The following information resources have been selected by the National Health Library and Knowledge Service Evidence Virtual Team in response to your question. The resources are listed in our estimated order of relevance to practicing healthcare professionals confronted with this scenario in an Irish context. In respect of the evolving global situation and rapidly changing evidence base, it is advised to use hyperlinked sources in this document to ensure that the information you are disseminating to the public or applying in clinical practice is the most current, valid and accurate. For further information on the methodology used in the compilation of this document—including a complete list of sources consulted—please see our National Health Library and Knowledge Service Summary of Evidence Protocol.

YOUR QUESTION

What are the physical sequelae for critically ill COVID-19 patients?

IN A NUTSHELL

The European Centre for Disease Control and Prevention[1] list respiratory and cardiovascular complications as possible sequelae of COVID-19 but the literature in general agrees that long-term sequelae of COVID-19 are still unknown.

A search of the literature found a systematic review as well as cross-sectional and prospective studies on SARS and MERS survivors that could potentially inform the question about long-term sequelae of COVID-19. Ahmed et al[3] conducted a systematic review and meta-analysis on the clinical outcomes of survivors of SARS and MERS outbreaks; the authors conclude that lung function abnormalities, psychological impairment and reduced exercise capacity were common in SARS and MERS survivors. Based on their findings, the authors advocate that clinicians anticipate and investigate similar long-term outcomes in COVID-19 survivors. Ong et al[12] conclude that one year after recovery from SARS, persistent pulmonary function impairment was found in about one third of patients. The health status of SARS survivors was also significantly worse compared with the healthy population. Hui et al[10] also conducted a 1 year cross-sectional survey of SARS survivors and came to the conclusion that significant impairment in DLCO [diffusing capacity of the lung for carbon monoxide] was noted in 23.7% of survivors 1 year after illness onset. Exercise capacity and health status of SARS survivors were remarkably lower than those of a normal population. Battawi et al[4] looked at MERS survivors who required hospitalization in Saudi Arabia during 2016-2017, approximately 1 year after diagnosis. They compared characteristics of MERS survivors against those of survivors of non-MERS Severe Acute Respiratory Infection (SARI). The

results show that functional scores were similar for MERS and non-MERS SARI survivors. However, MERS survivors of critical illness reported lower quality of life than survivors of less severe illness.

According to Zhang et al[18] the most severe sequelae after rehabilitation from SARS are femoral head necrosis and pulmonary fibrosis. The authors performed a 15-year follow-up on the lung and bone conditions of SARS patients. They evaluated the recovery from lung damage and femoral head necrosis in an observational cohort study of SARS patients using pulmonary CT scans, hip joint MRI examinations, pulmonary function tests and hip joint function questionnaires. They concluded that pulmonary interstitial damage and functional decline caused by SARS mostly recovered, with a greater extent of recovery within 2 years after rehabilitation. Femoral head necrosis induced by large doses of steroid pulse therapy in SARS patients was not progressive and was partially reversible.

According to Candan et al[6] research has focused in recent years on poor long-term functional outcomes in patients with Adult Respiratory Distress Syndrome (ARDS), often associated with ICU-acquired weakness, deconditioning, and myopathies and neuropathies. In addition to physical therapists providing respiratory support in the ICU, the literature unequivocally supports the view that early intervention for ICU management of patients with ARDS secondary to COVID-19 needs to focus on reducing contributors to impaired long-term function, with direct attention paid to preventing or managing ICU-acquired weakness, deconditioning, and myopathies and neuropathies, in conjunction with respiratory care.

Salehi et al[15] looked at long term pulmonary consequences of COVID-19. According to the authors, organizing pneumonia and diffuse alveolar damage seem to be, by far, the most common forms of lung injury associated with COVID-19, and both evolve in a fairly predictable manner. They suggest that long-term follow-up chest imaging of survivors is needed for a better understanding of the possible irreversible pulmonary damages of SARS-CoV-2 pneumonia. They advise follow-up evaluation of recovered patients by a respiratory physician.

Several studies look at the neurological sequelae of COVID-19 [2, 5, 11, 13, 16]. Abboud et al[2] discuss several neurological aspects reported in the literature to date, including the evidence and pathways of the neuro-invasion in

COVID-19, and the main neurological disorders reported in the literature to date, as well as the future perspectives and the potential long-term consequence of current neuro-infection in COVID-19 patients. In their review of the literature, Ogier et al[11] provide an overview of the current knowledge on neurologic sequelae of COVID-19 and their possible aetiology, and, based on available data, propose possible improvements in current medical care procedures. Papa et al[13] look at Parkinson's Disease and state that it is too early to know whether COVID- 19 will have long-term neurological complications. They observe that the facts that hyposmia is a common feature of early PD and that the olfactory system is an early predilection site for alpha-synuclein pathology might just be an intriguing coincidence but it is however notable that recent studies indicate that alpha-synuclein participates in the innate immune response to any viral infection. They believe that these observations could be important.

