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Compared characteristics, morbidity and mortality of COVID-19 and seasonal influenza: a nationwide population-based study

Lionel PIROTH, MD ^{1,2,3}, Jonathan COTTENET MSc ⁴, Anne-Sophie MARIET, MD ^{1,4}, Philippe BONNIAUD, MD ^{3,5,6}, Mathieu BLOT, MD ², Pascale TUBERT-BITTER, PhD ^{7*}, Catherine QUANTIN, MD ^{1,4,7*}

1 Inserm, CIC 1432, Dijon, France ; Dijon University Hospital, Clinical Investigation Center, clinical epidemiology/ clinical trials unit, Dijon, France

2 Infectious Diseases Department, Dijon University Hospital, BP 77908, 21079 Dijon, France

3 Faculty of Medicine, University of Bourgogne-Franche-Comté, Dijon, France

4 Biostatistics and Bioinformatics (DIM), Dijon University Hospital, BP 77908, 21079 Dijon, France; Bourgogne Franche-Comté University, Dijon, France ;

5 Reference Center for Rare Pulmonary Diseases, Pulmonary Medicine and Intensive Care Unit Department, Dijon University Hospital, BP 77908, 21079 Dijon, France

6 INSERM, LNC UMR1231, LipSTIC LabEx Team, Dijon, France

7 Université Paris-Saclay, UVSQ, Univ. Paris-Sud, Inserm, High-Dimensional Biostatistics for Drug Safety and Genomics, CESP, Villejuif, France;

* These two authors contributed equally to this work

Lionel Piroth, Philippe Bonniaud and Catherine Quantin are full professors.

Corresponding author

Pr Catherine QUANTIN

CHU de Dijon - Service de Biostatistique et d'Informatique Médicale - BP 77908 - 21079 Dijon CEDEX, France

Université Paris-Saclay, UVSQ, Univ. Paris-Sud, Inserm, High-Dimensional Biostatistics for Drug Safety and Genomics, CESP, Villejuif, France

Tel. (33) 3 80 29 34 65, Fax (33) 3 80 29 39 73 - catherine.quantin@chu-dijon.fr

Abstract (300 words)

Background: Though influenza epidemics have been considered suitable for use as a model for the COVID-19 epidemic, data comparing the two are scarce.

Methods: A nationwide retrospective cohort study was conducted using the French national administrative database (PMSI), which includes discharge summaries for all hospital admissions in France. All patients hospitalized for COVID-19 during March-April 2020 were included, as well as all patients hospitalized for influenza during the 2018-2019 influenza outbreak period.

Findings: The 89,350 COVID-19 patients were more likely to be overweight, diabetic, and hypertensive, whereas the 45,819 influenza patients were more likely to have heart failure, chronic respiratory disease, and cirrhosis. COVID-19 patients more often developed respiratory distress, pulmonary embolism, septic shock, or haemorrhagic stroke, but less often myocardial infarction or atrial fibrillation.

The in-hospital case fatality rate was higher in COVID-19 patients (16.9 vs 5.8%, $p < 0.01$), with a relative risk of death of 2.9 [2.8-3.0] and an age-standardized mortality ratio of 2.8.

When compared with those hospitalized with influenza, the paediatric population hospitalized with COVID-19 was under represented, but the need for intensive care support was higher in those younger than 5 years (14/613 for COVID-19, 2.3% vs 65/6,973 for influenza, 0.9%). The in-hospital case fatality rate in teenagers was tenfold higher (5/458, 1.1% vs 1/804, 0.1%, $p < 0.01$), and teenaged COVID-19 victims were more often obese or overweight.

Interpretation: There are significant differences in the presentation of COVID-19 and seasonal influenza requiring hospitalization. SARS-CoV2 is likely to have a higher potential for respiratory pathogenicity, leading to more respiratory complications and to higher case fatality rates. This is also likely true in the paediatric population (even if this age group need to be taken with caution considering the small number of deaths and ICU support) despite a lower rate of hospitalization than for influenza, in particular in overweight children. These findings highlight the importance of appropriate preventive measures as well as the need for a specific vaccine and treatment for SARS-CoV2.

Keywords: Covid-19; influenza; comparative study; morbidity; Mortality; administrative data; hospital; SARS-CoV-2; severity; France; age group

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

Introduction

In December 2019, a new disease now known as COVID-19 (Coronavirus Disease-19), caused by the new SARS-CoV-2 coronavirus, emerged as a major world threat. Considering its ability to spread and the relatively low case fatality rates initially reported in China, SARS-CoV2 was thought to be more similar to influenza than SARS-CoV-1 [1]. The preventive measures for this new infection were thus based on a comparison with the influenza virus since the viruses have similar modes of transmission and cause respiratory disease. It was anticipated that COVID-19 patients could also benefit from the clinical knowledge and care management of influenza.

