EUROPEAN RESPIRATORY *journal*

FLAGSHIP SCIENTIFIC JOURNAL OF ERS

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Original research article

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Please cite this article as: Beltramo G, Cottenet J, Mariet A-S, *et al*. Chronic respiratory diseases are predictors of severe outcome in COVID-19 hospitalised patients: a nationwide study. *Eur Respir J* 2021; in press (https://doi.org/10.1183/13993003.04474-2020).

This manuscript has recently been accepted for publication in the *European Respiratory Journal*. It is published here in its accepted form prior to copyediting and typesetting by our production team. After these production processes are complete and the authors have approved the resulting proofs, the article will move to the latest issue of the ERJ online.

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Chronic respiratory diseases are predictors of severe outcome in COVID-19 hospitalized patients: a nationwide study

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Abstract

Background: Influenza epidemics were initially considered to be a suitable model for the COVID-19 epidemic, but there is a lack of data concerning patients with chronic respiratory diseases (CRD), who were supposed to be at risk of severe forms of COVID-19.

Methods: This nationwide retrospective cohort study describes patients with prior lung disease hospitalized for COVID-19 (March-April 2020) or influenza (2018-2019 influenza outbreak). We compare the resulting pulmonary complications, need for intensive care and in-hospital mortality depending on respiratory history and virus.

Results: In the 89,530 COVID-19 cases, 16.03% had at least one CRD, which was significantly less frequently than in the 45,819 seasonal influenza patients. Patients suffering from chronic respiratory failure, chronic obstructive pulmonary disease, asthma, cystic fibrosis and pulmonary hypertension were underrepresented, contrary to those with lung cancer, sleep apnea, emphysema, and interstitial pulmonary diseases (ILD). COVID-19 patients with CRD developed significantly more ventilator-associated pneumonia and pulmonary embolism than influenza patients. They needed intensive care significantly more often and had a higher mortality rate (except for asthma) when compared to patients with COVID-19 but without CRD, or patients with influenza.

Conclusion: Patients with prior respiratory diseases were globally less likely to be hospitalized for COVID-19 than for influenza but were at higher risk of developing severe COVID-19 and had a higher mortality rate compared to influenza patients and patients without a history of respiratory illness.

Keywords: COVID-19; influenza; chronic respiratory diseases, pulmonary diseases, lung fibrosis, COPD, administrative data; SARS-CoV-2;

Funding: The project was funded by the French National Research Agency

Take home message

There was a higher risk of developing severe COVID-19 and a higher mortality rate among patients with chronic respiratory disease.

Our data suggest that these patients should have priority access to SARS-CoV2 vaccination.

Introduction

On March 11, 2020 a global pandemic caused by a new coronavirus (SARS-CoV-2) was declared. The virus, which was first identified in December 2019, is responsible for coronavirus disease (COVID-19), a new disease with a predominant respiratory tropism.

Patients suffering from chronic respiratory diseases (CRD) such as chronic respiratory failure, asthma, chronic obstructive pulmonary disease (COPD), interstitial lung diseases (ILD), pulmonary hypertension (PH), sarcoidosis or cystic fibrosis (CF), were immediately considered to be at risk of severe forms of COVID-19 (1). Indeed, COVID-19 is responsible for various respiratory symptoms, from cough with dyspnea to acute respiratory distress syndrome (ARDS) in its most severe presentation (2,3). In parallel, it has been shown that COVID-19 patients have an increased risk of venous thromboembolic disease (4). There is concern that the respiratory complications of COVID-19 could be deleterious in patients with prior CRD. However, clinical experience and published data covering the outbreak period have suggested that there was a surprisingly low proportion of patients with CRD among patients with COVID-19, especially in its most severe forms (1,5,6).

Other viral respiratory diseases, and in particular influenza, are well known for their ability to induce severe respiratory complications (7), including ARDS, mainly in frail elderly people and in patients with severe comorbidities (obesity, diabetes, heart or respiratory failure).(8) Thus, the first Chinese and Italian epidemiological data, both on the mode of transmission and the respiratory tropism of the SARS-CoV-2, initially led to a comparison of the pandemic with influenza epidemics in terms of spread and mortality (5). This also explains the early recommendations for the prevention of the spread of SARS-CoV-2 infection, which were heavily based on knowledge acquired through the management of influenza epidemics. Existing knowledge of influenza was also used to define populations at risk of severe disease, particularly individuals with CRD.

In a previous study by our group (9), including 89,530 in patients with COVID-19 identified over a two-month period and 45,819 seasonal influenza inpatients identified over a three-month period, we found that patients diagnosed with COVID-19 were significantly less likely to have a history of CRD than patients hospitalized for influenza.

The aim of our study was therefore, using the French national hospital database, to describe and compare CRD in hospitalized patients suffering from COVID-19 or influenza (2018-2019 season), and to describe and compare respiratory complications for COVID-19 patients with CRD to COVID-19 patients without CRD and to influenza patients.

Methods

Database

A retrospective cohort study was conducted using the national *Programme de Médicalisation des Systèmes d'Information* (PMSI) database, which is designed to include discharge summaries for all inpatient admissions to public and private hospitals in France. Diagnoses identified during the hospital stay are coded according to the 10th edition of the International Classification of Diseases (ICD-10), and procedures performed during hospitalisation are coded according to the French Common Classification of Medical Procedures (CCAM).

Study design and participants

Using the methodology described in the study by Piroth *et al.*(9), all patients hospitalized for COVID-19 from March 1st, 2020, to April 30th, 2020, were included and identified by the primary diagnoses (PD), related diagnoses (RD) or associated diagnoses (AD) by the ICD-10 codes U0710, U0711, U0712, U0714 or U0715, regardless of their age (i.e. 89,530 COVID-19 patients). For the influenza cohort, all patients hospitalized during the 2018-2019 influenza outbreak period (admitted from December 1st, 2018, to February 28th, 2019), and identified by ICD-10 codes J09, J10 or J11 (as PD, RD or AD) were included, whatever their age (i.e. 45,819 influenza patients).

For each inpatient stay, we extracted age, sex, transfer to an intensive care unit (ICU), and hospital death. We also identified all diagnoses recorded in the discharge abstracts for the included hospital stays (COVID-19 and influenza) related to CRD (chronic respiratory failure (CRF), lung cancer, PH, obstructive sleep apnea (OSA), COPD, emphysema, asthma, pulmonary sarcoidosis, interstitial lung disease (ILD), CF with pulmonary manifestations) and respiratory complications (acute respiratory failure, pulmonary embolism, ventilator-acquired pneumonia (VAP), pneumocystis pneumonia, aspergillosis pneumonia, pleural empyema, lung abscess, pneumothorax). We considered that patients suffered from VAP if they presented a community-acquired pneumonia and had a ventilation procedure. We also collected data on obesity, diabetes, hypertension, heart failure and atherosclerotic heart disease. ICD-10 and CCAM codes used are presented in **Supplementary Table 1**.

This study was approved by the *Comité Ethique et Scientifique pour les recherches, les études et les évaluations dans le domaine de la santé* (CESREES, Ethics and Scientific Committee for Research, Studies and Evaluation in Health, June 9 2020) and the Institut des Données de Santé (INDS, French Institute of Health Data, registration number 1611357, June 15, 2020) and authorized by the *Commission Nationale de l'Informatique et des Libertés* (CNIL, French Data Protection Authority, registration number DR-2020-250, July 3, 2020).