According to De Felice et al[8] emerging evidence suggests that SARS-CoV-2 is associated with neurological alterations in COVID-19 patients presenting with severe clinical manifestations. According to the authors, the impact of SARS-CoV-2 on the CNS could 1. lead to neurological alterations directly; 2. worsen pre-existing neurological conditions; and/or 3. increase susceptibility to or aggravate damage caused by other insults.

Other studies look at oral health[9], the development of a tool to ensure the full spectrum of functional outcomes following COVID-19[7], antimicrobial resistance[14] and the cardiovascular system[17].

IRISH AND INTERNATIONAL GUIDANCE

What do the European Centre for Disease Control and Prevention say?

Rapid Risk Assessment: Coronavirus disease 2019 (COVID-19) in the EU/EEA and the UK – ninth update[1]

In addition to respiratory sequelae, such as lung fibrosis, severe COVID-19 may lead to cardiovascular sequelae such as myocardial injury, arrhythmias, cardiomyopathy and heart failure.

INTERNATIONAL LITERATURE

What does the international literature say?

Abboud et al (2020) COVID-19 and SARS-Cov-2 Infection: Pathophysiology and Clinical Effects on the Nervous System[2]

The neurological disorders linked with COVID-19 can be grouped into several categories, ranging from non-specific and moderate symptoms such as headache, myalgia and hyposmia to severe symptoms including cerebrovascular disease and intracranial infections. Severe neurological symptoms such as acute cerebrovascular disease occur only in a minority of patients with usual risk factor, and are associated with poor outcome. However, most COVID-19 patients exhibit only minor or mild neurological symptoms. This review discusses several neurological aspects reported in the literature to date, including the evidence and pathways of the neuro-invasion in COVID-19, and the main neurological disorders reported in the literature to date, as well as the future perspectives and the potential long term consequence of current neuro-infection in COVID-19 patients.

Ahmed et al (2020) Long-term clinical outcomes in survivors of severe acute respiratory syndrome and Middle East respiratory syndrome coronavirus outbreaks after hospitalisation or ICU admission: A systematic review and meta-analysis[3]

Objective: To determine long-term clinical outcomes in survivors of severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome

(MERS) coronavirus infections after hospitalization or intensive care unit admission.
Data sources: Ovid MEDLINE, EMBASE, CINAHL Plus, and PsycINFO were searched.
Study selection: Original studies reporting clinical outcomes of adult SARS and MERS survivors 3 months after admission or 2 months after discharge were included.
Data extraction: Studies were graded using the Oxford Centre for Evidence-Based Medicine 2009 Level of Evidence Tool. Meta-analysis was used to derive pooled estimates for prevalence/severity of outcomes up to 6 months after hospital discharge, and beyond 6 months after discharge.
Data synthesis: Of 1,169 identified studies, 28 were included in the analysis. Pooled analysis revealed that common complications up to 6 months after discharge were: impaired diffusing capacity for carbon monoxide (prevalence 27%, 95% confidence interval (CI) 15–45%); and reduced exercise capacity (mean 6-min walking distance 461 m, CI 450–473 m). The prevalences of post-traumatic stress disorder (39%, 95% CI 31–47%), depression (33%, 95% CI 20–50%) and anxiety (30%, 95% CI 10–61) beyond 6 months after discharge were considerable. Low scores on Short-Form 36 were identified beyond 6 months after discharge.
Conclusion: Lung function abnormalities, psychological impairment and reduced exercise capacity were common in SARS and MERS survivors. Clinicians should anticipate and investigate similar long-term outcomes in COVID-19 survivors.

Batawi et al (2020) Quality of life reported by survivors after hospitalization for Middle East respiratory syndrome (MERS)[4]

Introduction: Data are lacking on impact of Middle East Respiratory Syndrome (MERS) on health-related quality of life (HRQoL) among survivors.
Methods: We conducted a cross-sectional survey of MERS survivors who required hospitalization in Saudi Arabia during 2016-2017, approximately 1 year after diagnosis. The Short-Form General Health Survey 36 (SF-36) was administered by telephone interview to assess 8 quality of life domains for MERS survivors and a sample of survivors of severe acute respiratory infection (SARI) without MERS. We compared mean SF-36 scores of MERS and non-MERS SARI survivors using independent t-test, and compared categorical variables using chi-square test. Adjusted analyses were performed using multiple linear regression.

