN USING THE ISARIC GLOBAL FOLLOW-UP PROTOCOL: A PROSPECTIVE COHORT STUDY

**Source:** The European Respiratory Journal; Jul 2021

**Abstract:** BACKGROUND The long-term sequelae of coronavirus disease 2019 (Covid-19) in children remain poorly characterised. This study aimed to assess long-term outcomes in children previously hospitalised with Covid-19 and associated risk factors. METHODS This is a prospective cohort study of children (≤18 years old) admitted with confirmed Covid-19. Children admitted to the hospital between April 2, 2020 and August 26, 2020, were included. Telephone interview using the International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) Covid-19 Health and Wellbeing paediatric follow-up survey. Persistent symptoms (>5 months) were further categorised by system(s) involved.FINDINGS518 of 853 (61%) of eligible children were available for the follow-up assessment and included in the study. Median age was 10.4 years (IQR, 3-15.2) and 270 (52.1%) were girls; median follow-up since hospital discharge was 256 (223-271) days. At the time of the follow-up interview 126 (24.3%) participants reported persistent symptoms among which fatigue (53, 10.7%), sleep disturbance (36, 6.9%,) and sensory problems (29, 5.6%) were the most common. Multiple symptoms were experienced by 44 (8.4%) participants. Risk factors for persistent symptoms were: older age "6-11 years" (odds ratio 2.74 (95% confidence interval 1.37 to 5.75) and "12-18 years" (2.68, 1.41 to 5.4); and a history of allergic diseases (1.67, 1.04 to 2.67).INTERPRETATION A quarter of children experienced persistent symptoms months after hospitalization with acute covid-19 infection, with almost one in ten experiencing multi-system involvement. Older age and allergic diseases were associated with higher risk of persistent symptoms at follow-up.
<https://erj.ersjournals.com/content/early/2021/06/10/13993003.01341-2021>

**REHABILITATION**

**Title:** OUTCOMES AMONG PATIENTS REFERRED TO OUTPATIENT REHABILITATION CLINICS AFTER COVID-19 DIAGNOSIS — UNITED STATES, JANUARY 2020–MARCH 2021

**Source**: CDC, 9th July 21

What is already known about this topic? COVID-19 patients might experience symptoms that persist months after initial infection. What is added by this report? Compared with control patients enrolled in a cancer rehabilitation program, adult post–COVID-19 patients referred for rehabilitation services reported poorer physical health and being less able to engage in physical activities and activities of daily living. Patients recovering from COVID-19 also had significantly higher health care use than control patients. What are the implications for public health practice? Patients recovering from COVID-19 might require tailored physical and mental health rehabilitation services. <https://www.cdc.gov/mmwr/volumes/70/wr/mm7027a2.htm?s_cid=mm7027a2_w>

**Title:** CORTICOSTEROIDS AND PULMONARY REHABILITATION REDUCING LONG-TERM MORBIDITY IN A PATIENT WITH POST-COVID-19 PNEUMONITIS: A CASE STUDY.

Source: Physiotherapy Research International: the journal for researchers and clinicians in physical therapy; Jul 2021; vol. 26 (no. 3); p. e1903

Whilst research efforts have focussed on treatment during the acute phase, little work has focussed on the long-term sequelae of COVID-19 infection. This case described a patient who remained symptomatic several weeks after discharge from hospital with what was diagnosed as a COVID-19 infection. There were significant deficits shown in his functional exercise testing, his pulmonary functions testing and there was evidence of fibrotic changes on his radiology. METHODS As part of a multidisciplinary clinic, he was started on steroids and a tailored pulmonary rehabilitation course over a course of 6-8 weeks. Thereafter, his exercise testing, pulmonary function tests and radiology were all repeated to see progress. RESULTS On completing the course of corticosteroids and concurrent personalised pulmonary rehabilitation, there was a dramatic improvement in the patient's symptom severity, radiology and pulmonary function. The most significant improvement noted was in his exercise testing, namely a 6-min walk test and 1 min of sit-to-stands. Before treatment, he had a Medical Research Council (MRC) score of 2, and after it returned to his baseline of 0.DISCUSSIONUsing corticosteroids and exercise training that allowed quantitative evaluation throughout the stages of recovery was a valuable tool to gauge progress and response to treatment. These therapies present opportunity to prevent the development of irreversible pulmonary fibrosis that could prove to be a major breakthrough in reducing long-term morbidity and improving the quality of life of those affected.
<https://pubmed.ncbi.nlm.nih.gov/33713539/>