Statistical analysis

We described and compared age, sex and all diagnoses related to CRD in patients hospitalized for COVID-19 or influenza. We also compared these CRD in COVID-19 and influenza patients, depending on age grouped into nine classes (under 18, 18-30, 31-40, 41-50, 51-60, 61-70, 71-80, 81-90 and > 90).
For each CRD, we then described and compared the need for ICU, in-hospital mortality and all diagnoses related to respiratory complications in the COVID-19 and seasonal influenza groups.
Next, we compared the need for ICU, in-hospital mortality and all diagnoses related to respiratory complications in the COVID-19 group between patients with and without CRD. COVID-19 patients with CRD were considered as a whole and then separately for each CRD in the sensitivity analyses. In the first sensitivity analysis, we classified our CRD patients as a single category. When several CRD codes were listed in the patient's discharge abstract, we prioritized in order to retain only one, in the following order: CF with pulmonary manifestations, lung cancer, COPD, asthma, pulmonary sarcoidosis, ILD, emphysema, OSA, PH and CRF (we selected the first CRD in this list). The second sensitivity analysis, to overcome the difficulty in prioritizing CRD, included patients with only one CRD.

All identified respiratory diseases or complications are accounted for in relation to the patient. In other words, if a patient had one of the conditions at least once during one of the stays for COVID-19 or for influenza, then the patient is considered to have had the condition.

Categorical data are provided as frequencies (percentage). Continuous data are provided as means ± standard deviation (SD) and as medians [interquartile range (Q1-Q3)].

The different variables studied were compared using the Chi-2 test or the Fisher's exact test for categorical data and Student's t test or Mann-Whitney test for continuous data.

To estimate the risk of transfer to an ICU and the risk of in-hospital death in COVID-19 patients with or without CRD, we performed three logistic regressions adjusting on obesity, diabetes, hypertension, heart failure, atherosclerotic heart disease, sex, and age as a continuous variable. First, a global model including CRD overall; second, we used the same model with CRD as disjunctive variables using the prioritization defined above (1^{st} sensitivity analysis); and third, a model with CRD as disjunctive variables for patients with only one CRD (2^{nd} sensitivity analysis). For each of the models, patients without CRD were considered as the reference. Adjusted odds ratios (aOR) with 95% confidence intervals (95% CI) are given.

The statistical significance threshold was set to < 0.05. All analyses were performed using SAS (SAS Institute Inc, Version 9.4, Cary, NC).

Results

The characteristics of the patients suffering from CRD among the 89,530 COVID-19 patients and the 45,819 influenza patients and for each of the viral epidemics are detailed in **Table 1**. Among the patients suffering from COVID and seasonal influenza, respectively 14,351 (16.03%) and 9,131 (19.93%) presented at least one CRD. Among COVID patients with CRD, 80.91% of them had only one CRD. There were significantly fewer patients with a history of chronic respiratory failure, COPD, asthma, CF and PH in the COVID-19 compared to the seasonal influenza cohort ($p<0.0001$ for all). On the contrary, COVID-19 patients were more likely to have a diagnosis of lung cancer, OSA, emphysema and ILD ($p<0.0001$ for all, except for lung cancer, $p=0.0098$). The proportion of pulmonary sarcoidosis did not significantly differ between the two groups. After stratification by age (Supplementary **Table 2**), lung cancer and emphysema were more often found among elderly COVID-19 patients (81-90 years and >71 years respectively), whereas sleep apnea was more often found in younger patients (31-40 years). PH, COPD, asthma and CF were less frequent among COVID-19 patients regardless of age strata, except, interestingly, for asthma in patients under 18 years.

Among the patients with CRD, we described and compared disease progression and prognosis in case of SARS-CoV2 or influenza infection. For the respiratory complications in patients with CRD stratified by disease (**Table 2 and Supplementary Table 3**), we found that COVID-19 patients developed significantly more VAP than influenza patients. Regarding underlying CRD, VAP was significantly more frequent in COVID-19 patients suffering from PH, sleep apnea, emphysema, asthma, pulmonary sarcoidosis and ILD. However, VAP was significantly more frequent for influenza patients suffering from CRF or lung cancer. No difference was observed for COPD and CF. On the contrary, COVID-19 patients presented pulmonary embolism significantly more often than influenza patients, except for those with lung cancer or pulmonary sarcoidosis. In the COVID-19 group, patients diagnosed with OSA, asthma, pulmonary sarcoidosis and ILD were significantly more likely to require intensive care than the other patients (**Table 2**). In contrast, in the influenza group, patients with chronic respiratory failure, lung cancer and COPD were significantly more often treated in ICU. Concerning in-hospital mortality (**Table 2**), patients with CRD were significantly more likely to die in the COVID-19 group, except for patients with CF.

Next, we compared the occurrence of respiratory complications, need for ICU, and mortality in patients suffering from COVID-19 with and without CRD. We observed a significant increase in the occurrence of each complication (except for pneumocystis pneumonia), need for ICU, and mortality in patients with CRD (**Table 3**). In multivariate analyses, the risk of both ICU care and in-hospital mortality was increased for COVID-19 patients with CRD compared to COVID-19 patients without CRD (aOR=1.34 [1.28-1.41] and aOR=1.19 [1.14-1.25] respectively). The 1st sensitivity analysis using CRD prioritization (**Table 4**) showed that COVID-19 patients with lung cancer, COPD, sleep apnea, emphysema and ILD had significantly more complications (for most complications) than COVID-19 patients without CRD. With the exceptions of CF and pulmonary sarcoidosis, patients with CRD had significantly more acute respiratory failure. With the exception of CF and CRF, patients with CRD had significantly more VAP. Excluding CF, lung cancer and CRF, all other CRD increased significantly the risk of need of ICU (**Table 4** and crude OR in **Table 5**). Excluding CF, asthma and emphysema, all other CRD increased significantly the risk of in-hospital death (**Table 4** and crude OR in **Table 5**). It should be noted that lung cancer reduced the risk of VAP and need for ICU and that asthma reduced the risk of in-hospital death. In multivariate analyses in COVID-19 patients (**Table 5)**, we still found that, compared to patients without CRD, lung cancer reduced the risk of needing ICU (aOR=0.77 [0.63-0.94]), while the other CRD increased it (except for CF and CRF). Concerning mortality, multivariate analysis (**Table 5)** showed that sleep apnea and PH were no longer associated with the risk of death, while pulmonary sarcoidosis became associated with this risk (aOR=2.11 [1.36-3.26]). Because of the relationship between OSA and obesity (36.5% of obesity in OSA patients and 7.11% in patients without CRD), we took into account this possible interaction in our model, but it did not influence our results. The other CRD were still associated with the risk of in-hospital death (except for emphysema). This was particularly true for lung cancer, which multiplied the risk of death by more than 3.5 (aOR=3.67 [3.20-4.21]).

The results of the 2nd sensitivity analysis, including COVID-19 patients with only one CRD, were generally consistent with the previous results (**Supplementary Tables 4 and 5).** However, patients with COPD were no longer associated with the risk of needing ICU care, and patients with ILD were no longer associated with the risk of in-hospital death in multivariate analysis (**Supplementary Table 5**).

Discussion

This nationwide survey highlights that patients with COPD, asthma and chronic respiratory failure were less frequent among patients hospitalized during the first wave of the COVID-19 epidemic when compared with previous seasonal influenza epidemics. In contrast, patients with lung cancer, OSA, emphysema, and ILD were overrepresented among patients hospitalized for COVID-19 when compared with influenza. Compared to COVID-19 patients without CRD, those with CRD were more likely to need ICU care and to die. However, patients with chronic respiratory failure, lung cancer and COPD in the COVID-19 group were significantly less likely to be admitted to intensive care compared to the influenza group. Moreover, when comparing risk of requiring intensive care, we observed that patients with lung cancer were admitted less frequently than patients without CRD, which may have been the result of ethical considerations during the crisis. However, all patients with a respiratory

disease in the COVID-19 group had a higher mortality risk compared with the influenza group.