Results: Of 355 MERS survivors, 83 were eligible and 78 agreed to participate. MERS survivors were younger than non-MERS SARI survivors (mean ± SD): (44.9 years ±12.9) vs (50.0 years ±13.6), p = 0.031. Intensive care unit (ICU) admissions were similar for MERS and non-MERS SARI survivors (46.2% vs. 57.1%), p = 0.20. After adjusting for potential confounders, there were no significant differences between MERS and non-MERS SARI survivors in physical component or mental component summary scores. MERS ICU survivors scored lower than MERS survivors not admitted to an ICU for physical function (p = 0.05), general health (p = 0.01), vitality (p = 0.03), emotional role (p = 0.03) and physical component summary (p < 0.02). **Conclusions:** Functional scores were similar for MERS and non-MERS SARI survivors. However, MERS survivors of critical illness reported lower quality of life than survivors of less severe illness. Efforts are needed to address the long-term medical and psychological needs of MERS survivors.

Bhidayasiri et al (2020) COVID-19: An Early Review of Its Global Impact and Considerations for Parkinson's Disease Patient Care[5]

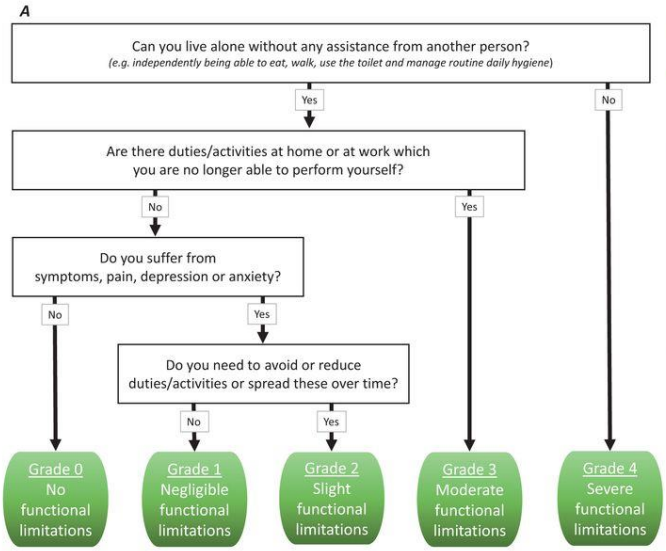
Parkinson's disease (PD) shares a common profile as an age-dependent degenerative disorder, frequently associated with comorbidities, particularly cardiovascular diseases, so PD patients will almost certainly fall into the high-risk group. Therefore, the aim of this review is to explore the risk of COVID-19 in PD based on the susceptibility to severe disease, its impact on PD disease severity, potential long-term sequelae, and difficulties of PD management during this outbreak, where neurologists face various challenges on how we can maintain effective care for PD patients without exposing them, or ourselves, to the risk of infection. It is less than six months since the identification of the original COVID-19 case on New Year's Eve 2019, so it is still too early to fully understand the natural history of COVID-19 and the evidence on COVID-19-related PD is scant. Though the possibilities presented are speculative, they are theory-based, and supported by prior evidence from other neurotrophic viruses closely related to SARS-CoV-2. Neurologists should be on high alert and vigilant for potential acute and chronic complications when encountering PD patients who are suspected of having COVID-19.

Candan et al (2020) Consideration of prevention and management of long-term consequences of post-acute respiratory distress syndrome in patients with COVID-19[6]

This manuscript provides support for physical therapists to focus on the long-term, as well as the short-term, consequences of acute respiratory distress syndrome (ARDS) associated with COVID-19. Since late November 2019, COVID-19 has become a global health pandemic and threat. Although most people have no or mild symptoms, COVID-19 spreads aggressively and can lead to ARDS rapidly in a proportion of individuals. The evidence supports that gas exchange and countering the negative effects of bed rest and immobility are priorities in severely affected patients admitted to the intensive care unit (ICU). However, in recent years, research has focused on poor long-term functional outcomes in patients with ARDS, often associated with ICU-acquired weakness, deconditioning, and myopathies and neuropathies. In addition to physical therapists providing respiratory support in the ICU, the literature unequivocally supports the view that early intervention for ICU management of patients with ARDS secondary to COVID-19 needs to focus on reducing contributors to impaired long-term function, with direct attention paid to preventing or managing ICU-acquired weakness, deconditioning, and myopathies and neuropathies, in conjunction with respiratory care.