**Title:** FOLLOW-UP OF FUNCTIONAL EXERCISE CAPACITY IN PATIENTS WITH COVID-19: IT IS IMPROVED BY TELEREHABILITATION

**Source**: Respiratory medicine; Jul 2021; vol. 183; p. 106438

The impact of the COVID-19 pandemic on functional exercise capacity seemed quickly clinically evident. The objective of this study was to assess the functional exercise capacity of patients with severe COVID-19 and to evaluate the effect of a telerehabilitation program in the specific context of the COVID-19 pandemic. METHOD Patients hospitalized for severe or critical COVID-19 were recruited. The functional exercise capacity (1-min sit-to-stand test (STST)) was prospectively quantified at discharge. A telerehabilitation program was then proposed. A control group was composed with the patients refusing the program. RESULTS At discharge, none of the 48 recruited patients had a STST higher than the 50th percentile and 77% of them were below the 2.5th percentile. SpO2 was 92.6 ± 3.0% after STST and 15 patients had oxygen desaturation. After 3-months of follow-up, the number of repetitions during STST significantly increased either in telerehabilitation (n = 14) (p < 0.001) or in control groups (n = 13) (p = 0.002) but only one patient had a result higher than the 50th percentile (in Telerehabilitation group) and 37% of them were still under the 2.5th percentile for this result. The improvement was significantly and clinically greater after the telerehabilitation program (p = 0.005). No adverse events were reported by the patients during the program. CONCLUSIONS Patients hospitalized for COVID-19 have a low functional exercise capacity at discharge and the recovery after three months is poor. The feasibility and the effect of a simple telerehabilitation program were verified, this program being able to substantially improve the functional recovery after three months.
<https://covid19.elsevierpure.com/en/publications/follow-up-of-functional-exercise-capacity-in-patients-with-covid->

**Title:** PROVIDING REHABILITATION TO PATIENTS RECOVERING FROM COVID-19: A SCOPING REVIEW

**Source**: PM&R: the journal of injury, function, and rehabilitation; Jul 2021 Publication Date Jul 2021

To synthesize the nature and extent of research on rehabilitation care provision to COVID-19 (COVID) patients. Specifically, we aimed to: (1) Describe the impact of COVID on patients and associated rehabilitation needs; (2) Outline the adaptations and preparations required to enable the provision of COVID rehabilitation; (3) Describe the types of rehabilitation services and treatments provided to COVID patients; and (4) Identify barriers and facilitators to delivering COVID rehabilitation.
<https://onlinelibrary.wiley.com/doi/abs/10.1002/pmrj.12669>

**Title:** IS TELE-REHABILITATION SUPERIOR TO HOME EXERCISE PROGRAM IN COVID-19 SURVIVORS FOLLOWING DISCHARGE FROM INTENSIVE CARE UNIT? - A STUDY PROTOCOL OF A RANDOMIZED CONTROLLED TRIAL

**Source**: Physiotherapy research international: the journal for researchers and clinicians in physical therapy; Jul 2021; p. e1920

This is a randomized assessor blinded control trial with two groups; tele-rehabilitation and home exercise. One hundred twenty-two COVID-19 survivors following discharge from intensive care unit will be allocated into two groups. The tele-rehabilitation group will receive breathing, aerobic, posture, stretching, strengthening exercises at their home under remote supervision via Internet for 3 days/week for 10 weeks. Home exercise group will receive the same program at their home on their own and they will be called weekly. The patients will be evaluated at the beginning, at the end of the program, 6th and 12th months following the rehabilitation. The primary outcome is the change in 6-minute walking distance; the secondary outcomes are changes in quality of life, physical function, health status, dyspnea and muscle strength. Impact statement: This detailed description of the rehabilitation protocol will guide to plan the rehabilitation program and help how to design an efficacy study comparing different models of rehabilitation in COVID-19 survivors following discharge from intensive care unit with evidence-based contribution to the literature.
<https://pubmed.ncbi.nlm.nih.gov/34237184/>