Obesity (10), diabetes (11), hypertension (12) and especially age (13) have been widely described as the main risk factors for developing severe forms of COVID-19. On the contrary, patients with respiratory diseases, in particular asthma and COPD, seem to be less likely to be severely affected (12,14–17). For example, two studies conducted in the New York City area, which was an early COVID-19 hotspot, found that COPD was a comorbid condition in only 5.4% of cases (18,19), while it was found in 18% of patients hospitalized for influenza from November 15, 1999, to April 15, 2000 (20). Regarding asthma (3.66% in our national COVID-19 cohort), a low prevalence is also generally reported (21,22), with some exceptions (23). This is also the case with patients with CF, for whom the incidence of severe COVID-19 seems to be lower than in the general population (24,25).

Our study adds data for COPD, asthma, and CF, which were also less frequent in the COVID-19 group. This could be explained by several reasons. First, these fragile individuals may have been more careful and implemented more strict preventive measures, as already reported (17,26). Second, the general lockdown applied during most of the study period led to a considerable decrease in air pollution (27), which is known to favor lung disease exacerbation (28), even in COVID-19 (29). Third, the COVID-19 epidemic occurred later in the year than influenza, and the weather was unusually warm. Since the cold is also described as influencing respiratory health, the effect of climate could be advocated here (30). Fourth, COPD, asthma, and CF are often treated by inhaled corticosteroids (ICS). This treatment might have protected against COVID-19 since some in-vitro models show that certain ICS suppress coronavirus replication and cytokine production (14,31). However no study has confirmed this hypothesis, and there is currently no evidence that ICS use protects against COVID-19 (26,32,33).

On the contrary, emphysema, lung cancer, ILD, and OSA were more frequent in patients hospitalized for COVID-19 than for influenza. The results for emphysema and lung cancer differed according to patient age. There were more patients with emphysema only among hospitalized COVID-19 patients older than 70 years. The same was observed for lung cancer, which was only significantly more present in elderly patients (81 to 90 years) in the COVID-19 group. No previous data support an increased risk of COVID-19 for these two conditions. The difference between emphysema and COPD seemed to be linked to the patient's profile. Indeed, only 30% of patients with emphysema had COPD and only 3.3% had ILD (combined pulmonary fibrosis and emphysema). These cases may correspond to smokers with emphysema but without obstructive syndrome. COVID-19 patients had significantly more emphysema in the oldest age groups; these were probably patients with emphysema without obstructive syndrome, for whom age seems to be the most important risk factor for developing COVID-19. Some publications underline the risk of severe COVID-19 and increased mortality risk in patients with interstitial lung disease (34). However, Guiot *et al*. found that only 1% of patients with interstitial lung disease were hospitalized for COVID-19 (1 in ICU) among 401 patients in a single Belgian center (35). Our results suggest the need to be cautious regarding ILD patients and the risk of SARS-Cov2 infection.

The high prevalence of OSA syndrome in the population of patients hospitalized for COVID-19 could be explained by the fact that the risk factors for severe SARS CoV-2 pneumonia (obesity, hypertension and diabetes, as previously described) are also well-known comorbidities of OSA (36). Accounting for a potential interaction between obesity and OSA did not change our results for ICU and mortality risk. Moreover, OSA has been identified as a risk factor for severe COVID-19 (including hospitalization, ICU admission, mechanical

ventilation, or death (37)), and it may be an important predictor of poor outcomes in obese patients (38).

We identified several key points in our analysis of pulmonary complications and prognosis in patients hospitalized for COVID-19 with a history of respiratory disease. First, these patients developed significantly more VAP. Previous work reports that COVID-19 patients developed less respiratory bacterial co-infections than patient hospitalized for influenza (39). The small number of patients with COVID-19 who developed respiratory bacterial co-infections made it possible (due to a lack of specific code for VAP and inconsistent ICU practices) to consider community-acquired pneumonia crossed with codes for ventilation acts as VAP. Secondly, they developed significantly more pulmonary embolism than patients hospitalized for influenza and significantly more pulmonary complications than patients without CRD hospitalized for COVID-19 (40). Third, we found that patients hospitalized for COVID-19 and presenting CRD were more likely to be admitted to ICU, and mortality was increased compared with both patients hospitalized for influenza (except for lung cancer and COPD) and patients hospitalized for COVID-19 without CRD. These data confirm that pulmonary diseases including chronic respiratory failure and asthma are associated with a risk of severe disease and mortality in SARS-CoV-2 infection, as indicated by national studies in the UK (31) and Sweden (41). Nevertheless, while Bloom *et al.* observed an increased mortality for patients with severe asthma and COVID-19, we observed a significant decrease in mortality compared to patients without CRD. This decrease could be explained by protective effect of ICS, as previously suggested by Bloom *et al*., and by the small proportion (around 10% - 10.8% in Bloom's study) of severe asthma in our nationwide population. In COVID-19 patients with COPD (5.4%), admission to intensive care was less frequent, but we also observed higher in-hospital mortality in the COVID-19 than in the influenza group. These data are consistent with previously cited publications and several reviews (42,43). In contrast to influenza infection, only few publications underline the role of CRD in the development of severe forms of COVID-19 and even less so for hospital admission for COVID-19. This can be seen in a meta-analysis by Zheng *et al.* (44), which reported that underlying respiratory disease had an odds ratio of 5.15 for critical care or death. Regarding mortality, Khan *et al.* found that the mortality risk in COVID-19 doubled in patients with respiratory disease (45)

We were unable to assess whether vaccination against influenza could explain the differences in morbidity and mortality in our study. Indeed, influenza vaccination, which is recommended for patients with CRD, may have protected them from most severe forms of influenza. Regardless, our data suggest that this category of patients should benefit from greater vigilance and be hospitalized at the slightest clinical sign of severe COVID-19. A more aggressive therapeutic approach may also be worth considering. Finally, our data suggest that patients with CRD should have priority access to the SARS-CoV2 vaccination.

Our study has several limitations. Firstly, there may have been testing biases between viruses because probably more patients were tested for COVID-19 than for influenza during the 2018-19 season. Testing practices were also more standardized during the sanitary crisis than during typical seasonal influenza epidemics. However, tests systematically done in the ambulatory setting for COVID-19 likely did not influence the number of hospitalized patients, particularly those admitted to intensive care units. Secondly, the comparison between COVID-19 and seasonal influenza was done on two different years and the 2018-2019 influenza season is not necessarily representative of all seasonal influenzas, even if it was one of the most severe epidemic in the past 5 years in France. Though some COVID-19 patients may have had influenza at the same time, the influenza epidemic was ending at the start of the COVID-19 epidemic, limiting this possibility. Our study concerns only hospitalized patients, and the characteristics of patients who died from COVID-19 outside of hospitals

may not reflect those described in our study. For respiratory history, certain CRD may have been diagnosed during hospitalization, potentially inducing a bias regarding the increased number of these diseases. For COVID-19 patients, this bias could include lung cancer, emphysema and ILD due to the more frequent use of computed tomography (CT) pulmonary angiogram for COVID-19 diagnosis, and because of the risk of pulmonary embolism, as previously reported (46). Another possible limitation is misclassification-related or under-detection-related bias for comorbidities even if coding quality is checked by medical information professionals in each hospital to correct diagnoses and to increase the recorded comorbidity level. These potential biases may concern comorbidities which were only identified during the stays for COVID-19 or for influenza, seeing as we cannot always distinguish between acute and chronic conditions. However, this misclassification bias is likely to be non-differential for the majority of comorbidities, except for ILD, for which the same code is used for pre-existing ILD and for ILD linked to the fibrosing ARDS complication. Finally, some relevant variables were not available, such as treatments or tobacco consumption, which is not always coded in the discharge abstract because it does not necessarily impact patient care during hospitalisation.

