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Incidence of SARS-CoV-2 in people with cystic fibrosis in Europe between February and June 2020



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ABSTRACT

Background: Viral infections can cause significant morbidity in cystic fibrosis (CF). The current Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) pandemic could therefore have a serious impact on the health of people with CF (pwCF).

Methods: We used the 38-country European Cystic Fibrosis Society Patient Registry (ECFSPR) to collect case data about pwCF and SARS-CoV-2 infection.

Results: Up to 30 June 2020, 16 countries reported 130 SARS-CoV-2 cases in people with CF, yielding an incidence of 2.70/1000 pwCF. Incidence was higher in lung-transplanted patients (n=23) versus non-transplanted patients (n=107) (8.43 versus 2.36 cases/1000). Incidence was higher in pwCF versus the age-matched general population in the age groups <15, 15–24, and 25–49 years (p<0.001), with similar trends for pwCF with and without lung transplant. Compared to the general population, pwCF (regardless of transplantation status) had significantly higher rates of admission to hospital for all age groups with available data, and higher rates of intensive care, although not statistically significant.

Most pwCF recovered (96.2%), however 5 died, of whom 3 were lung transplant recipients. The case fatality rate for pwCF (3.85%, 95% CI: 1.26–8.75) was non-significantly lower than that of the general population (7.46%; p=0.133).

Conclusions: SARS-CoV-2 infection can result in severe illness and death for pwCF, even for younger patients and especially for lung transplant recipients. PwCF should continue to shield from infection and should be prioritized for vaccination.

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1. Background

SARS-CoV-2, the novel Severe Acute Respiratory Syndrome Coronavirus 2 causing Covid-19, was declared a pandemic in March 2020 by the World Health Organization (WHO). Western Europe was heavily affected in the first half of 2020. Covid-19 morbidity and mortality are highest in the elderly and in people with underlying chronic illnesses [1].

Cystic fibrosis (CF) arises from gene mutations in cystic fibrosis transmembrane conductance regulator (*CFTR*), which lead to chronic CF lung disease and compromised function of multiple other organ systems. Repeated cycles of respiratory infection and chronic inflammation cause progressive lung function decline. Pulmonary exacerbations can be triggered by infection with viruses such as influenza [2]. The 2009–2010 H1N1 pandemic caused significant morbidity in people with CF (pwCF) [3]. Therefore, the SARS-CoV-2 pandemic caused considerable anxiety in the CF community [4]. Early case series of pwCF in various regions who tested positive for SARS-CoV-2 suggest that pwCF have better outcomes than expected [5–8].

We aimed to assess the incidence, clinical course and outcome of SARS-CoV-2 infection in pwCF versus the general population from February to June 2020 in countries that report data to the European Cystic Fibrosis Society Patient Registry (ECFSPR).

2. Methods

2.1. Study design

This observational study was nested within the ECFSPR. We collected case reports for pwCF diagnosed with polymerase chain reaction (PCR)-confirmed SARS-CoV-2 infection between 01 February 2020 and 30 June 2020, with data follow-up until 07 January 2021. Case definitions were based on WHO guidance [9–11].

ECFSPR's 38 member countries provided data under existing ethical approvals and data governance structures. Most countries contributed data directly to ECFSPR. Belgium, France, Germany and the UK contributed via their national registries. Italy contributed via their national registry and the Italian CF society. Turkey contributed via their national registry and directly to ECFSPR. No cases were doubly reported from Italy or Turkey. ECFSPR covers 35–99% of the CF population per country [12]; 9 countries have coverage <80% (Armenia, Belarus, Bulgaria, Lithuania, Poland, Romania, Spain, Turkey and Ukraine) [12] in 2018.

The ECFSPR structure and operations have been previously described [13] (www.ecfs.eu/ecfspr). Participating pwCF provide written informed consent, including consent to use their data for future research. This provided the framework for collecting data regarding SARS-CoV-2 infection, as confirmed in writing by the ECFSPR data protection officer.

2.2. Data collected

A case report form, developed collaboratively within ECFS, was used to collect anonymized data about demographics, pre-infection CF characteristics (medical history data taken pre-infection or from 2019 registry data) and SARS-CoV-2 infection (symptoms, treatment, complications, and outcomes). Most national registries collected data in a different format, then shared a core dataset of patient-level data. One national registry shared aggregated data.

