



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 outcomes for people with cystic fibrosis who contract COVID-19?

IN A NUTSHELL

BMJ Best Practice³ categorise cystic fibrosis patients as a high-risk population in terms of COVID-19. HSE guidance¹ gives clear advice on how to keep well for patients who have contracted COVID-19. BMJ Best Practice³ recommends that for patients with known or suspected COVID-19, airway clearance should be carried out in a well-ventilated room, separate from other people, if possible, as it is a potentially infectious aerosol-generating procedure.

Very little reliable research and data on clinical outcomes of cystic fibrosis patients who have contracted COVID-19 has yet been published. A multinational cohort study by Cosgriff et al⁵ concludes that there is good recovery from SARS-CoV-2 in the heterogeneous CF cohort investigated. The disease course does not seem to differ from that in the general population, but the current numbers are too small to draw firm conclusions, and people with CF should continue to follow public health advice to protect themselves from infection. Colombo et al⁴ base their recommendations on the 2009 influenza pandemic, H1N1 virus, which caused substantial morbidity in patients with cystic fibrosis and which, in a subgroup with severe lung disease, was associated with respiratory deterioration, mechanical ventilation and even death. As the clinical features of COVID-19 are distinct from the symptoms of cystic fibrosis, COVID-19 in people with cystic fibrosis should be clearly distinguishable, but it is suggested that mild disease might be categorised as being within the normal spectrum of symptoms for some

cystic fibrosis patients. The authors recommend a low threshold for testing in the cystic fibrosis population.

Several countries are now reporting COVID-19 case data of people with a confirmed diagnosis of CF to the European Cystic Fibrosis Society patient registry. The ECFS present a weekly update⁶ of centralised, anonymised data on CF admissions throughout Europe. The data is preliminary, incomplete, might change over time, and the number of cases is low; therefore, the information in the ECFS registry should not be used to direct clinical decisions. The data published on 20 May, 2020 shows that 41 patients in Europe were hospitalised (six in the ICU), and 2 patients required ventilation. 11 patients were asymptomatic. The top five symptoms were fever, increased cough, fatigue, increased sputum production and increased breathlessness.

Siuba M et al⁷ looked at mortality in individuals with cystic fibrosis requiring invasive mechanical ventilation (IMV) for respiratory failure. They concluded that mortality per hospitalization in adults with cystic fibrosis who are not bridging to lung transplant and require emergent IMV is 44.5%, suggesting IMV is not futile and that these findings may help providers, families and patients with cystic fibrosis weigh the risks and benefits of IMV for respiratory failure.

Farfour et al⁸ report the case of a SARS-CoV-2 infection in a lung-transplanted patient for cystic fibrosis characterized by several singularities. The case highlights three significant observations: (1) in its early stages, COVID-19 presents in a non-specific manner; (2) swab testing appears to be less sensitive among cystic fibrosis patients who present with primarily respiratory symptoms; (3) the identification of another respiratory pathogen should not exclude a SARS-CoV-2 infection, at least in patients presenting severe pathology. Poli et al⁹ briefly report a case of COVID-19 in an infant with CF in Italy. The patient never developed fever or any symptoms or signs of infection.



IRISH AND INTERNATIONAL GUIDANCE

What does the HSE say?

[National Clinical Programme for Cystic Fibrosis - Guidance for People with Cystic Fibrosis and Their Families Regarding COVID-19¹](#)

The HSE stresses that it is essential for CF patients to keep taking all their medications and treatments including nutritional treatments regularly as prescribed by their CF team. Failure to take regular treatments could increase patients' risk of developing COVID-19 or other infections.

CF patients should keep their prescriptions up to date. Patients are advised to phone their pharmacy in advance to arrange for prescription preparation. Patients are urged not to go to the pharmacy, but instead to ask the pharmacy to deliver or ask neighbours, family or friends to collect their medications and to leave them outside their door

For family and carers, airway clearance and nebulizer treatments for CF patients should be carried out regularly and, if possible, away from anyone else in a well-ventilated room.

The HSE stresses the importance of regular exercise while maintaining physical isolation. HSE CF teams are available for advice regarding modification of exercise programmes.

Patients are strongly encouraged to phone or email the CF Nurse/CF Centre if they become unwell.