In conclusion, our study highlights, on a national scale, that patients with chronic respiratory diseases including COPD, asthma and chronic respiratory failure were underrepresented among hospitalized COVID-19 patients compared with hospitalized influenza patients. Nevertheless, we also confirmed that patients with respiratory diseases were at risk of developing severe COVID-19 and had a high mortality rate. The low proportion of patients with respiratory conditions found among the COVID-19 population could potentially be because vulnerable individuals followed the lockdown rules more stringently. We must therefore bear in mind that these patients are at risk of severe disease and not drop our guard too fast, even if only few of them were hospitalized during the first wave of COVID-19. Influenza and SARS-CoV 2 vaccination will be a key public health priority for these patients.

Contributors

GB, PB, LP, CQ, PTB were involved in the conception and design of the study. CQ was the coordinator of the study. JC, ASM, CQ were responsible for the data collection, GB wrote the first draft. JC was in charge of the analysis. JC and CQ accessed and verified the data. GB, PB, MG, LP, CQ, PTB, ASM, JC were involved in the interpretation, critically reviewed the first draft, and approved the final version.

Declaration interests

Dr. Bonniaud reports personal fees and other from Roche, personal fees and other from Boehringer, personal fees and other from Novartis, personal fees from TEVA, other from Chiesi, personal fees from AstraZeneca, other from Stallergene, other from SANOFI, outside the submitted work

Other authors declare no competing interests.

Acknowledgements

The authors thank Suzanne Rankin for reviewing the English.

Bibliography

1. Ahrenfeldt LJ, Nielsen CR, Möller S, Christensen K, Lindahl-Jacobsen R. Burden and prevalence of risk factors for severe COVID-19 disease in the ageing European population - A SHARE-based analysis. Res Sq. 9 sept 2020;
2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet Lond Engl. 15 févr 2020;395(10223):497‑506.
3. Chung M, Bernheim A, Mei X, Zhang N, Huang M, Zeng X, et al. CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV). Radiology. avr 2020;295(1):202‑7.
4. Poissy J, Goutay J, Caplan M, Parmentier E, Duburcq T, Lassalle F, et al. Pulmonary Embolism in Patients With COVID-19: Awareness of an Increased Prevalence. Circulation. 14 juill 2020;142(2):184‑6.
5. Petersen E, Koopmans M, Go U, Hamer DH, Petrosillo N, Castelli F, et al. Comparing SARS-CoV-2 with SARS-CoV and influenza pandemics. Lancet Infect Dis. sept 2020;20(9):e238‑44.
6. Burn E, You SC, Sena AG, Kostka K, Abedtash H, Abrahão MTF, et al. An international characterisation of patients hospitalised with COVID-19 and a comparison with those previously hospitalised with influenza. MedRxiv Prepr Serv Health Sci. 25 avr 2020;
7. Barker WH, Mullooly JP. Pneumonia and influenza deaths during epidemics: implications for prevention. Arch Intern Med. janv 1982;142(1):85‑9.
8. Reacher M, Warne B, Reeve L, Verlander NQ, Jones NK, Ranellou K, et al. Influenza-associated mortality in hospital care: a retrospective cohort study of risk factors and impact of oseltamivir in an English teaching hospital, 2016 to 2017. Euro Surveill Bull Eur Sur Mal Transm Eur Commun Dis Bull. oct 2019;24(44).
9. Piroth L, Cottenet J, Mariet A-S, Bonniaud P, Blot M, Tubert-Bitter P, et al. Comparison of the characteristics, morbidity, and mortality of COVID-19 and seasonal influenza: a nationwide, population-based retrospective cohort study. Lancet Respir Med. mars 2021;9(3):251‑9.
10. Kwok S, Adam S, Ho JH, Iqbal Z, Turkington P, Razvi S, et al. Obesity: A critical risk factor in the COVID-19 pandemic. Clin Obes. déc 2020;10(6):e12403.
11. Apicella M, Campopiano MC, Mantuano M, Mazoni L, Coppelli A, Del Prato S. COVID-19 in people with diabetes: understanding the reasons for worse outcomes. Lancet Diabetes Endocrinol. sept 2020;8(9):782‑92.
12. Guan W-J, Liang W-H, Zhao Y, Liang H-R, Chen Z-S, Li Y-M, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. Eur Respir J. mai 2020;55(5).
13. Hazeldine J, Lord JM. Immunesenescence: A Predisposing Risk Factor for the Development of COVID-19? Front Immunol. 2020;11:573662.
14. Halpin DMG, Faner R, Sibila O, Badia JR, Agusti A. Do chronic respiratory diseases or their treatment affect the risk of SARS-CoV-2 infection? Lancet Respir Med. mai 2020;8(5):436‑8.
15. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. JAMA. 28 avr 2020;323(16):1574‑81.
16. Izquierdo JL, Almonacid C, González Y, Del Rio-Bermudez C, Ancochea J, Cárdenas R, et al. The impact of COVID-19 on patients with asthma. Eur Respir J. 2021;57(3):2003142.
17. Liang En Wee, Edwin Philip Conceicao, Jing Yuan Tan, Jean Xiang Ying Sim, Indumathi Venkatachalam. Reduction in asthma admissions during the COVID-19 pandemic: consequence of public health measures in Singapore. Eur Respir J. 2021;
18. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA. 26 mai 2020;323(20):2052‑9.

19. Goyal P, Choi JJ, Pinheiro LC, Schenck EJ, Chen R, Jabri A, et al. Clinical Characteristics of Covid-19 in New York City. N Engl J Med. 11 juin 2020;382(24):2372‑4.
20. Walsh EE, Cox C, Falsey AR. Clinical features of influenza A virus infection in older hospitalized persons. J Am Geriatr Soc. sept 2002;50(9):1498‑503.
21. Choi YJ, Park J-Y, Lee HS, Suh J, Song JY, Byun MK, et al. Effect of Asthma and Asthma Medication on the Prognosis of Patients with COVID-19. Eur Respir J. 25 sept 2020;
22. Lovinsky-Desir S, Deshpande DR, De A, Murray L, Stingone JA, Chan A, et al. Asthma among hospitalized patients with COVID-19 and related outcomes. J Allergy Clin Immunol. nov 2020;146(5):1027‑1034.e4.
23. Hughes-Visentin A, Paul ABM. Asthma and COVID-19: What do we know now. Clin Med Insights Circ Respir Pulm Med. 2020;14:1179548420966242.
24. Cosgriff R, Ahern S, Bell SC, Brownlee K, Burgel P-R, Byrnes C, et al. A multinational report to characterise SARS-CoV-2 infection in people with cystic fibrosis. J Cyst Fibros Off J Eur Cyst Fibros Soc. mai 2020;19(3):355‑8.
25. Colombo C, Burgel P-R, Gartner S, van Koningsbruggen-Rietschel S, Naehrlich L, Sermet-Gaudelus I, et al. Impact of COVID-19 on people with cystic fibrosis. Lancet Respir Med. mai 2020;8(5):e35‑6.
26. Halpin DMG, Singh D, Hadfield RM. Inhaled corticosteroids and COVID-19: a systematic review and clinical perspective. Eur Respir J. mai 2020;55(5).
27. Le Quéré C, Jackson RB, Jones MW, Smith AJP, Abernethy S, Andrew RM, et al. Temporary reduction in daily global CO2 emissions during the COVID-19 forced confinement. Nat Clim Change. 1 juill 2020;10(7):647‑53.
28. Guan W-J, Zheng X-Y, Chung KF, Zhong N-S. Impact of air pollution on the burden of chronic respiratory diseases in China: time for urgent action. Lancet Lond Engl. 15 oct 2016;388(10054):1939‑51.
29. Pozzer A, Dominici F, Haines A, Witt C, Münzel T, Lelieveld J. Regional and global contributions of air pollution to risk of death from COVID-19. Cardiovasc Res. 27 oct 2020;
30. D'Amato M, Molino A, Calabrese G, Cecchi L, Annesi-Maesano I, D'Amato G. The impact of cold on the respiratory tract and its consequences to respiratory health. Clin Transl Allergy. 2018;8:20.
31. Bloom CI, Drake TM, Docherty AB, Lipworth BJ, Johnston SL, Nguyen-Van-Tam JS, et al. Risk of adverse outcomes in patients with underlying respiratory conditions admitted to hospital with COVID-19: a national, multicentre prospective cohort study using the ISARIC WHO Clinical Characterisation Protocol UK. Lancet Respir Med. 2021;
32. Schultze A, Walker AJ, MacKenna B, Morton CE, Bhaskaran K, Brown JP, et al. Risk of COVID-19-related death among patients with chronic obstructive pulmonary disease or asthma prescribed inhaled corticosteroids: an observational cohort study using the OpenSAFELY platform. Lancet Respir Med. nov 2020;8(11):1106‑20.
33. Eger K, Bel EH. Asthma and COVID-19: do we finally have answers? Eur Respir J [Internet]. 2021 [cité 1 avr 2021];57(3). Disponible sur: https://erj.ersjournals.com/content/57/3/2004451
34. Drake TM, Docherty AB, Harrison EM, Quint JK, Adamali H, Agnew S, et al. Outcome of Hospitalization for COVID-19 in Patients with Interstitial Lung Disease: An International Multicenter Study. Am J Respir Crit Care Med. 2 oct 2020;
35. Guiot J, Henket M, Frix AN, Delvaux M, Denis A, Giltay L, et al. Single-center experience of patients with interstitial lung diseases during the early days of the COVID-19 pandemic. Respir Investig. 19 sept 2020;58(6):437‑9.
36. Gaines J, Vgontzas AN, Fernandez-Mendoza J, Bixler EO. Obstructive sleep apnea and the metabolic syndrome: The road to clinically-meaningful phenotyping, improved prognosis, and personalized treatment. Sleep Med Rev. déc 2018;42:211‑9.
37. Cade BE, Dashti HS, Hassan SM, Redline S, Karlson EW. Sleep Apnea and COVID-19 Mortality and Hospitalization. Am J Respir Crit Care Med. 15 nov 2020;202(10):1462‑4.