The CF population seen in the calendar year per country was from the most recent ECFSPR report (2018) [12] (and the 2017 report for France). Country-specific SARS-CoV-2 aggregate data up to 30 June 2020 for the general population (cases, deaths, hospitalizations and intensive care admissions) were from the European Centre for Disease Prevention and Control (ECDC) [14–16]. General

population data were only available by different age groups for incidence (<15, 15–24, 25–49, 50–64, 65–79, >80 years) and hospitalization/ICU (0–9, 10–19, 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, >80 years). Incidence by age group was available only for a subset of 24 countries: Austria, Belgium, Croatia, Czech Republic, Cyprus, Denmark, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden. Hospitalization/ICU data were available for a different subset of 30 countries (the 24 countries above plus Bulgaria, Estonia, Finland, Iceland, Malta, United Kingdom) [14]. Of note, pwCF are included in these data reported for the general European population.

2.3. Statistics

Standard ECFSPR definitions applied to all variables (www.ecfs.eu/projects/ecfs-patient-registry/Variables-Definitions). Percent predicted forced expiratory volume was calculated using Global Lung Initiative reference values [17]. Patient-level data were summarized, then aggregate data were added where available. Continuous data were categorized and presented as number and percentage (computed excluding missing data).

Clinical and demographic characteristics of pwCF with SARS-CoV-2 infection (and the subgroups of non-lung-transplanted and lung-transplanted pwCF) are reported using descriptive statistics. SARS-CoV-2 incidence was estimated in pwCF, and by country and age group. 95% confidence intervals (CIs) were computed using binomial exact distribution. Age-specific SARS-CoV-2 incidence rates were compared in pwCF versus the general population in corresponding countries, using the exact binomial test and p-values are provided [18]. P-values below 0.05 were considered statistically significant.

ECFSPR statisticians analyzed data using SAS (v9.4, SAS Institute Inc., Cary, NC, USA) and R v4.0. . Maps were produced using www.datawrapper.de.

3. Results

3.1. Participation and patient characteristics

Of the 38 ECFSPR member countries, 22 reported zero known cases and 16 reported 130 PCR-confirmed cases up to 30 June 2020 (Fig. 1). We also received notification of 31 patients seropositive for SARS-CoV-2 but without confirmatory PCR. We excluded these patients from analyses.

Of the 130 pwCF with SARS-CoV-2 infection, 72 (55.4%) were male and 39 (30.0%) were aged <18 years. Demographics and pre-infection disease characteristics are presented by pwCF with lung transplant (n=23) and without (n=107, including 1 patient with a liver transplant) (Table 1). Compared to those without transplant, lung-transplanted pwCF were older, had higher pre-infection BMI, higher lung function, more frequent CF-related diabetes (CFRD) and pancreatic insufficiency and lower use of CFTR modulators. Lung-transplanted pwCF more frequently used azithromycin maintenance therapy (although data were often missing for this variable).

3.2. Symptoms of SARS-CoV-2 infection in pwCF

We had data about at least one symptom for 128 pwCF, but data collection was not uniform across all countries. Of the 128 pwCF with partial data available, 101 pwCF (78.9%) had symptoms of SARS-CoV-2 infection, while 27 (21.1%) were asymptomatic. Lung-transplanted pwCF had a higher rate of symptomatic SARS-CoV-2 than non-lung transplanted pwCF (91.3% versus 76.2%). PwCF most commonly reported general symptoms (≥ 1 event of