What do the Centers for Disease Control and Prevention (United States) say?

[Groups at Higher Risk for Severe Illness²](#)

Chronic lung diseases such as chronic obstructive pulmonary disease (COPD) [including emphysema and chronic bronchitis], idiopathic pulmonary fibrosis and cystic fibrosis may put people at higher risk for severe illness from COVID-19.

CDC also urges CF patients: to continue taking their current medications including those with steroids in them; and to avoid triggers that make their symptoms worse.

Based on data from other viral respiratory infections, such as influenza, it is believed that COVID-19 might cause flare-ups of chronic lung diseases leading to severe illness.



POINT-OF-CARE TOOLS

What does BMJ Best Practice say?

[Management of coexisting conditions in the context of COVID-19³](#)

Patients with cystic fibrosis (CF) are at higher risk for severe COVID-19 illness and should carefully follow public health advice.

UK guidance advises that patients and their families and carers should continue with all usual self-care, including airway clearance, regular medication, and home exercise. Exacerbations should be managed as previously advised, including taking rescue medication and contacting their CF team.

If the patient is known or suspected to have COVID-19, airway clearance should be done in a well-ventilated room, separate from other people, if possible, as it is a potentially infectious aerosol-generating procedure. UK guidelines advise that nebulisers will not generate infectious aerosols as the aerosol comes from fluid in the nebuliser chamber, not the patient, so may be used as normal; however, carers should use appropriate hand hygiene when helping patients with masks. However, the Global Initiative for Asthma (GINA) does consider nebulisation to have aerosol-generating potential... Guidelines from the US Centers for Disease Control and Prevention also consider nebuliser therapy to be a high-risk aerosol generating procedure.

Patients are managed remotely where possible. Lung function tests should only be done in hospital if the results will have a direct impact on management; home spirometry should be used where possible.

INTERNATIONAL LITERATURE

What does the international literature say?

[Colombo, C et al \(2020\) Impact of COVID-19 on people with cystic fibrosis⁴](#)

Viral respiratory tract infections are more severe in patients with cystic fibrosis than in the general population, with an increased risk of complications and a negative impact on lung function. During the 2009 influenza pandemic, H1N1 virus caused substantial morbidity in patients with



cystic fibrosis, and in a subgroup with severe lung disease, H1N1 infection was associated with respiratory deterioration, mechanical ventilation, and even death. People with cystic fibrosis have a phenotypic spectrum ranging from excellent respiratory health to chronic airways disease with productive cough and respiratory compromise. The clinical features of COVID-19 — dry cough, myalgia, and fever — are quite distinct from the symptoms of cystic fibrosis. Therefore, most COVID-19 in people with cystic fibrosis should be recognisable, but mild disease might be labelled as within the normal spectrum of symptoms for that individual. A low threshold for testing is therefore needed in this population.

[**Cosgriff, R et al \(2020\) A multinational report to characterise SARS-CoV-2 infection in people with cystic fibrosis⁵**](#)

Information is lacking on the clinical impact of the novel coronavirus, SARS-CoV-2, on people with cystic fibrosis (CF). Our aim was to characterise SARS-CoV-2 infection in people with cystic fibrosis. **METHODS:** Anonymised data submitted by each participating country to their National CF Registry was reported using a standardised template, then collated and summarised. **RESULTS:** 40 cases have been reported across 8 countries. Of the 40 cases, 31 (78%) were symptomatic for SARS-CoV-2 at presentation, with 24 (60%) having a fever. Among the 40 cases, 70% had recovered, 30% remained unresolved at the time of reporting, and no deaths were reported. **CONCLUSIONS:** This early report shows good recovery from SARS-CoV-2 in this heterogeneous CF cohort. The disease course does not seem to differ from the general population, but the current numbers are too small to draw firm conclusions and people with CF should continue to strictly follow public health advice to protect themselves from infection.

[**European Cystic Fibrosis Society \(2020\) COVID-CF project in Europe⁶**](#)

CF patient registries throughout Europe are collecting data about people with CF who become infected with SARS-Cov-2, causing the illness COVID-19. Countries that contribute annual data to the ECFS Patient Registry (ECFSPR) were invited to report COVID-19 case data of people with a confirmed diagnosis of CF. The results are presented in the ECFSPR 2020 report. However, it must be stated that the data is preliminary, incomplete, might change over time, and the number of cases is low. Therefore this information should be used only with caution and should not be used directly to assist clinical decisions.