38. Memtsoudis SG, Ivascu NS, Pryor KO, Goldstein PA. Obesity as a risk factor for poor outcome in COVID-19-induced lung injury: the potential role of undiagnosed obstructive sleep apnoea. Br J Anaesth. août 2020;125(2):e262‑3.
39. Verroken A, Scohy A, Gérard L, Wittebole X, Collienne C, Laterre P-F. Co-infections in COVID-19 critically ill and antibiotic management: a prospective cohort analysis. Crit Care Lond Engl. 9 juill 2020;24(1):410.
40. Piroth L, Cottenet J, Mariet A-S, Bonniaud P, Blot M, Tubert-Bitter P, et al. Compared characteristics, morbidity and mortality of COVID-19 and seasonal influenza: a nationwide population-based study. Lancet Respir Med. nov 2020;
41. Bergman J, Ballin M, Nordström A, Nordström P. Risk factors for COVID-19 diagnosis, hospitalization, and subsequent all-cause mortality in Sweden: a nationwide study. Eur J Epidemiol [Internet]. 2021 [cité 1 avr 2021]; Disponible sur: https://doi.org/10.1007/s10654-021-00732-w
42. Leung JM, Niikura M, Yang CWT, Sin DD. COVID-19 and COPD. Eur Respir J. août 2020;56(2).
43. Alqahtani JS, Oyelade T, Aldhahir AM, Alghamdi SM, Almehmadi M, Alqahtani AS, et al. Prevalence, Severity and Mortality associated with COPD and Smoking in patients with COVID-19: A Rapid Systematic Review and Meta-Analysis. PloS One. 2020;15(5):e0233147.
44. Zheng Z, Peng F, Xu B, Zhao J, Liu H, Peng J, et al. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. J Infect. août 2020;81(2):e16‑25.
45. Khan MMA, Khan MN, Mustagir MG, Rana J, Islam MS, Kabir MI. Effects of underlying morbidities on the occurrence of deaths in COVID-19 patients: A systematic review and meta-analysis. J Glob Health. déc 2020;10(2):020503.
46. Tsakok MT, Qamhawi Z, Lumley SF, Xie C, Matthews P, Gleeson F, et al. COVID-19 CT pulmonary angiogram examinations and reported pulmonary embolism incidence: comparison between peak first wave and early second wave. Clin Radiol. 5 févr 2021;

Table 1· Respiratory history of patients hospitalized in France for COVID-19 (from March 1 to April 30, 2020) or seasonal influenza (from December 1, 2018, to February 28, 2019)

	COVID-19	2018-2019 seasonal influenza	p-value
Number of patients	89530	45819	
Sex (men)	47495 (53.05)	22118 (48.27)	<0.0001
Age Mean ± std	65 ± 20	59 ± 32	<0.0001
Obesity (BMI≥30 kg/m²)	8611 (9.62)	2491 (5.44)	<0.0001
Diabetes	17050 (19.04)	7352 (16.05)	<0.0001
Hypertension	29622 (33.09)	12921 (28.20)	<0.0001
Heart failure	7134 (7.97)	6266 (13.68)	<0.0001
Chronic respiratory failure n (%)	1433 (1.60)	**1830 (3.99)**	<0.0001
Sleep apnea	**3581 (4.00)**	1443 (3.15)	<0.0001
Pulmonary hypertension	341 (0.38)	**247 (0.54)**	<0.0001
Chronic obstructive pulmonary disease	4866 (5.44)	**4637 (10.12)**	<0.0001
Asthma	3273 (3.66)	**2230 (4.87)**	<0.0001
Cystic fibrosis with pulmonary manifestations	20 (0.02)	**79 (0.17)**	<0.0001
Lung cancer	**977 (1.09)**	431 (0.94)	0.0098
Emphysema	**1426 (1.59)**	553 (1.21)	<0.0001
Pulmonary sarcoidosis	159 (0.18)	81 (0.18)	0.9732
Interstitial lung diseases	**1611 (1.80)**	471 (1.03)	<0.0001

Groups where prevalence is significantly increased are bolded

Table 2· Respiratory morbidity of the patients hospitalized in France for COVID-19 (from March 1 to April 30, 2020) or seasonal influenza (from December 1, 2018, to February 28, 2019), according to pulmonary comorbidity at admission

COVID19

	CRF	Lung cancer	PH	Sleep apnea	COPD	Emphysema	Asthma	Pulmonary sarcoidosis	ILD	CF
Number of patients	1433	977	341	3581	4866	1426	3,273	159	1611	20
Pulmonary embolism (%)	36 (2.5) *	44 (4.5)	38 (11.1) *	152 (4.2) *	151 (3.1) *	101 (7.1) *	114 (3.5) *	8 (5.0)	93 (5.8) *	0 (0.0)
Ventilator -acquired pneumonia (%)	117 (8.2) $	49 (5.0) $	49 (14.4) *	692 (19.3) *	457 (9.4)	237 (16.6) *	354 (10.8) *	30 (18.9) *	311 (19.3) *	1 (5.0)
Pneumocystis pneumonia (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Aspergillosis pneumonia (%)	13 (0.9)	1 (0.1) $	1 (0.3)	18 (0.5)	32 (0.7)	17 (1.2)	23 (0.7)	0 (0.0)	15 (0.9)	1 (5.0)
Pleural empyema (%)	1 (0.1)	6 (0.6)	0 (0.0)	3 (0.1) $	3 (0.1)	2 (0.1)	2 (0.1)	1 (0.6)	3 (0.2)	0 (0.0)
Lung abscess (%)	2 (0.1)	6 (0.6)	0 (0.0)	5 (0.1)	3 (0.1)	6 (0.4)	2 (0.1)	0 (0.0)	9 (0.6)	0 (0.0)
Pneumothorax (%)	8 (0.6)	10 (1.0)	4 (1.2)	29 (0.8)	25 (0.5)	39 (2.7)	14 (0.4)	1 (1.6)	25 (1.6)	1 (5.0)
ICU (%)	320 (22.3) $	117 (12.0) $	97 (28.5)	1172 (32.7) *	986 (20.6) $	405 (28.4)	640 (19.6) *	53 (33.3) *	527 (32.7) *	2 (10.0)
In-hospital death (%)	413 (28.8) *	402 (41.2) *	96 (28.2) *	672 (18.8) *	1229 (25.3) *	312 (21.8) *	310 (9.5) *	32 (20.1) *	363 (22.5) *	0 (0.0)