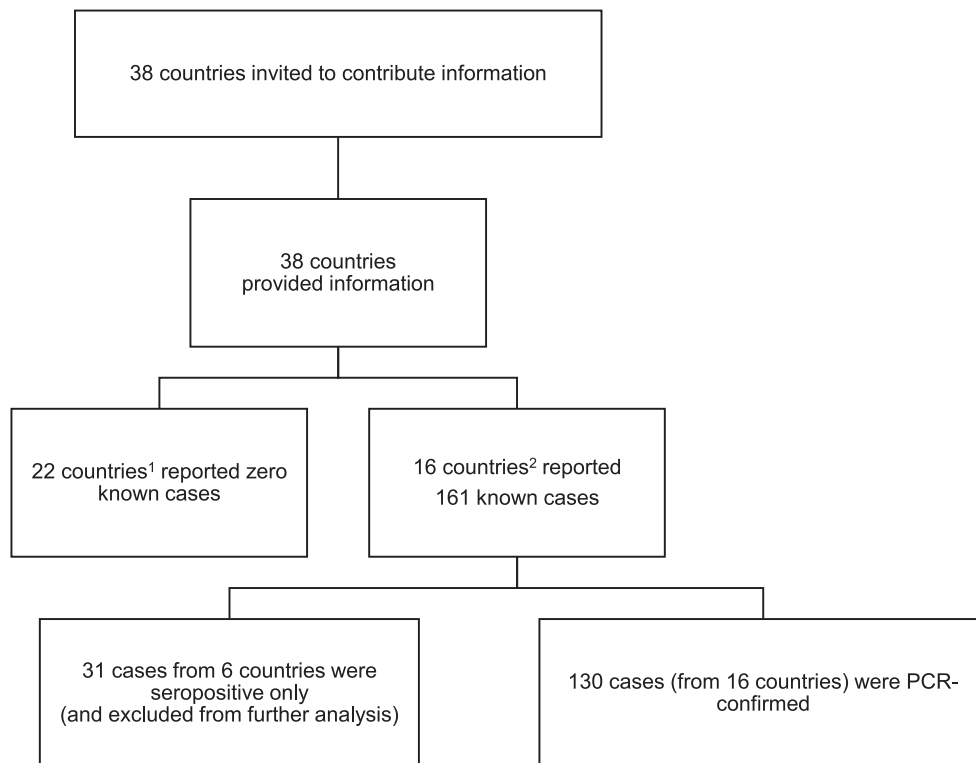


Fig. 1. Flow chart on SARS-CoV-2 data collection.

1 Albania, Armenia, Austria, Belarus, Bulgaria, Croatia, Cyprus, Czech Republic, Georgia, Hungary, Israel, Latvia, Lithuania, Luxembourg, Republic of Moldova, North Macedonia, Portugal, Romania, Serbia, Slovak Republic, Slovenia, Ukraine

2 Belgium, Denmark, France, Germany, Greece, Ireland, Italy, Netherlands, Norway, Poland, Russia, Spain, Sweden, Switzerland, Turkey, United Kingdom

fever, fatigue, headache, arthralgia/myalgia) (84/122 [68.9%] with information about these symptoms), followed by pulmonary symptoms (66/112; 58.9%) (≥ 1 event of increased cough, dyspnea, chest tightness, wheezing, sputum production, hemoptysis).

3.3. Incidence of SARS-CoV-2 infection in pwCF

The incidence of PCR-confirmed SARS-CoV-2 in pwCF (2.70 cases per 1000; 95% CI: 2.25–3.20) was not statistically different to that of the general population (3.10/1000; 95% CI: 3.10–3.11) of the entire 38-country ECFSPR area in the same period. SARS-CoV-2 infections were concentrated in Western Europe both in pwCF and the general population (Fig. 2), although this could be due to differing rates of testing between countries. Incidence per 1000 pwCF by country varied from 1.11 to 7.26, with large confidence intervals for all countries (Supplementary Table 1).

SARS-CoV-2 incidence was significantly higher in lung-transplanted pwCF (8.43/1000, 95% CI: 5.35–12.62) versus non-lung transplanted pwCF (2.36/1000, 95% CI: 1.94–2.86).

When incidence was considered by age group for the 24 countries with data for both populations, SARS-CoV-2 incidence was significantly higher in pwCF versus the general population for those aged <15, 15–24, and 25–49 years ($p < 0.001$). This pattern was maintained when incidence by age group was considered for pwCF with and without lung transplant (Fig. 3, Supplementary Table 2).

3.4. Management and outcomes

Overall, 75 pwCF (58.1%) were admitted to hospital and 12 (9.2%) to intensive care (Table 2). Lung-transplanted pwCF had higher rates than non-lung transplanted pwCF of hospital (82.6%

versus 52.8%) and intensive care (26.1% versus 5.6%) admission (Fig. 3, Supplementary Tables 4 and 5).

Compared to the general population, pwCF (regardless of transplantation status) had significantly higher rates of admission to hospital for all age groups with available data. Importantly, this pattern of higher hospitalization rates in pwCF was maintained even when we excluded pwCF lung transplant from the analysis (Fig. 3, Supplementary Table 4).

The rate of intensive care admissions was notably higher in pwCF versus the general population. Some differences were observed by age group when pwCF with and without lung transplant were compared versus the general population (Fig. 3, Supplementary Table 5), but low numbers in some subgroups prevent robust comparisons.

PwCF with SARS-CoV-2 infection were most commonly treated with additional intravenous antibiotics (49.5%) and additional oral antibiotics (36.8%) (Supplementary Table 3).

Oxygen was administered to 24/86 (27.9%) pwCF and 10/80 (12.5%) received some form of respiratory support. Five pwCF received non-invasive ventilation, 5 required invasive ventilation and 2 had an additional extracorporeal membrane oxygenation (ECMO). Most pwCF recovered (96.2%), however 5 (3.8%) died.

Of the 5 pwCF who died, 3 had received a lung transplant and 2 did not. Complete case information was available for 3 of the 5 patients who died. All 3 patients had general and pulmonary symptoms of SARS-CoV-2 infection. They were all F508del homozygous lung transplant recipients with pancreatic insufficiency and aged over 20 years at the time of SARS-CoV-2 infection. Two had CFRD. All 3 had invasive ventilation in intensive care (2 of whom required ECMO) and 2 received treatment with steroids.