Klok et al (2020) The Post-COVID-19 Functional Status (PCFS) Scale: a tool to measure functional status over time after COVID-19[7]

We propose an ordinal tool to measure the full spectrum of functional outcomes following COVID-19. This "Post-COVID-19 Functional Status (PCFS) Scale" can be used for tracking functional status over time as well as for research purposes.



B

How much are you currently affected in your everyday life by COVID-19? Please indicate which one of the following statements applies to you most.	Corresponding PCFS scale grade
I have no limitations in my everyday life and no symptoms, pain, depression or anxiety related to the infection.	0
I have negligible limitations in my everyday life as I can perform all usual duties/activities, although I still have persistent symptoms, pain, depression or anxiety.	1
I suffer from limitations in my everyday life as I occasionally need to avoid or reduce usual duties/activities or need to spread these over time due to symptoms, pain, depression or anxiety. I am, however, able to perform all activities without any assistance.	2
I suffer from limitations in my everyday life as I am not able to perform all usual duties/activities due to symptoms, pain, depression or anxiety. I am, however, able to take care of myself without any assistance.	3
I suffer from severe limitations in my everyday life: I am not able to take care of myself and therefore I am dependent on nursing care and/or assistance from another person due to symptoms, pain, depression or anxiety.	4

De Felice et al (2020) Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and the Central Nervous System[8]

Emerging evidence indicates that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the etiologic agent of coronavirus disease 2019 (COVID-19), can cause neurological complications. We provide a brief overview of these recent observations and discuss some of their possible implications. In particular, given the global dimension of the current pandemic, we highlight the need to consider the possible long-term impact of COVID-19, potentially including neurological and neurodegenerative disorders.

Dziedzic and Wojtyczka (2020) The impact of coronavirus infectious disease 19 (COVID-19) on oral health[9]

Due to indirect complex effect, intensified COVID-19 therapies and multi-drug treatment, it is believed that some oral conditions could be aggravated by COVID-19 disease, particularly those with autoimmune aetiology, linked to compromised immune system or long-term pharmacotherapy.

Hui et al (2020) The 1-year impact of severe acute respiratory syndrome on pulmonary function, exercise capacity, and quality of life in a cohort of survivors[10]

Objective: To examine pulmonary function, exercise capacity, and health-related quality of life (HRQoL) among severe acute respiratory syndrome (SARS) survivors.

Methods: We evaluated survivors with confirmed SARS at the Prince of Wales Hospital, Hong Kong, at 3, 6, and 12 months after symptom onset. Our assessment included: lung volume (total lung capacity [TLC], vital capacity, residual volume, functional residual capacity), spirometry (FVC, FEV1), diffusing capacity of the lung for carbon monoxide (D(LCO)), inspiratory and expiratory respiratory muscle strength, 6-min walk distance (6MWD), chest radiographs (CXRs), and HRQoL by Medical Outcomes Study 36-Item Short-Form General Health Survey questionnaire.

Results: Ninety-seven patients completed the serial assessments. There were 39 male and 58 female patients, and 63 patients (70%) were health-care workers (mean age, 36.9 years [SD, 9.5 years]; body mass index, 23.7 kg/m2 [SD, 4.0 kg/m2]). At 1 year, 27 patients (27.8%) had abnormal CXR findings. Four patients (4.1%), 5 patients (5.2%), and 23 patients (23.7%) had FVC, TLC, and D(LCO) values < 80% of predicted values, respectively. The 6MWD at 12 months was 511.0 m (SD, 89.8 m), which was higher than at 3 months (mean difference, 47.0 m; 95% confidence interval [CI], 31.8 to 62.1 m; p < 0.01) but not different from 6 months (mean difference, 9.7 m; 95% CI, -4.4 to 23.8 m; p = 0.18). The 6MWD was lower than that for normal control subjects of the same age groups, and there was impairment of HRQoL at 12 months. Patients who required ICU admission (n = 31) showed higher CXR scores (1.6 [SD, 3.1]; vs 0.4 [SD, 1.1]; p = 0.04) and lower percentage of predicted FVC, TLC, and Dlco than those who did not, but there were no differences in 6MWD and health status.

Conclusion: Significant impairment in Dlco was noted in 23.7% of survivors 1 year after illness onset. Exercise capacity and health status of SARS survivors were remarkably lower than those of a normal population.