Seasonal influenza

Number of patients	1830	431	247	1443	4637	553	2230	81	471	79
Pulmonary embolism (%)	28 (1.5) *	16 (3.7)	6 (2.4) *	16 (1.1) *	59 (1.3) *	11 (2.0) *	14 (0.6) *	1 (1.2)	10 (2.1) *	1 (1.3)
Ventilator-acquired pneumonia (%)	250 (13.7) $	39 (9.1) $	17 (6.9) *	138 (96.6) *	423 (9.1)	62 (11.2) *	91 (4.1) *	4 (4.9) *	58 (12.3) *	2 (2.5)
Pneumocystis pneumonia (%)	0 (0.0)	2 (0.5)	0 (0.0)	1 (0.1)	1 (0.0)	0 (0.0)	2 (0.1)	2 (2.5)	1 (0.2)	0 (0.0)
Aspergillosis pneumonia (%)	16 (0.9)	6 (1.4) $	1 (0.4)	10 (0.7)	34 (0.7)	11 (2.0)	12 (0.5)	1 (1.2)	7 (1.5)	4 (5.1)
Pleural empyema (%)	3 (0.2)	1 (0.2)	0 (0.0)	5 (0.4) $	3 (0.1)	0 (0.0)	2 (0.1)	1 (1.2)	3 (0.6)	0 (0.0)
Lung abscess (%)	2 (0.1)	3 (0.7)	0 (0.0)	2 (0.1)	8 (0.2)	2 (0.4)	1 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pneumothorax (%)	7 (0.4)	3 (0.7)	1 (0.4)	6 (0.4)	15 (0.3)	13 (2.4)	8 (0.4)	0 (0.0)	7 (1.5)	2 (2.5)
ICU (%)	621 (33.9) $	92 (21.4) $	74 (30.0)	376 (26.1) *	1121 (24.2) $	175 (31.7)	274 (12.3) *	12 (14.8) *	122 (25.9) *	4 (5.1)
In-hospital death (%)	201 (11.0) *	87 (20.2) *	28 (11.3) *	77 (5.3) *	383 (8.3) *	39 (7.1) *	55 (2.5) *	5 (6.2) *	65 (13.8) *	1 (1.3)

* significantly more frequent in the COVID-19 group ($p<0.05$)

$ significantly more frequent in the seasonal influenza group ($p<0.05$)

CRF: chronic respiratory failure, PH: pulmonary hypertension, COPD: chronic obstructive pulmonary disease, ILD: interstitial lung disease, CF: cystic fibrosis

Table 3· Respiratory morbidity, need for ICU, and mortality of patients hospitalized in France for COVID-19 (from March 1 to April 30, 2020), according to presence of chronic respiratory disease

	Chronic respiratory disease	**No chronic respiratory disease**	**p-value**
Number of patients	14351	75179	
Pulmonary embolism n (%)	**590 (4.11)**	2496 (3.32)	<0.0001
Respiratory bacterial co-infection n (%)	**1841 (12.83)**	5962 (7.93)	<0.0001
Pneumocystis pneumonia n (%)	0 (0.00)	3 (0.00)	1.0000
Aspergillosis pneumonia n(%)	**80 (0.56)**	130 (0.17)	<0.0001
Pleural empyema n (%)	**19 (0.13)**	53 (0.07)	0.0165
Lung abscess n (%)	**28 (0.20)**	75 (0.10)	0.0020
Pneumothorax n (%)	**123 (0.86)**	251 (0.33)	<0.0001
Acute respiratory failure (%)	**5387 (37.54)**	18930 (25.18)	<0.0001
ICU (%)	**2985 (20.80)**	12119 (16.12)	<0.0001
In-hospital death (%)	**3363 (23.43)**	11222 (14.93)	<0.0001

Groups where prevalence is significantly increased are bolded

Table 4· Respiratory morbidity, need for ICU and mortality of the patients hospitalized in France for COVID-19 (from March 1 to April 30, 2020): comparison between patients with and without chronic respiratory disease (disjunctive variables using prioritization[a])

	CF	Lung cancer	COPD	Asthma	Pulmonary sarcoidosis	ILD	Emphysema	Sleep apnea	PH	CRF	No CRD
Number of patients (%)	20 (0.1)	977 (6.8)	4682 (32.6)	2973 (20.7)	138 (1.0)	1385 (9.7)	794 (5.5)	2623 (18.3)	230 (1.6)	529 (3.7)	
Pulmonary embolism n (%)	0 (0)	44 (4.5) *	142 (3.0)	106 (3.6)	8 (5.8)	81 (5.9) *	58 (7.3%) *	112 (4.3) *	27 (11.7) *	12 (2.3%)	3.3%
VAP n (%)	1 (5.0)	49 (5.0) $	445 (9.5) *	323 (10.9) *	26 (18.8) *	277 (20.0) *	132 (16.6) *	517 (19.7) *	33 (14.4) *	39 (7.4)	7.9%
Pneumocystis pneumonia n (%)	0	0	0	0	0	0	0	0	0	0	0%
Aspergillosis pneumonia n(%)	1 (5.0) *	1 (0.1)	32 (0.7) *	15 (0.5) *	0 (0.0)	13 (0.9) *	6 (0.8) *	8 (0.3)	1 (0.5)	3 (0.6)	0.2%
Pleural empyema n (%)	0 (0)	6 (0.6) *	3 (0.1)	2 (0.1)	1 (0.7)	3 (0.2)	2 (0.3)	2 (0.1)	0 (0)	0 (0)	0.1%
Lung abscess n (%)	0 (0)	6 (0.6) *	2 (0.0)	2 (0.1)	0 (0)	9 (0.7) *	6 (0.8) *	2 (0.1)	0 (0)	1 (0.2)	0.1%
Pneumothorax n (%)	1 (5.0)	10 (1.0) *	25 (0.5) *	13 (0.4)	1 (0.7)	23 (1.7) *	26 (3.3) *	19 (0.7) *	2 (0.9)	3 (0.6)	0.3%
Acute respiratory failure (%)	3 (15.0)	344 (35.2) *	1845 (39.4) *	853 (28.7) *	43 (31.2)	632 (45.6) *	297 (37.4) *	1068 (40.7) *	99 (43.0) *	203 (38.4) *	25.2%
ICU (%)	2 (10.0)	117 (12.0) $	960 (20.5) *	570 (19.2) *	47 (34.1) *	453 (32.7) *	213 (26.8) *	851 (32.4) *	59 (25.7) *	91 (17.2)	14.9%
In-hospital death (%)	0 (0)	402 (41.2) *	1163 (24.8) *	266 (9.0) $	29 (21.0)	296 (21.4) *	147 (18.5)	466 (17.8) *	64 (27.8) *	152 (28.7) *	16.1%

[a] each CRD patient was classified in only one single CRD category. When there were several CRD codes on the discharge abstract of a patient, we decided to prioritize in order to retain only one, using the following order: CF with pulmonary manifestations, lung cancer, COPD, asthma, pulmonary sarcoidosis, ILD, emphysema, sleep apnea, PH and CRF

* significantly more frequent in the chronic respiratory disease group compared to the group with no chronic respiratory disease ($p<0.05$)

$ significantly less frequent in the chronic respiratory disease group compared to the group with no chronic respiratory disease ($p<0.05$)