Case fatality rates were calculated for pwCF and the general population of the 16 countries with SARS-CoV-2 cases in both pop-

Table 1
Demographics and pre-infection characteristics of people with cystic fibrosis with SARS-CoV-2.

	Total N=130	Non-lung transplant ¹ N=107	Lung-transplant N=23
Age, years, n (%)			
0-11	15 (11.5%)	15 (14%)	0 (0%)
12-17	24 (18.5%)	24 (22.4%)	0 (0%)
18-29	37 (28.5%)	33 (30.8%)	4 (17.4%)
30-49	49 (37.7%)	30 (28%)	19 (82.6%)
50+	5 (3.8%)	5 (4.7%)	0 (0%)
Sex, n (%)			
Female	58 (44.6%)	50 (46.7%)	8 (34.8%)
Male	72 (55.4%)	57 (53.3%)	15 (65.2%)
Genotype, n (%)			
F508del homozygous	57 (43.8%)	45 (42.1%)	2 (8.7%)
F508del heterozygous	46 (35.4%)	37 (34.6%)	9 (39.1%)
Other	27 (20.8%)	25 (23.4%)	12 (52.2%)
Unknown	0	0	0
BMI², kg/m², n (%)			
<18.5	31 (26.3%)	27 (28.1%)	4 (18.2%)
18.5-30	82 (69.5%)	64 (66.7%)	18 (81.8%)
>30	5 (4.2%)	5 (5.2%)	0 (0%)
Unknown	8	7	1
Azithromycin (maintenance therapy pre-infection), n (%)			
Yes	30 (39.0%)	23 (35.4%)	7 (58.3%)
No	47 (61.0%)	42 (64.6%)	5 (41.7%)
Unknown	53	42	11
ppFEV₁³, n (%)			
≤40%	31 (26.5%)	27 (28.4%)	4 (18.2%)
41-70%	31 (26.5%)	28 (29.5%)	3 (13.6%)
>70%	55 (47.0%)	40 (42.1%)	15 (68.2%)
Unknown	5	4	1
Pseudomonas aeruginosa⁴, n (%)			
Yes	65 (51.2%)	53 (50.5%)	12 (54.5%)
No	62 (48.8%)	52 (49.5%)	10 (45.5%)
Unknown	3	2	1
CF related diabetes, n (%)			
Yes	40 (32.0%)	26 (25.2%)	14 (63.6%)
No	85 (68.0%)	77 (74.8%)	8 (36.4%)
Unknown	5	4	1
Pancreatic insufficiency, n (%)			
Yes	82 (79.6%)	62 (75.6%)	20 (95.2%)
No	21 (20.4%)	20 (24.4%)	1 (4.8%)
Unknown	27	25	2
CFTR modulator therapy, n (%)			
Yes	31 (24.6%)	30 (29.1%)	1 (4.3%)
No	95 (75.4%)	73 (70.9%)	22 (95.7%)
Unknown	4	4	0

Abbreviations: BMI=body mass index, CFTR=cystic fibrosis transmembrane conductance regulator, ppFEV₁=percent predicted forced expiratory volume in one second

Percentages are calculated based on non-missing data.

¹This group included 1 patient with a liver transplant

² BMI was only calculated for patients aged 2 years and older. Data were not available to calculate z-scores.

³ Percent predicted FEV₁ was only calculated for patients not lung transplanted and aged 6 years and older.

⁴ In the last 12 months.

Table 2
Outcome of SARS-CoV-2 infection in people with cystic fibrosis, by lung transplant status.

	Total (N=130)	Non-lung transplant N=107	Lung-transplant N=23
Hospital admission			
Yes	75 (58.1%)	56 (52.8%)	19 (82.6%)
No	54 (41.9%)	50 (47.2%)	4 (17.4%)
Missing	1	1	0
Intensive care unit			
Yes	12 (9.2%)	6 (5.6%)	6 (26.1%)
No	118 (90.8%)	101 (94.4%)	17 (73.9%)
Missing	0	0	0
Death			
Yes	5 (3.8%)	2 (1.9%)	3 (13%)
No	125 (96.2%)	105 (98.1%)	20 (87%)
Missing	0	0	0