Ogier et al (2020) How to detect and track chronic neurologic sequelae of COVID-19? Use of auditory brainstem responses and neuroimaging for long-term patient follow-up[11]

This review intends to provide an overview of the current knowledge on neurologic sequelae of COVID-19 and their possible etiology, and, based on available data, proposes possible improvements in current medical care procedures. We conducted a thorough review of the scientific literature on neurologic manifestations of COVID-19, the neuroinvasive propensity of known coronaviruses (CoV) and their possible effects on brain structural and functional integrity. It appears that around one third of COVID-19 patients admitted to intensive care units (ICU) for respiratory difficulties exhibit neurologic symptoms. This may be due to progressive brain damage and dysfunction triggered by severe hypoxia and hypoxemia, heightened inflammation and SARS-CoV-2 dissemination into brain parenchyma, as suggested by current reports and analyses of previous CoV outbreaks. Viral invasion of the brain may particularly target and alter brainstem and thalamic functions and, consequently, result in sensorimotor dysfunctions and psychiatric disorders. Moreover, data collected from other structurally homologous CoV suggest that SARS-CoV-2 infection may lead to brain cell degeneration and demyelination similar to multiple sclerosis (MS). Hence, current evidence warrants further evaluation and long-term follow-up of possible neurologic sequelae in COVID-19 patients. It may be particularly relevant to evaluate brainstem integrity in recovered patients, as it is suspected that this cerebral area may particularly be dysfunctional following SARS-CoV-2 infection. Because CoV infection can potentially lead to chronic neuroinflammation and progressive demyelination, neuroimaging features and signs of MS may also be evaluated in the long term in recovered COVID-19 patients.

Ong et al (2020) 1-year pulmonary function and health status in survivors of severe acute respiratory syndrome[12]

Study objectives: To characterize the long-term pulmonary function and health status in a prospectively identified cohort of patients who survived the severe acute respiratory syndrome (SARS).
Design: Prospective follow-up cohort study.
Setting: University-affiliated hospital.
Patients: Ninety-four patients who recovered from SARS were assessed at a uniform time point of 1 year after hospital discharge.

Measurements: The study included the measurement of static and dynamic lung volumes, the determination of the diffusing capacity of the lung for carbon monoxide (D(LCO)), and a health status evaluation using the St. George Respiratory Questionnaire (SGRQ).
Results: Eleven patients (12%) had mild impairment of FVC, 20 (21%) had mild impairment of FEV1, 5 (5%) had mild impairment of the FEV1/FVC ratio, and 17 (18%) had mild impairment of the D(LCO). There was one patient (1%) who had moderate impairment of FVC, one patient (1%) who had moderate impairment of the FEV1/FVC ratio, and three patients (3%) who had moderate impairment of the D(LCO). No pulmonary function abnormalities were detected in 59 patients (63%). Mean scores were significantly higher (ie, worse) than the population norms in the activity ($p < 0.001$), impacts ($p < 0.001$), and total ($p < 0.001$) domains of the SGRQ.
Conclusions: One year after recovery from SARS, persistent pulmonary function impairment was found in about one third of patients. The health status of SARS survivors was also significantly worse compared with the healthy population. The main determinants of morbidity in recovered SARS patients need to be further defined.

Papa et al (2020) Impact of the COVID-19 Pandemic on Parkinson's Disease and Movement Disorders[13]

It is too early to know whether COVID- 19 will have long- term neurological complications of exposure to SARS- CoV- 2. The 1918 "Spanish" flu pandemic was caused by influenza A (H1N1). A viral etiology of encephalitis lethargica and postencephalitic parkinsonism, which followed temporally from the flu pandemic, has been suspected although is still not proven, with some evidence implicating an enterovirus. Thus far, coronaviruses have not been linked to specific long- term neurological sequelae. Nonetheless, the observations of anosmia and ageusia are worthy of future study. The facts that hyposmia is a common feature of early PD (often even present in the prodrome) and that the olfactory system is an early predilection site for alpha- synuclein pathology might just be an intriguing coincidence. However, it is notable that recent studies indicate that alpha- synuclein participates in the innate immune response to any viral infection, suggesting that these observations could be important.

Rawson et al (2020) COVID-19 and the potential long-term impact on antimicrobial resistance[14]

Whilst the pandemic has focused society on the threat of emerging infections and hand hygiene, certain infection control and antimicrobial stewardship policies may have to be relaxed. It is unclear whether the unintended consequences of these changes will have a net-positive or -negative impact on rates of antimicrobial resistance. Whilst the urgent focus must be on controlling this pandemic, sustained efforts to address the longer-term global threat of antimicrobial resistance should not be overlooked.