**GASTROENTEROLOGY**

**Title:** CHOLANGIOPATHY AFTER SEVERE COVID-19: CLINICAL FEATURES AND PROGNOSTIC IMPLICATIONS

**Source**: The American Journal of Gastroenterology; Jul 2021; vol. 116 (no. 7); p. 1414-1425

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 virus, is a predominantly respiratory tract infection with the capacity to affect multiple organ systems. Abnormal liver tests, mainly transaminase elevations, have been reported in hospitalized patients. We describe a syndrome of cholangiopathy in patients recovering from severe COVID-19 characterized by marked elevation in serum alkaline phosphatase (ALP) accompanied by evidence of bile duct injury on imaging. METHODS We conducted a retrospective study of COVID-19 patients admitted to our institution from March 1, 2020, to August 15, 2020, on whom the hepatology service was consulted for abnormal liver tests. Bile duct injury was identified by abnormal liver tests with serum ALP > 3x upper limit of normal and abnormal findings on magnetic resonance cholangiopacreatography. Clinical, laboratory, radiological, and histological findings were recorded in a Research Electronic Data Capture database. … DISCUSSION Cholangiopathy is a late complication of severe COVID-19 with the potential for progressive biliary injury and liver failure. Further studies are required to understand pathogenesis, natural history, and therapeutic interventions.
<https://journals.lww.com/ajg/Fulltext/2021/07000/Cholangiopathy_After_Severe_COVID_19__Clinical.16.aspx>

**ORTHOPAEDICS**

**Title:** AVASCULAR NECROSIS AS A PART OF 'LONG COVID-19'

**Source**: BMJ case reports; Jul 2021; vol. 14 (no. 7)

**Abstract:** Long COVID-19' can affect different body systems. At present, avascular necrosis (AVN) as a sequalae of 'long COVID-19' has yet not been documented. By large-scale use of life-saving corticosteroids in COVID-19 cases, we anticipate that there will be a resurgence of AVN cases. We report a series of three cases in which patients developed AVN of the femoral head after being treated for COVID-19 infection. The mean dose of prednisolone used in these cases was 758 mg (400-1250 mg), which is less than the mean cumulative dose of around 2000 mg steroid, documented in the literature as causative for AVN. Patients were symptomatic and developed early AVN presentation at a mean of 58 days after COVID-19 diagnosis as compared with the literature which shows that it generally takes 6 months to 1 year to develop AVN post steroid exposure.
<https://casereports.bmj.com/content/14/7/e242101>

**NEW RESEARCH STUDIES**

**Title:** NEW RESEARCH INTO TREATMENT AND DIAGNOSIS OF LONG COVID

**Source**: Gov.uk, 18th July 2021

15 new studies across the UK will expand research into long COVID to support thousands of vulnerable people, backed by nearly £20 million through the NIHR, including:

* STIMULATE-ICP at University College London Hospitals NHS Trust which will be the largest long COVID trial to date, recruiting more than 4,500 people with the condition. With £6.8 million of funding, the project will test the effectiveness of existing drugs to treat long COVID by measuring the effects of 3 months’ treatment, including on people’s symptoms, mental health and outcomes such as returning to work. It will also assess the use of MRI scans to help diagnose potential organ damage, as well as enhanced rehabilitation through an app to track their symptoms
* The immunologic and virologic determinants of long COVID at Cardiff University with nearly £800,000, which will look at the role of the immune system in long-term disease and whether overactive or impaired immune responses could drive long COVID by causing widespread inflammation
* ReDIRECT at University of Glasgow backed by nearly £1 million, which will assess whether a weight management programme can reduce symptoms of long COVID in people who are overweight or obese
* LOCOMOTION at University of Leeds with £3.4 million, which focuses on identifying and promoting the most effective care, from accurate assessments in long COVID clinics to the best advice and treatment in surgeries, as well as home monitoring methods that can show flare-ups of symptoms. The research aims to establish a gold standard of care that can be shared across England and the rest of the UK
* EXPLAIN at University of Oxford backed by £1.8 million, which will seek to diagnose ongoing breathlessness in people with COVID-19 who were not admitted to hospital, using MRI scans to trace inhaled gas moving into and out of the lungs to assess their severity and whether they improve over time

<https://www.gov.uk/government/news/new-research-into-treatment-and-diagnosis-of-long-covid>

**news & local SERVICE DEVelopments**

**Title:** Accolade for city’s specialist post-Covid-19 healthcare services

**Source**: STH, 15th July 2021

A new specialist service aiming at helping patients suffering with the long-term effects of Covid-19 has been shortlisted for a national Health Service Journal Patient Safety Award. The Sheffield Long Covid Programme, which was set up by Sheffield Teaching Hospitals NHS Foundation Trust and NHS Sheffield Clinical Commissioning Group to support patients with Long Covid, is one of eight finalists in the ‘Service User Engagement and Co-production category’. The award recognises healthcare initiatives which are designed and planned with patients and their families.
<https://www.sth.nhs.uk/news/news?action=view&newsID=1319>