Abbreviations: SARS-CoV-2=Severe Acute Respiratory Syndrome Coronavirus 2

Percentages are calculated based on non-missing data

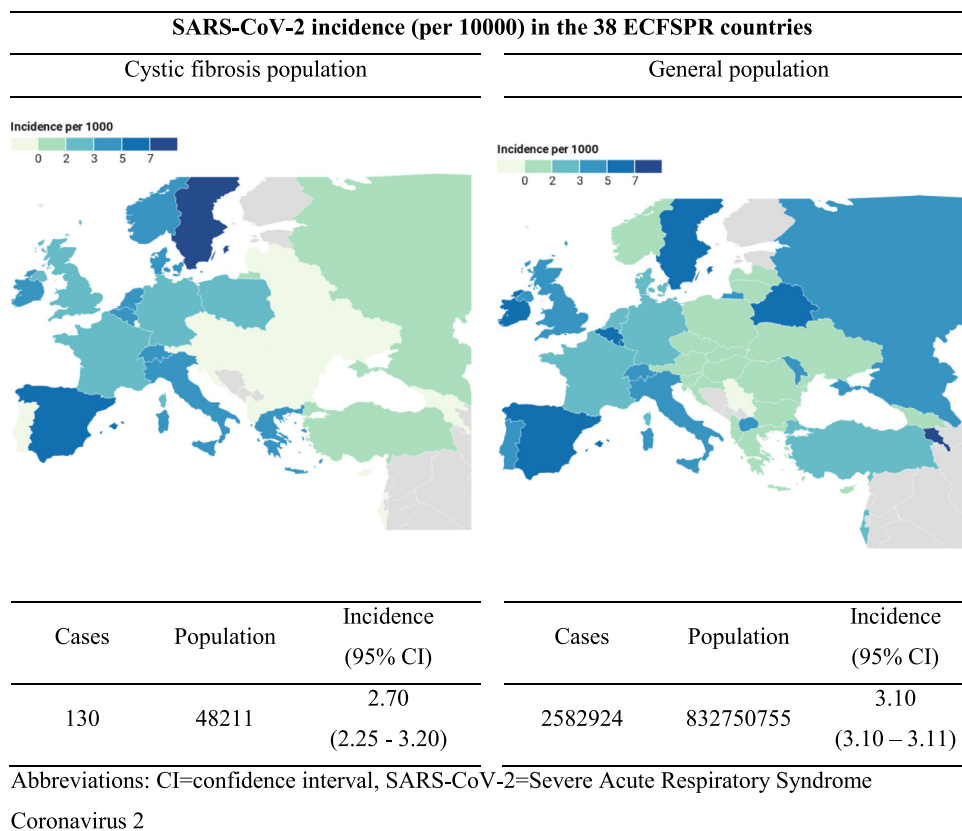


Fig. 2. Incidence of SARS-CoV-2 infection up to 30 June 2020 in people with cystic fibrosis and in the general population by country.

Abbreviations: CI=confidence interval, SARS-CoV-2=Severe Acute Respiratory Syndrome Coronavirus 2

Notes: All cases of SARS-CoV-2 in pwCF and the general population were PCR-confirmed. Incidence was calculated as (SARS-CoV-2 cases/number of people in the population)*1000.

CF population size was from the 2018 ECFSPR report.

ulations. The case fatality rate for pwCF (3.85%, 95% CI: 1.26-8.75) was non-significantly lower than that of the general population (7.46%; 95% CI: 7.43-7.49; p=0.133).

4. Discussion

We used the 38-country ECFSPR framework to collect case data about PCR-confirmed SARS-CoV-2 infection in pwCF. Up to 30 June 2020 we report that incidence was significantly higher in pwCF versus the age-matched general population, where comparisons could be made. PwCF had significantly higher rates of hospitalization, even when lung-transplanted pwCF were excluded and notably higher rates of intensive care admissions.

In the ECFSPR geographic area, the overall incidence of SARS-CoV-2 in pwCF was not significantly different to the incidence of that of the corresponding general population (2.70 versus 3.10/1000). SARS-CoV-2 was lower in pwCF versus the general population in studies from a global group (0.7/1000 versus 1.5/1000 up to mid-April 2020) [7], Spain (3.2/1000 versus 4.9/1000 up to 16 May 20) [19], France (4.1/1000 pwCF up to 30 June 20) [5], Italy (15.8/1000 versus 29.1/1000 up to November 2020) [20] and Verona, Italy (1.9/1000 versus 4/1000 up to 23 July 20) [21].

However, age represents a major confounding factor to these comparisons of incidence, due to different age distributions in pwCF versus the general population. PwCF have a shorter lifespan than the general population, with a median age of survival in the range of 40-55 years and the median age at death of 31.2 years [22]. We addressed this confounder with subgroup analysis of incidence by age group and found that SARS-CoV-2 incidence was significantly higher in pwCF versus the general population for all

age groups up to 49 years of age (p<0.001). According to the 2018 ECFSPR report, 96% of pwCF are aged below 50 years [12]. Therefore, for the vast majority of the European CF population, incidence of SARS-CoV-2 is significantly higher than in the age-matched general population.