Salehi et al (2020) Long-term Pulmonary Consequences of Coronavirus Disease 2019 (COVID-19): What We Know and What to Expect[15]

Over the last couple of months, the clinical and imaging features of COVID-19 pneumonia have been discussed in numerous publications, and the major imaging findings of the disease have been described in detail. However, the post recovery course of the disease, including its physical and psychological sequela, is not yet clear. The long-term effect of COVID-19 on lung parenchyma and pulmonary function remains an outstanding question. Although it is too early to completely answer this question, our limited observations demonstrate significant pulmonary sequela of the disease in some of the survivors. In general, survivors of viral pneumonias are at risk of psychological and physical complications of the disease itself, as well as treatment-related lung damage and other organ injuries. Long-term lung disability is not uncommon in patients who have recovered from severe viral pneumonias. Although most survivors can return to work and normal life, a significant number of them will show residual ventilation and blood-gas diffusion abnormalities.

Serrano-Castro et al (2020) Impact of SARS-CoV-2 infection on neurodegenerative and neuropsychiatric diseases: a delayed pandemic?[16]

Introduction: In view of the magnitude of the epidemic, we conducted a speculative review of possible medium- and long-term neurological consequences of SARS-CoV-2 infection, with particular emphasis on neurodegenerative and neuropsychiatric diseases of neuroinflammatory origin, based on the available evidence on neurological symptoms of acute SARS-CoV-2 infection.

Development: We systematically reviewed the available evidence about the pathogenic mechanisms of SARS-CoV-2 infection, the immediate and lasting effects of the cytokine storm on the central nervous system, and the consequences of neuroinflammation for the central nervous system.
Conclusions: SARS-CoV-2 is a neuroinvasive virus capable of triggering a cytokine storm, with persistent effects in specific populations. Although our hypothesis is highly speculative, the impact of SARS-CoV-2 infection on the onset and progression of neurodegenerative and neuropsychiatric diseases of neuroinflammatory origin should be regarded as the potential cause of a delayed pandemic that may have a major public health impact in the medium to long term. Cognitive and neuropsychological function should be closely monitored in COVID-19 survivors.

Xiong et al (2020) Coronaviruses and the cardiovascular system: acute and long-term implications[17]

Heightened systemic inflammatory and pro-coagulant activity can persist in survivors of hospitalization for community-acquired pneumonia long after resolution of the index infection. The clinical effects of pneumonia have been linked to increased risk of cardiovascular disease up to 10-year follow-up and it is likely that cases infected via respiratory virus outbreaks will experience similar adverse outcomes. Therapeutic use of corticosteroids further augments the possibility of adverse cardiovascular events. However, long-term follow-up data concerning the survivors of respiratory virus epidemics are scarce. Lipid metabolism remained disrupted 12 years after clinical recovery in a metabolomic study amongst 25 SARS survivors, whereas cardiac abnormalities observed during hospitalisation in eight patients with H7N9 influenza returned to normal at 1-year follow-up. Whilst viral phenotype, baseline clinical characteristics, initial disease severity, and immediate management impact on short-term survival, long-term prognosis following outbreaks of respiratory virus infection may equally depend upon the extra-pulmonary manifestations. Serial follow-up studies amongst the survivors of acute infection are sorely needed.

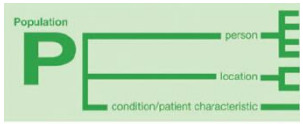
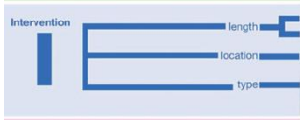
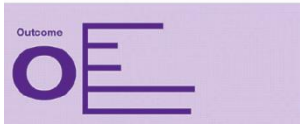
Zhang et al (2020) Long-term bone and lung consequences associated with hospital-acquired severe acute respiratory syndrome: a 15-year follow-up from a prospective cohort study[18]

The most severe sequelae after rehabilitation from SARS are femoral head necrosis and pulmonary fibrosis. We performed a 15-year follow-up on the lung and bone conditions of SARS patients. We evaluated the recovery from

lung damage and femoral head necrosis in an observational cohort study of SARS patients using pulmonary CT scans, hip joint MRI examinations, pulmonary function tests and hip joint function questionnaires. Eighty medical staff contracted SARS in 2003. Two patients died of SARS, and 78 were enrolled in this study from August 2003 to March 2018. Seventy-one patients completed the 15-year follow-up. The percentage of pulmonary lesions on CT scans diminished from 2003 (9.40 ± 7.83)% to 2004 (3.20 ± 4.78)% ($P < 0.001$) and remained stable thereafter until 2018 (4.60 ± 6.37)%. Between 2006 and 2018, the proportion of patients with interstitial changes who had improved pulmonary function was lower than that of patients without lesions, as demonstrated by the one-second ratio (FEV1/FVC%, $t = 2.21$, $P = 0.04$) and mid-flow of maximum expiration (FEF25%-75%, $t = 2.76$, $P = 0.01$). The volume of femoral head necrosis decreased significantly from 2003 (38.83 ± 21.01)% to 2005 (30.38 ± 20.23)% ($P = 0.000\ 2$), then declined slowly from 2005 to 2013 (28.99 ± 20.59)% and plateaued until 2018 (25.52 ± 15.51)%. Pulmonary interstitial damage and functional decline caused by SARS mostly recovered, with a greater extent of recovery within 2 years after rehabilitation. Femoral head necrosis induced by large doses of steroid pulse therapy in SARS patients was not progressive and was partially reversible.