CRD: chronic respiratory disease, CRF: chronic respiratory failure, PH: pulmonary hypertension, COPD: chronic obstructive pulmonary disease, ILD: interstitial lung disease, CF: cystic fibrosis, VAP: ventilator-associated pneumonia

Table 5· Risk of requiring intensive care and mortality for patients hospitalized in France for COVID-19 (from March 1 to April 30, 2020) according to chronic respiratory disease (disjunctive variables using prioritization[a])

	ICU		Death	
	OR [95% IC]	Adjusted OR [95% IC]	OR [95% IC]	Adjusted OR [95% IC]
No CRD	1	1	1	1
CF	0.63 [0.15-2.73]	0.60 [0.1-2.60]	-	-
Lung cancer	**0.78 [0.64-0.94]**	**0.77 [0.63-0.94]**	3.64 [3.20-4.14]	3.67 [3.20-4.21]
COPD	1.47 [1.37-1.58]	1.16 [1.07-1.26]	1.72 [1.61-1.84]	1.14 [1.06-1.22]
Asthma	1.35 [1.23-1.48]	1.23 [1.12-1.36]	**0.51 [0.45-0.58]**	**0.82 [0.71-0.94]**
Pulmonary sarcoidosis	2.94 [2.07-4.19]	2.65 [1.83-3.84]	1.38 [0.92-2.09]	2.11 [1.36-3.26]
ILD	2.77 [2.47-3.11]	2.42 [2.14-2.72]	1.41 [1.24-1.61]	1.20 [1.05-1.38]
Emphysema	2.09 [1.78-2.45]	1.83 [1.56-2.16]	1.18 [0.99-1.42]	1.01 [0.83-1.22]
Sleep apnea	2.74 [2.52-2.98]	1.39 [1.27-1.53]	1.12 [1.02-1.25]	0.95 [0.85-1.06]
PH	1.97 [1.46-2.65]	1.73 [1.27-2.37]	2.01 [1.50-2.68]	1.24 [0.91-1.67]
CRF	1.18 [0.94-1.49]	1.03 [0.81-1.30]	2.10 [1.74-2.54]	1.30 [1.06-1.59]

Chronic respiratory diseases significantly less at risk are bolded

[a] each CRD patient was classified in only one single CRD category. When there were several CRD codes on the discharge abstract of a patient, we decided to prioritize in order to retain only one, using the following order: CF with pulmonary manifestations, lung cancer, COPD, asthma, pulmonary sarcoidosis, ILD, emphysema, sleep apnea, PH and CRF

OR adjusted on obesity, diabetes, hypertension, heart failure, atherosclerotic heart disease, sex, and age as a continuous variable.

CRF: chronic respiratory failure, PH: pulmonary hypertension, COPD: chronic obstructive pulmonary disease, ILD: interstitial lung disease, CF: cystic fibrosis, VAP: ventilator-associated pneumonia, No CRD: No chronic respiratory disease

Supplemental material

Supplementary Table 1: ICD-10 and CCAM codes used to identify chronic respiratory diseases, respiratory complications, and potential confounding factors

Codes	Respiratory disease
Chronic respiratory disease	
J961	Chronic respiratory failure
C34 and C45	Lung cancer
I270	Pulmonary hypertension - PH
G473	Sleep apnea
J40, J41, J42 and J44	Chronic obstructive pulmonary disease - COPD
J43 and J982	Emphysema
J45 and J46	Asthma
D86	Pulmonary sarcoidosis
J84	Interstitial lung disease
E840	Cystic fibrosis with pulmonary manifestations
Respiratory complication	
J10, J11, J12, J13, J14, J15, J16, J17, and J18 associated with CCAM codes GLLD006, GLLD015, GLLD008, GLLD004, GLLD007, GLLD009	Ventilator-acquired pneumonia
B206 and B59	Pneumocystis pneumonia
B440 and B441	Aspergillosis pneumonia
J86	Pleural empyema
J85	Lung abscess
J93	Pneumothorax
J96	Acute respiratory failure
I26	Pulmonary embolism

Potential confounding factors	
E66 except E6603, E6613, E6683, E6693	Obesity
E10, E11, E12, E13, E14, O24	Diabetes
I10, I11, I12, I13, I15, O10, O13 and O16	Hypertension
I50	Heart failure

Supplementary Table 2: Respiratory history of patients hospitalized in France for COVID-19 (from March 1 to April 30, 2020) or seasonal influenza (from December 1, 2018 to February 28, 2019), according to their age at admission

COVID19

Age strata (years)	**<18**	**18-30**	**31-40**	**41-50**	**51-60**	**61-70**	**71-80**	**81-90**	**>90**
Number of patients	1,227	4,384	6,065	8,892	13,110	15,345	16,265	17,841	6,401
Chronic respiratory failure (%)	10 (0.81) *	5 (0.11) $	18 (0.3) $	46 (0.52) $	110 (0.84) $	276 (1.8) $	410 (2.52) $	435 (2.44) $	123 (1.92)
Sleep apnea (%)	4 (0.33)	10 (0.23)	71 (1.17) *	212 (2.38) $	599 (4.57)	979 (6.38)	987 (6.07)	635 (3.56)	87 (1.31)
Pulmonary hypertension (%)	0 (0)	2 (0.05)	2 (0.03) $	8 (0.09)	24 (0.18) $	63 (0.41)	91 (0.56)	112 (0.63) $	39 (0.61)
Chronic obstructive pulmonary disease (%)	3 (0.24)	8 (0.18) $	31 (0.51) $	129 (1.45) $	448 (3.42) $	1,120 (7.3) $	1,469 (9.03) $	1,342 (7.52) $	316 (4.94) $
Asthma (%)	105 (8.56) *	248 (5.66) $	308 (5.08) $	504 (5.67) $	601 (4.58) $	562 (3.66) $	456 (2.80) $	375 (2.10) $	114 (1.78) $
Cystic fibrosis with pulmonary manifestations (%)	4 (0.33)	6 (0.14) $	4 (0.07) $	6 (0.07)	0 (0) $	0 (0)	0 (0)	0 (0)	0 (0)
Lung cancer (%)	0 (0)	2 (0.05)	5 (0.08)	32 (0.36) $	135 (1.03) $	312 (2.03) $	311 (1.91)	158 (0.89) *	22 (0.34)
Emphysema (%)	1 (0.08)	7 (0.16)	21 (0.35)	83 (0.93)	192 (1.46) $	418 (2.72) $	392 (2.41) *	260 (1.46) *	52 (0.81) *
Pulmonary sarcoidosis (%)	0 (0)	3 (0.07)	12 (0.20)	21 (0.24)	35 (0.27)	41 (0.27) $	33 (0.20)	12 (0.07)	2 (0.03)
Interstitial lung diseases (%)	10 (0.81) *	23 (0.52) *	46 (0.76)	99 (1.11)	223 (1.70)	350 (2.28) *	403 (2.48) *	379 (2.12) *	78 (1.22) *