[**Siuba M, et al Mortality in Adults with Cystic Fibrosis Requiring Mechanical Ventilation. Cross-Sectional Analysis of Nationwide Events⁷**](#)

Rationale: Survival in patients with cystic fibrosis (CF) is improving over time. Traditionally, there has been concern about high mortality in individuals with CF requiring invasive mechanical ventilation (IMV) for respiratory failure. Objectives: We hypothesized that mortality has decreased over time in this population because of improvements in disease-specific therapies. Methods: The U.S. Nationwide Healthcare Cost and Utilization Project database was used to identify adult patients with CF undergoing IMV between 2002 and 2014. Patients with nonurgent/nonemergent admissions, pregnancy, and encounters related to lung transplantation were excluded. Demographic, geographic, and comorbidities were analyzed. The Cochran-Armitage trend test was used to examine trends in mortality over time. Multivariate mixed effects logistic regression was used to account for possible differences in hospital mortality patterns. Results: We identified 58,799 CF admissions from 2002 to 2014, with 3,727 (6.3%) undergoing IMV. After exclusions, 1,711 admissions remained. In 762 (44.5%) of adult hospitalizations, the patient died. Annual mortality per hospitalization ranged from 29.9 to 55.3%. The Cochran-Armitage trend test suggested an increased probability of survival over time. Factors significantly associated with mortality in multivariate analysis included female sex (odds ratio [OR], 1.54; 95% confidence interval [CI], 1.14–2.09), acute renal failure (OR, 1.99; 95% CI, 1.32–3.01), and malnutrition (OR, 1.44; 95% CI, 1.01–2.06). IMV greater than 96 hours was associated with increased mortality in univariate analysis (OR, 1.51; 95% CI, 1.14–1.98); however, after adjustment for potential confounders, the association was no longer statistically significant (OR, 1.05; 95% CI, 0.77–1.43). Conclusions: Mortality per hospitalization in adults with CF who are not bridging to lung transplant and require emergent IMV is 44.5%, suggesting IMV is not futile. Furthermore, mortality decreased over the study period. These findings may help providers, families, and patients with CF weigh the risks and benefits of IMV for respiratory failure. These results must be interpreted with caution, however, as only 3% of the original patient sample remained after all exclusions were applied.

[**Farfour, E et al \(2020\) COVID-19 in lung-transplanted and cystic fibrosis patients: Be careful⁸**](#)

Although COVID-19 has yet to be well-described among cystic fibrosis and lung-transplanted patients, these patients are probably at major risk of



presenting a severe form of the disease. Farfour and colleagues report the case of a SARS-CoV-2 infection in a lung-transplanted patient for cystic fibrosis characterized by several singularities.

The authors conclude that lung-transplanted and cystic fibrosis patients might be at major risk of developing a severe SARS-CoV-2 infection. To date, the presentation of the disease is unknown in these patients. A wide screening is probably needed in symptomatic patients, including those presenting minor symptoms. The recovery of another pathogen should not exclude a SARS-CoV-2 infection. In the pandemic context, all these findings would help to improve the rapid identification of SARS-CoV-2-infected patients and therefore their medical management but also the implementation of specific infection prevention and control measures.

[**Poli, P et al \(2020\) Asymptomatic case of COVID-19 in an infant with cystic fibrosis⁹**](#)

Since February 2020, pandemic coronavirus disease 2019 (COVID-19) rapidly spread throughout Italy and caused varying degrees of illness, which is particularly severe in vulnerable subsets of patients. To date, only one adult case with mild symptoms of COVID-19 has been reported in Italian patients affected by Cystic Fibrosis (CF). No data are available in regard to incidence and outcomes within the paediatric CF population. Here we briefly report our first case of COVID-19 in an infant with CF.