Several caveats exist for incidence estimates. First, testing in early 2020 was restricted to symptomatic cases with usual respiratory symptoms, therefore many cases of asymptomatic or mild infections probably went undetected, both in pwCF and the general population. ECDC data show that the rate of testing for SARS-CoV-2 increased steadily throughout the reported period and varied widely between countries [23]. Second, cases could have been under-reported by overwhelmed hospital teams. Third, pwCF may have been tested more frequently than the general population due to increased vigilance and established care routines, particularly for younger age groups. Testing rates by age group are not available from the ECDC. Conversely, we also know that many CF teams switched to conducting care and clinical trial visits remotely as much as possible to minimize the risk of exposure [19, 24] which could have led to missed opportunities to test asymptomatic and mildly ill pwCF for SARS-CoV-2 infection. Fourth, comparing incidence by country (either in our study or in other published reports) is difficult due to differing impacts of the pandemic, case definitions and public health measures between countries. Fifth, pwCF and their families are expert in infection control. Anecdotal evidence suggests that they took early action to avoid infection and effectively started lockdown or shielding earlier than it was imposed in countries across Europe to proactively avoid infection [25]. Sixth, we do not know details about the type of PCR tests

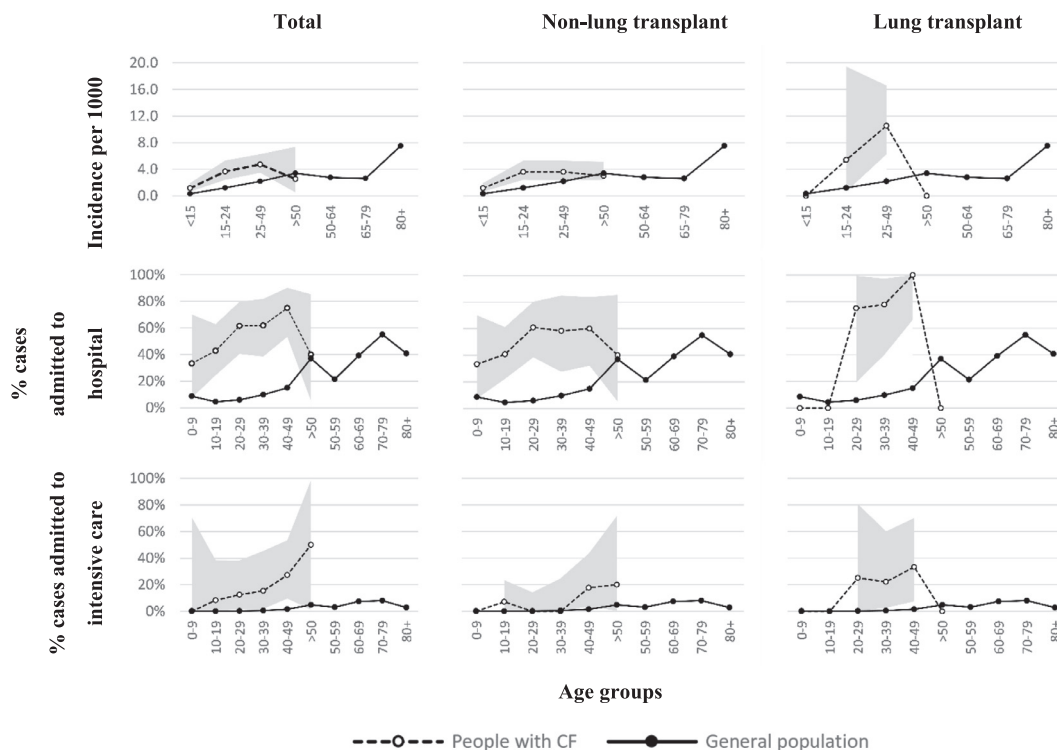


Fig. 3. Incidence and rates of hospitalization and intensive care admission by age group and transplant status in people with cystic fibrosis compared to the general population.

Notes: Confidence intervals shown as grey shaded area. People with CF aged ≥ 50 years were grouped together due to low numbers.

The 24 countries included in age-banded analysis of incidence in people with CF and the general population were: Austria, Belgium, Croatia, Czech Republic, Cyprus, Denmark, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden.

The 30 countries included in age-banded analysis of hospital and intensive care admission in people with CF and the general population were the 24 countries above plus Bulgaria, Estonia, Finland, Iceland, Malta, United Kingdom.

used to diagnosis SARS-CoV-2 infection in pwCF across the different countries. PCR tests vary in brand, sensitivity and the platform used [26]. Given these caveats, the true incidence in pwCF will only become apparent with large scale, comprehensive and timely serological studies.

Nonetheless, our data show the importance that pwCF continue to protect themselves from infection by maintaining good lung health (via exercise, physiotherapy and medical treatment) and by shielding, reducing social contacts, wearing a mask and maintaining high standards of hand hygiene.