Produced by the members of the National Health Library and Knowledge Service Evidence Team†. Current as at 5 June 2020.This evidence summary collates the best available evidence at the time of writing and **does not replace clinical judgement or guidance**. Emerging literature or subsequent developments in respect of COVID-19 may require amendment to the information or sources listed in the document. Although all reasonable care has been taken in the compilation of content, the National Health Library and Knowledge Service Evidence Team makes no representations or warranties expressed or implied as to the accuracy or suitability of the information or sources listed in the document. This evidence summary is the property of the National Health Library and Knowledge Service and subsequent re-use or distribution in whole or in part should include acknowledgement of the service.

The following PICO(T) was used as a basis for the evidence summary:

	COVID-19 SURVIVORS
	
	
	LONG-TERM PHYSICAL AND NEUROLOGICAL SEQUELAE

The following search strategy was used:

(COVID-19 OR CORONAVIRUS OR "CORONA VIRUS" OR WUHAN NEAR/3 VIRUS OR (("2018-NCOV" OR "2019 NCOV")) OR "SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2" OR "2019 NOVEL CORONAVIRUS" OR "2019 NEW CORONAVIRUS" OR "SARS-COV-2")

AND

("LONG-TERM" NEAR/3 (SEQUELAE OR IMPAIRMENT OR CONDITION$ OR COMPLICATION$ OR FUNCTION$ OR CONSEQUENCE$) OR TOPIC ("LONG-TERM" NEAR/3 (SEQUELAE OR IMPAIRMENT OR CONDITION$ OR COMPLICATION$ OR FUNCTION$ OR CONSEQUENCE$)

† Isabelle Delaunois, Medical Librarian, HSE Mid-West, University of Limerick Hospitals, Limerick [Author]; Dr. Declan McKeown, Consultant in Public Health Medicine [Editor]; Brendan Leen, Area Library Manager, HSE South [Editor