Based on available evidence, it remains unknown why the children have such a low incidence and benign clinical course across the world. Field authorities hypothesize that this may be due to the high plasticity of their immune system, low expression of ACE2 receptors, or to the exposure of other coronaviruses which are generally common in kids. The Italian Cystic Fibrosis Research Foundation contacted all affiliated centers to obtain data on co-infection incidence in the CF population. They identified one adult and one child affected by COVID-19. While the adult presented mild symptoms, the toddler did not present any signs of the infection.



Produced by the members of the National Health Library and Knowledge Service Evidence Team†. Current as at 19 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:

	CYSTIC FIBROSIS PATIENTS
	COVID-19
	CLINICAL OUTCOMES

The following search strategy was used:

'CORONAVIRIDAE'/EXP OR 'COVID-19':AB, TI OR CORONAVIRUS:AB, TI OR 'CORONA VIRUS':AB, TI OR '2019-NCOV':AB, TI OR '2019 NCOV':AB, TI OR 'SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2':AB, TI OR 'SARS-COV-2':AB, TI OR WUHAN:AB, TI AND ADJ3:AB, TI AND VIRUS:AB, TI OR ('2019':AB, TI AND NEW:AB, TI AND CORONAVIRUS:AB, TI) OR ('2019':AB, TI AND NOVEL:AB, TI AND CORONAVIRUS:AB, TI)

AND

'CYSTIC FIBROSIS'/EXP OR ((CYSTIC NEAR/2 FIBROSIS):AB, TI) OR MUCOVISCIDOSIS:AB, TI OR MUCOVISCOIDOSIS:AB, TI OR 'PANCREAS FIBROCYSTIC DISEASE':AB, TI OR 'FIBROCYSTIC DISEASE OF PANCREAS':AB, TI OR 'FIBROCYSTIC DISEASE':AB, TI OR 'PANCREATIC CYSTIC DISEASE':AB, TI

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- ¹ COVID-19 HSE Clinical Guidance and Evidence (2020), National Clinical Programme for Cystic Fibrosis - Guidance for People with Cystic Fibrosis and their Families Regarding COVID-19 (CD19-049_001/03.04.20), available <https://hse.drsteevenslibrary.ie/COVID19V2/respiratory> [Accessed 25 May 2020]
- ² Centres for Disease, P. and Control (2020) People Who Are at Higher Risk for Severe Illness | Coronavirus | COVID-19 | CDC, available: <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/groups-at-higher-risk.html> [accessed 25 May 2020]
- ³ BMJ Best practice (2020) Management of coexisting conditions in the context of COVID-19 - Summary of relevant conditions | BMJ Best Practice, available: <https://bestpractice.bmj.com/topics/en-gb/3000190> [accessed 25 May 2020].
- ⁴ The Lancet Respiratory Medicine, 8(5), e35-e36, available: [http://dx.doi.org/10.1016/S2213-2600\(20\)30177-6](http://dx.doi.org/10.1016/S2213-2600(20)30177-6)
- ⁵ Cosgriff, R., et al (2020) 'A multinational report to characterise SARS-CoV-2 infection in people with cystic fibrosis', J Cyst Fibros, available: <http://dx.doi.org/10.1016/j.jcf.2020.04.012>
- ⁶ ECFS (2020), COVID-CF project in Europe, available <https://www.ecfs.eu/sites/default/files/general-content-images/news/ECFS%20infographic%20Week%204-2.pdf> [Accessed 25 May 2020]
- ⁷ Siuba M, Attaway A, Zein J, et al Mortality in Adults with Cystic Fibrosis Requiring Mechanical Ventilation. Cross-Sectional Analysis of Nationwide Events. *Ann Am Thorac Soc.* 2019;16(8):1017- 1023. doi:10.1513/AnnalsATS.201804-268OC
- ⁸ Farfour E, Picard C, Beaumont L, et al COVID-19 in lung-transplanted and cystic fibrosis patients: Be careful [published online ahead of print, 2020 May 10]. *J Cyst Fibros.* 2020;S1569-1993(20)30113-2. doi:10.1016/j.jcf.2020.03.021
- ⁹ Poli P, Timpano S, Goffredo M, Padoan R, Badolato R. Asymptomatic case of COVID-19 in an infant with cystic fibrosis [published online ahead of print, 2020 Apr 13]. *J Cyst Fibros.* 2020;S1569-1993(20)30096-5. doi:10.1016/j.jcf.2020.03.017