4.1. Disease course and outcomes

SARS-CoV-2 caused symptomatic illness in 101/128 (78.9%) of our cohort, where data about symptoms were available, lower than the 82–100% reported in other studies in CF [5, 7, 19] but comparable to the reported rate of symptomatic illness in the general population in the first half of 2020 (80%) [27]. In our cohort of pwCF, the most common symptoms were general or pulmonary, in line with symptoms commonly experienced by the general population. Just over half of pwCF with SARS-CoV-2 were admitted to hospital and 9.2% were admitted to intensive care. PwCF were more frequently admitted to hospital and intensive care than the general population in all age groups up to 49 years (after which age too few cases in pwCF are available for robust comparison). The use of hospitalization as a proxy for severe Covid-19 should be interpreted with caution, as hospitalization could have been precautionary, or for reasons other than Covid-19. Of note, a meta-analysis has identified male sex as a risk factor for death and intensive care admission in the general population [28]. It is therefore possible

that the over-representation of male pwCF in our cohort (55.4%) could have partly driven rates of intensive care.

The case fatality rate in pwCF was lower (but not significantly) than the general population (3.85% vs 7.46%, $p=0.133$). More data is required to confirm this, and to untangle whether this could be due to the younger age and/or the absence of other risk factors for more severe course of the infection in our cohort of pwCF with SARS-CoV-2, or the heterogeneous testing and reporting between countries.

People with solid organ transplants have an increased risk of severe disease from SARS-CoV-2 infection [29]. ECFSPR 2018 data report that 1816 pwCF (4.4% of the ECFSPR population) were living with a lung transplant [12], representing a large group at risk for severe complications if infected with SARS-CoV-2. Our cohort included 23 pwCF with lung transplant. Upon SARS-CoV-2 infection, lung-transplanted pwCF were more frequently symptomatic, were admitted to hospital 1.7-fold more frequently and required intensive care 8-fold more frequently than pwCF without lung transplant. Previous studies also found that solid organ transplant recipients require more treatment and medical care upon SARS-CoV-2 infection, whether transplant was for CF [5, 7] or other reasons [30, 31].

4.2. Limitations and future directions

Our study had several limitations, as well as the caveats related to testing and incidence discussed above. Throughout the study period, countries had differing impact of the pandemic and heterogeneous access to testing. Case definitions were also heterogeneous between countries, as reflected in the different case definitions in published studies in CF [5, 7, 19, 21]. Reporting to ECFSPR was vol-

untary, therefore cases may be under-reported with possible selection bias for more severe cases. In addition, ECFSPR has low coverage in some countries, especially in Eastern Europe [12]. Since these countries reported a low incidence of SARS-CoV-2 in the general population during our study period, we do not believe this to be problematic. However, it could however skew future updates of incidence, as SARS-CoV-2 cases have risen significantly in these countries since summer 2020, whether through increased testing or increased impact of the pandemic. The denominator for calculating SARS-CoV-2 incidence in pwCF was from the 2018 ECFSPR report. It is possible that the CF population has increased since then. In some countries and regions, lung transplanted pwCF are treated by another care team or at another hospital. Therefore, it is possible that some lung-transplanted pwCF no longer participate in ECFSPR and the number of infections in pwCF living with a transplant could be under-reported here. Of note, pwCF from 11 countries in our study were also included in the global study [7] and in national or center-based studies [5, 19, 21, 32] in pwCF.

We sourced comparator data for the general population from the ECDC and included only pwCF with PCR-confirmed SARS-CoV-2 to facilitate comparisons. However, ECDC datasets were limited to certain subsets of countries and age groups, forcing us to exclude some cases in pwCF from comparisons.

Finally, some comparisons reported here should be interpreted with caution due to low sample sizes, particularly in subgroup analyses. We are currently enlarging our dataset by collecting cases up to the end of 2020. This will increase the robustness of our analyses and will facilitate multivariate analyses to identify risk factors associated with severe disease and worse outcomes. We also plan to assess the long-term effect of SARS-CoV-2 infection on lung function and pulmonary exacerbations in pwCF, as well any effects of concomitant CFTR modulator therapy. This is important since pulmonary exacerbation and lung function decline have been previously associated with viral infection by H1N1 [3], RSV [2] and influenza B [33].

5. Conclusion

Since the case cutoff of 30 June 2020 in this study, the number of cases has risen significantly, with expansion into Eastern Europe (1126 cases reported up to 08 March 2021, www.ecfs.eu). At the time of writing, several vaccines have been approved by the EMA and vaccination campaigns have started. Here we show that, versus the age-matched general population, pwCF have a higher incidence of SARS-CoV-2 infection and hospitalization, especially lung-transplanted pwCF. Although more data are required to confirm these findings, it is clear that SARS-CoV-2 infection can result in severe illness and death for pwCF, especially for those with lung transplants. PwCF should continue to protect their health by shielding and maintaining good adherence to treatments and exercise. Governments should prioritize pwCF of all ages for vaccination, by listing CF as an underlying condition with an increased risk of more severe disease.