Seasonal influenza

Age strata (years)	**<18**	**18-30**	**31-40**	**41-50**	**51-60**	**61-70**	**71-80**	**81-90**	**>90**
Number of patients	8,942	1,836	1,568	1,626	3,164	5,624	7,693	11,276	4,090
Chronic respiratory failure (%)	31 (0.35) *	25 (1.36) $	21 (1.34) $	60 (3.69) $	191 (6.04) $	448 (7.97) $	498 (6.47) $	478 (4.24) $	78 (1.91)
Sleep apnea (%)	11 (0.12)	7 (0.38)	8 (0.51) *	56 (3.44) $	142 (4.49)	349 (6.21)	455 (5.91)	378 (3.35)	37 (0.90)
Pulmonary hypertension (%)	3 (0.03)	2 (0.11)	6 (0.38) $	3 (0.18)	12 (0.38) $	31 (0.55)	49 (0.64)	106 (0.94) $	35 (0.86)
Chronic obstructive pulmonary disease (%)	16 (0.18)	12 (0.65) $	17 (1.08) $	128 (7.87) $	522 (16.5) $	1,186 (21.09) $	1,295 (16.83) $	1,208 (10.71) $	253 (6.19) $
Asthma (%)	528 (5.9) *	147 (8.01) $	132 (8.42) $	177 (10.89) $	232 (7.33) $	265 (4.71) $	314 (4.08) $	337 (2.99) $	98 (2.40) $
Cystic fibrosis with pulmonary manifestations (%)	19 (0.21)	32 (1.74) $	20 (1.28) $	4 (0.25)	2 (0.06) $	0 (0)	1 (0.01)	1 (0.01)	0 (0)
Lung cancer (%)	0 (0)	2 (0.11)	2 (0.13)	12 (0.74) $	64 (2.02) $	147 (2.61) $	123 (1.60)	73 (0.65) *	8 (0.20)
Emphysema (%)	9 (0.1)	4 (0.22)	7 (0.45)	22 (1.35)	98 (3.1) $	182 (3.24) $	126 (1.64) *	89 (0.79) *	16 (0.39) *
Pulmonary sarcoidosis (%)	0 (0)	2 (0.11)	6 (0.38)	8 (0.49)	15 (0.47)	26 (0.46) $	16 (0.21)	7 (0.06)	1 (0.02)

Interstitial lung diseases (%)	12 (0.13) *	3 (0.16) *	15 (0.96)	22 (1.35)	41 (1.30)	83 (1.48) *	130 (1.69) *	133 (1.18) *	32 (0.78) *

* significantly more frequent in the COVID-19 group ($p<0.05$)

$ significantly more frequent in the seasonal influenza group ($p<0.05$)

Supplementary Table 3: Respiratory complications of patients hospitalized in France for COVID-19 (from March 1 to April 30, 2020) or seasonal flu (from December 1, 2018 to February 28, 2019)

	COVID-19	2018-2019 seasonal flu	p-value
Number of patients	89,530	45,819	
Pulmonary embolism n (%)	**3086 (3.45)**	412 (0.90)	<0.0001
Ventilator-acquired pneumonia n (%)	7803 (8.72)	**1710 (3.73)**	<0.0001
Pneumocystis pneumonia n (%)	3 (0.00)	**22 (0.05)**	<0.0001
Aspergillosis pneumonia n(%)	210 (0.23)	112 (0.24)	0.7240
Pleural empyema n (%)	72 (0.08)	44 (0.10)	0.3531
Lung abscess n (%)	103 (0.12)	60 (0.13)	0.4247
Pneumothorax n (%)	**374 (0.42)**	89 (0.19)	<0.0001

Groups where prevalence is significantly increased are bolded

Supplementary Table 4: Respiratory morbidity, need for ICU and mortality of the patients hospitalized in France for COVID-19 (from March 1 to April 30, 2020): comparison between patients with and without chronic respiratory disease (for patients with CRD, we included patients with only one CRD)

	CF	Lung cancer	COPD	Asthma	Pulmonary sarcoidosis	ILD	Emphysema	Sleep apnea	CRF	PH	No CRD
Number of patients (%)	13 (0.1)	698 (4.3)	3013 (26.0)	2641 (22.8)	115 (1.0)	1171 (10.1)	734 (6.3)	2480 (21.4)	529 (4.6)	217 (1.9)	
Pulmonary embolism n (%)	0 (0)	30 (4.3)	85 (2.8)	84 (3.2)	8 (7.0)	69 (5.9) *	54 (7.4) *	106 (4.3) *	12 (2.3)	26 (12.0) *	3.32%
VAP n (%)	1 (7.7)	32 (4.6) $	234 (7.8)	254 (9.6) *	21 (18.3) *	230 (19.6) *	123 (16.8) *	499 (20.1) *	38 (7.2)	32 (14.8) *	7.9%
Pneumocystis pneumonia n (%)	0	0	0	0	0	0	0	0	0	0	0%
Aspergillosis pneumonia n (%)	1 (7.7) *	0 (0)	10 (0.3) *	10 (0.4) *	0 (0)	9 (0.8) *	6 (0.8) *	8 (0.3)	3 (0.6)	1 (0.5)	0.2%
Pleural empyema n (%)	0 (0)	6 (0.9) *	3 (0.1)	2 (0.1)	1 (0.9)	2 (0.2)	1 (0.1)	2 (0.1)	0 (0)	0 (0)	0.1%
Lung abscess n (%)	0 (0)	4 (0.6) *	2 (0.1)	0 (0)	0 (0)	9 (0.1) *	6 (0.1) *	2 (0.1)	1 (0.2)	0 (0)	0.1%
Pneumothorax n (%)	1 (7.7) *	9 (1.3) *	15 (0.5)	7 (0.3)	0 (0)	15 (1.3) *	24 (3 .3) *	19 (0.8) *	3 (0.6)	2 (0.9)	0.3%
Acute respiratory failure (%)	2 (15.4)	241 (34.5) *	1062 (35.3) *	716 (27.1) *	29 (25.2)	516 (44.1) *	271 (37.0) *	1003 (40.4) *	203 (38.4) *	94 (43.3) *	25.2%
ICU (%)	1 (7.7)	74 (10.6) $	503 (16.7) *	463 (17.5) *	35 (30.4)	364 (31.1) *	200 (27.3) *	807 (32.5) *	91 (17.2)	57 (26.3) *	14.9%
In-hospital death (%)	0 (0)	293 (42.0) *	750 (24.9) *	223 (8.4) $	24 (20.9)	227 (19.4) *	135 (18.4)	426 (17.2)	152 (28.7) *	60 (27.7) *	16.1%

* significantly more frequent in the chronic respiratory disease group compared to the group with no chronic respiratory disease ($p<0.05$)
$ significantly less frequent in the chronic respiratory disease group compared to the group with no chronic respiratory disease ($p<0.05$)
CRF: chronic respiratory failure, PH: pulmonary hypertension, COPD: chronic obstructive pulmonary disease, ILD: interstitial lung disease, CF: cystic fibrosis, VAP: ventilator-associated pneumonia, No CRD: No chronic respiratory disease

Supplementary Table 5· Risk of intensive care requiring and mortality for the patients hospitalized in France for COVID-19 (from March 1 to April 30, 2020) according to their chronic respiratory disease (only one CRD)

	ICU	Death
	Adjusted OR [95% IC]	Adjusted OR [95% IC]
No CRD	1	1
CF	0.46 [0.1-3.60]	-
Lung cancer	**0.72 [0.57-0.93]**	3.95 [3.36-4.64]
COPD	0.96 [0.87-1.07]	1.09 [1.01-1.19]
Asthma	1.15 [1.04-1.28]	**0.81 [0.70-0.94]**
Pulmonary sarcoidosis	2.22 [1.47-3.38]	2.12 [1.31-3.243]
ILD	2.29 [2.01-2.61]	1.07 [0.92-1.25]
Emphysema	1.92 [1.62-2.28]	1.01 [0.83-1.23]
Sleep apnea	1.38 [1.26-1.52]	0.93 [0.83-1.04]
CRF	1.02 [0.80-1.29]	1.30 [1.06-1.58]
PH	1.81 [1.31-2.49]	1.21 [0.88-1.66]

Chronic respiratory diseases significantly less at risk are bolded

OR adjusted on obesity, diabetes, hypertension, heart failure, atherosclerotic heart disease, sex, and age as a continuous variable.

CRF: chronic respiratory failure, PH: pulmonary hypertension, COPD: chronic obstructive pulmonary disease, ILD: interstitial lung disease, CF: cystic fibrosis, VAP: ventilator-associated pneumonia, No CRD: No chronic respiratory disease