[1] Coronavirus disease 2019 (COVID-19) in the EU/EEA and the UK – ninth update , 23 April 2020. Stockholm: ECDC; 2020 available : https://www.ecdc.europa.eu/en/publications-data/rapid-risk-assessment-coronavirus-disease-2019-covid-19-pandemic-ninth-update#no-link [Accessed 5 June 2020].
[2] Abboud H, et al (2020) COVID-19 and SARS-Cov-2 Infection: Pathophysiology and Clinical Effects on the Nervous System [published online ahead of print, 2020 May 28]. World Neurosurg. 2020;S1878-8750(20)31164-5. doi:10.1016/j.wneu.2020.05.193 [Accessed 5 June 2020].
[3] Ahmed H, et al (2020) Long-term clinical outcomes in survivors of severe acute respiratory syndrome and Middle East respiratory syndrome coronavirus outbreaks after hospitalisation or ICU admission: A systematic review and meta-analysis [published online ahead of print, 2020 May 25]. J Rehabil Med. 2020;10.2340/16501977-2694. doi:10.2340/16501977-2694 https://pubmed.ncbi.nlm.nih.gov/32449782/ [Accessed 5 June 2020].
[4] Batawi S, et al (2020) Quality of life reported by survivors after hospitalization for Middle East respiratory syndrome (MERS). Health Qual Life Outcomes. 2019;17(1):101. Published 2019 Jun 11. doi:10.1186/s12955-019-1165-2 https://pubmed.ncbi.nlm.nih.gov/31186042/ [Accessed 5 June 2020].
[5] Bhidayasiri R, et al (2020) COVID-19: An Early Review of Its Global Impact and Considerations for Parkinson's Disease Patient Care [published online ahead of print, 2020 Apr 30]. J Mov Disord. 2020;10.14802/jmd.20042. doi:10.14802/jmd.20042 https://pubmed.ncbi.nlm.nih.gov/32344993/ [Accessed 5 June 2020].
[6] Candan SA, et al (2020) Consideration of prevention and management of long-term consequences of post-acute respiratory distress syndrome in patients with COVID-19. Physiother Theory Pract. 2020;36(6):663- 668. doi:10.1080/09593985.2020.1766181 https://pubmed.ncbi.nlm.nih.gov/32419564/ [Accessed 5 June 2020].
[7] Klok FA, , et al The Post-COVID-19 Functional Status (PCFS) Scale: a tool to measure functional status over time after COVID-19 [published online ahead of print, 2020 May 12]. Eur Respir J. 2020;2001494. doi:10.1183/13993003.01494-2020 https://erj.ersjournals.com/content/early/2020/05/12/13993003.01494-2020 [Accessed 5 June 2020].
[8] De Felice FG, et al (2020) Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and the Central Nervous System. Trends Neurosci. 2020;43(6):355- 357. doi:10.1016/j.tins.2020.04.004 https://www.sciencedirect.com/science/article/pii/S0166223620300916 [Accessed 5 June 2020].
[9] Dziedzic A, Wojtyczka R. The impact of coronavirus infectious disease 19 (COVID-19) on oral health [published online ahead of print, 2020 Apr 18]. Oral Dis. 2020;10.1111/odi.13359. doi:10.1111/odi.13359 https://pubmed.ncbi.nlm.nih.gov/32304276/ [Accessed 5 June 2020].
[10] Hui DS, Wong KT, Ko FW, et al The 1-year impact of severe acute respiratory syndrome on pulmonary function, exercise capacity, and quality of life in a cohort of survivors. Chest. 2005;128(4):2247- 2261. doi:10.1378/chest.128.4.2247 https://pubmed.ncbi.nlm.nih.gov/16236881/ [Accessed 5 June 2020].
[11] Ogier M, et al (2020) how to detect and track chronic neurologic sequelae of covid-19? Use of auditory brainstem responses and neuroimaging for long-term patient follow-up [published online ahead of print, 2020 May 15]. Brain Behav Immun Health. 2020;5:100081. doi:10.1016/j.bbih.2020.100081 https://pubmed.ncbi.nlm.nih.gov/32427134/ [Accessed 5 June 2020].
[12] Ong KC, Ng AW, Lee LS, et al 1-year pulmonary function and health status in survivors of severe acute respiratory syndrome. Chest. 2005;128(3):1393- 1400. doi:10.1378/chest.128.3.1393 https://journal.chestnet.org/article/S0012-3692%2815%2952164-8/abstract [Accessed 5 June 2020].
[13] Papa SM, et al (2020) Impact of the COVID-19 Pandemic on Parkinson's Disease and Movement Disorders. Mov Disord. 2020;35(5):711- 715. doi:10.1002/mds.28067 https://pubmed.ncbi.nlm.nih.gov/32373651/ [Accessed 5 June 2020].
[14] Rawson TM, et al (2020) COVID-19 and the potential long-term impact on antimicrobial resistance [published online ahead of print, 2020 May 20]. J Antimicrob Chemother. 2020;dkaa194. doi:10.1093/jac/dkaa194 https://pubmed.ncbi.nlm.nih.gov/32433765/ [Accessed 5 June 2020].
[15]Salehi S, et al (2020) Long-term Pulmonary Consequences of Coronavirus Disease 2019 (COVID-19): What We Know and What to Expect [published online ahead of print, 2020 May 12]. J Thorac Imaging. 2020;10.1097/RTI.0000000000000534. doi:10.1097/RTI.0000000000000534 https://pubmed.ncbi.nlm.nih.gov/32404798/ [Accessed 5 June 2020].
[16] Serrano-Castro PJ, et al (2020) Impact of SARS-CoV-2 infection on neurodegenerative and neuropsychiatric diseases: a delayed pandemic? [published online ahead of print, 2020 Apr 17]. Influencia de la infección SARS-CoV-2 sobre enfermedades neurodegenerativas y neuropsiquiátricas: ¿una pandemia demorada? [published online ahead of print, 2020 Apr 17]. Neurologia. 2020;S0213-4853(20)30067-0. doi:10.1016/j.nrl.2020.04.002 https://doi.org/10.1016/j.nrleng.2020.04.002 [Accessed 5 June 2020].
[17] Xiong TY, et al (2020) Coronaviruses and the cardiovascular system: acute and long-term implications. Eur Heart J. 2020;41(19):1798- 1800. doi:10.1093/eurheartj/ehaa231 https://pubmed.ncbi.nlm.nih.gov/32186331/ [Accessed 5 June 2020].
[18] Zhang P, et al (2020) Long-term bone and lung consequences associated with hospital-acquired severe acute respiratory syndrome: a 15-year follow-up from a prospective cohort study. Bone Res. 2020;8:8. Published 2020 Feb 14. doi:10.1038/s41413-020-0084-5 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7018717/ [Accessed 5 June 2020].