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All authors have read and agreed to the published version of the manuscript.

Declaration of Competing Interest

Dr. Naehrlich reports that he has received institutional fees for site participation in clinical trials from Vertex Pharmaceuticals and Boehringer Ingelheim; Dr. Orenti has nothing to disclose; Dr. Dunlevy reports institutional grants from Chiesi, during the conduct of the study; Dr. Kasmi has nothing to disclose; Dr. Harutyunyan has nothing to disclose; Dr. Pflieger has nothing to disclose; Dr. Bobrovnichy has nothing to disclose; Dr. Keegan has nothing to disclose; Dr. Daneau has nothing to disclose; Dr. Petrova has nothing to disclose; Dr. Bambir has nothing to disclose; Dr. Vukić Dugac has nothing to disclose; Dr. Tješić-Drinković has nothing to dis-

close; Dr. Yiallourous has nothing to disclose; Dr. Drevinek reports personal fees from Vertex Pharmaceuticals, outside the submitted work; Prof. Milan Macek reports grants from Vertex Pharmaceuticals, outside the submitted work; Mrs. Bilkova has nothing to disclose; Dr. Olesen has nothing to disclose; Dr. Burgel reports personal fees from Astra-Zeneca, personal fees from Boehringer Ingelheim, personal fees from Chiesi, personal fees from GSK, personal fees from Insmmed, personal fees from Novartis, personal fees from Pfizer, grants and personal fees from Vertex, personal fees from Zambon, outside the submitted work; Dr. Corvol has nothing to disclose; Ms. Lemmonier has nothing to disclose; Dr. Parulava has nothing to disclose; Dr. Hatziagorou has nothing to disclose; Dr. Diamantea has nothing to disclose; Dr. Párniczky has nothing to disclose; G. Fletcher has nothing to disclose; Prof. McKone reports travel support from A Menarini, speaker fees from Roche Pharmaceuticals, consultancy fees from Insmmed, consultancy fees from Janssen Pharmaceuticals, grants to institution and consultancy fees from Vertex, outside the submitted work; Dr. Mei-Zahav has nothing to disclose; Dr. Padoan has nothing to disclose; Dr. Salvatore has nothing to disclose; Dr. Colombo has nothing to disclose; Dr. Aleksejeva has nothing to disclose; Dr. Malakauskas has nothing to disclose; Dr. Schlesser has nothing to disclose; Dr. Fustik has nothing to disclose; Dr. Turcu has nothing to disclose; V. Gulmans has nothing to disclose; D. Zomer-van Ommen has nothing to disclose; Dr. Wathne has nothing to disclose; Dr. Bakkeheim has nothing to disclose; Dr. Woźniacki has nothing to disclose; Dr. Pereira has nothing to disclose; Dr. Pop has nothing to disclose; Dr. Kondratyeva has nothing to disclose; Dr. Amelina has nothing to disclose; Dr. Zhekaite has nothing to disclose; Dr. O. Simonova has nothing to disclose; Dr. Kashirskaya has nothing to disclose; Dr. Rodic has nothing to disclose; Dr. Kayserova has nothing to disclose; Dr. Krivec has nothing to disclose; Dr. Mondejar-Lopez has nothing to disclose; Dr. Pastor-Vivero has nothing to disclose; Dr. de Monestrol reports grants from Vertex, outside the submitted work; Dr. Lindblad has nothing to disclose; Dr. Dogru has nothing to disclose; Dr. Gokdemir has nothing to disclose; Dr. Pekcan has nothing to disclose; Dr. Makukh has nothing to disclose; Dr. Brownlee has nothing to disclose; Ms. Cosgriff has nothing to disclose; Mr. McClenaghan has nothing to disclose; Dr. Carr reports personal fees from Chiesi Pharmaceuticals, personal fees and non-financial support from Vertex, personal fees from Zambon, personal fees from Insmmed, outside the submitted work; Dr. Lammertyn has nothing to disclose; Dr. Zolin has nothing to disclose; Ms. Fox reports grants from ECFS, during the conduct of the study; Mr. Krasnyk has nothing to disclose; Mrs. Van Rens has nothing to disclose; Dr. van Koningsbruggen-Rietschel reports grants and personal fees from Algipharma (HORIZON2020), personal fees from Deutsches Zentrum für Infektionsforschung, personal fees from Antibio, personal fees from Proteostasis, personal fees from Roche, personal fees from Vertex, outside the submitted work; Dr. Jung reports grants from Chiesi Pharmaceuticals, during the conduct of the study.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.jcf.2021.03.017](https://doi.org/10.1016/j.jcf.2021.03.017).

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