**Title:** OVER 2 MILLION ADULTS IN ENGLAND MAY HAVE HAD LONG COVID - IMPERIAL REACT

**Source**: Imperial College, 24th June 2021

A study of over half a million adults in England found that one in 20 had persistent COVID-19 symptoms. The research looked at survey data from the Imperial College London-led REACT-2 study, collected from random samples of the population between September and February. Nearly 27,000 (around 6%) reported experiencing at least one of 29 symptoms linked with COVID-19 for 12 weeks or more.
<https://www.imperial.ac.uk/news/224853/over-million-adults-england-have-long/>

**Title:** COVID AND THE BRAIN: RESEARCHERS ZERO IN ON HOW DAMAGE OCCURS

**Source**: Nature,

Growing evidence suggests that the coronavirus causes ‘brain fog’ and other neurological symptoms through multiple mechanisms.
<https://www.nature.com/articles/d41586-021-01693-6>

**Title:** HEALTH SYSTEMS SHOULD BE PREPARED’: DOCTORS BRACE FOR TSUNAMI OF LONG COVID

**Source**: The Guardian, 28th June 2021

As the debilitating post-viral condition affects millions around the world, medical experts are scrambling to nail down what causes it – and how to treat it.
<https://www.theguardian.com/australia-news/2021/jun/28/health-systems-should-be-prepared-doctors-brace-for-tsunami-of-long-covid>

**Title:** ARE LATENT VIRUSES CAUSING LONG COVID-19 SYMPTOMS? PATIENT GROUPS PUSH FOR TESTING

**Source**: Wall Street Journal, 13th July 2021

A new theory that reactivated older viruses are driving some of the coronavirus’s debilitating symptoms is gaining traction among some patient advocates.
<https://www.wsj.com/articles/are-latent-viruses-causing-long-covid-19-symptoms-patient-groups-push-for-testing-11626181200>

**Title:** LONG COVID SHOULD BE TREATED AS DISABILITY, SAYS TUC

**Source**: The Guardian, 20th June 2021

Employees need protection in the workplace, with half experiencing some form of discrimination or disadvantage.
<https://www.theguardian.com/society/2021/jun/20/long-covid-should-be-treated-as-disability-says-tuc>

**Title:** DELTA SURGE ‘COULD LEAVE HUNDREDS OF THOUSANDS WITH LONG COVID’

**Source**: The Guardian, 13th July 2021

Unvaccinated younger sufferers more at risk of debilitating long-term symptoms, study finds.
<https://www.theguardian.com/society/2021/jul/13/delta-surge-could-leave-hundreds-of-thousands-with-long-covid>

**Title:** MEETING THE NEED OF LONG COVID (Nisreen A. Alwan)

**Source**: Science, 30th July 2021

The public health response to the COVID-19 pandemic needs to adequately address the direct long-term effects of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in the context of the ongoing pandemic. An adequate response should incorporate the 4 Rs: Reporting, Recognition (including Rehabilitation), and Research.
<https://science.sciencemag.org/content/373/6554/491/tab-figures-data>

**Title:** WE MUST TAKE LONG COVID INTO ACCOUNT WHEN EASING COVID RESTRICTIONS

**Source**: BMJ, 6th July 2021

As the UK government announce plans to roll back covid-19 restrictions in England, a group of patient advocates with long covid write an open letter to Sajid Javid, the secretary of state for health and social care.
<https://blogs.bmj.com/bmj/2021/07/06/we-must-take-long-covid-into-account-when-easing-covid-restrictions/>

**Title:** DOCTORS WORRY THAT MEMORY PROBLEMS AFTER COVID-19 MAY SET THE STAGE FOR ALZHEIMER'S

**Source**: NPR, 26th July 2021

…Researchers at UT Health San Antonio are studying patients like Hernandez, trying to understand why their cognitive problems persist and whether their brains have been changed in ways that elevate the risk of developing Alzheimer's disease.
<https://www.npr.org/sections/health-shots/2021/07/26/1019875347/doctors-worry-that-memory-problems-after-covid-19-may-set-stage-for-alzheimers>

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We

[TRFT Library & Knowledge Service](https://www.trftlibraryknowledge.com/) aim to bring together the latest guidelines, research and news on Covid-19 through our [Covid-19 portal](https://www.trftlibraryknowledge.com/coronavirus.html). For daily updates on Covid-19 visit our '[Latest Health](https://trfthealthweeklydigest.wordpress.com/)' newsfeed, or use the hashtag [#covid19rftlks](https://twitter.com/hashtag/covid19rftlks?src=hashtag_click) to see our latest tweets on Covid-19 research, guidelines and news.

We also produce a range of subject-specific news feeds to ensure our clinical and professional teams stay up to date with developments in their work areas. Please visit our [website](http://www.trftlibraryknowledge.com/) for more information

<https://www.trftlibraryknowledge.com/health-newsfeeds.html>