On July 10th, 2020, more than 12 million cases of COVID-19 and 554,000 COVID-19-related deaths had been identified worldwide. In France, it had already caused more than 30,000 deaths, nearly 20,000 of which were in hospital. At this point, COVID-19 had developed into a pandemic associated with substantial morbidity and mortality, putting significant strain on hospitals and the health system in general.

The case fatality rate in COVID-19 appears to be higher than in seasonal influenza, even though both mainly affect frail older adults. This may be due to a difference in underlying comorbidities, the pathogenicity of the virus, population immunity, and host response to infection. For example, there are available vaccines and treatments for influenza but not for COVID-19. Moreover, the massive strain that was put on hospitals within a short period of time led to limitations in available care for the frailest patients.

Few studies have directly compared the respective burdens of the two epidemics [2] [3]. Nevertheless, underscoring the risk factors for hospitalization and comprehensively assessing their respective mortality risk factors and rates seems of the utmost importance. Such data could be used to identify risk factors and specific at-risk populations, strengthen and focus specific preventive measures in these populations, and help define the future needs of health care facilities.

The aim of the present study was thus to compare, using French nationwide data, the population hospitalized for COVID-19 and the population hospitalized for influenza during the 2018-2019 season, and to assess the differences in terms of risk factors, clinical characteristics and outcomes.

Methods

Study design and participants

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 inpatients admitted to public and private hospitals in France. Inspired by the American DRG (diagnosis-related groups) model, the gathering of national administrative health data was established in France in 1991 and extended to all French healthcare facilities in 1997. This coding system was initially designed to analyse hospital activity and to contribute to the development of strategic healthcare plans. Since 2008, each hospital's budget depends on the medical activity described in a specific computer program that compiles discharge abstracts for all admissions. The information in these abstracts is anonymous and covers both medical and administrative data. Diagnoses identified during the hospital stay are coded according to the 10th edition of the International Classification of Diseases (ICD10), and procedures performed during the hospitalisation are coded according to the French Common Classification of Medical Procedures. Each facility produces its own standardised anonymous data set, and these are compiled to create a national data set. The

fact that these national data are used for the allocation of hospital budgets encourages improvement in data quality in terms of coherence, accuracy and exhaustiveness.

In France, Stage 1 of the COVID-19 epidemic was declared on February 23, Stage 2 was declared on February 29, and Stage 3 on March 14, 2020. The peak of the epidemic occurred during the second week of April, 2020. While during Stage 1 and 2 all patients with COVID-19 were hospitalized regardless of clinical presentation, only those in serious clinical condition were admitted to hospital during Stage 3. A PMSI database was developed for COVID-19, and hospitals were asked to perform accelerated data transmission for COVID-19 patients from March 2020 onwards on the request of the government, according to the decree dated April 21, 2020.

For the COVID-19 cohort, all patients hospitalized for COVID-19 from March 1st, 2020, to April 30th, 2020, were included, regardless of their age. Patients were followed up until the end of their hospital stay, even if that date was after April. Hospital stays for COVID-19 were identified by the primary diagnoses (PD), related diagnoses (RD) or associated diagnoses (AD) by the ICD-10 codes U0710, U0711, U0712, U0714 or U0715. 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.

This study was approved by the *Comité Ethique et Scientifique pour les Recherches, les Etudes et les Evaluations 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

The following variables were extracted for each inpatient stay: age, sex, transfer to an intensive care unit (ICU), and hospital death. We also included all diagnoses (PD, RD and AD, ICD-10 codes) recorded in the discharge abstracts for the included hospital stays (COVID-19 and influenza) in order to analyse comorbidities (hypertension, diabetes, dementia, HIV, heart failure, chronic respiratory and kidney diseases, cirrhosis, peripheral vascular disease, overweight, dyslipidemia, deficiency anemia, pulmonary bacterial infection, immunocompromised status) and complications (acute respiratory and kidney diseases, stroke, myocardial infarction, atrial fibrillation, venous thrombosis including pulmonary embolism). Deficiency anemia included iron anemia and other causes of deficiency anemia. Immunocompromised patients were those with agranulocytosis, immunodeficiency, medullar aplasia and cancer treated by chemotherapy. We also identified ventilation procedures. The Charlson comorbidity index [4] and the Elixhauser comorbidity score [5] were retrieved. We also used the social deprivation index (taking into account the socio-economic environment of the patient) [6]. In theory, this index ranges from -6.4 for the least deprived areas to 21.2 for the most deprived areas. Thus, the higher the score, the more disadvantaged the municipality. We divided this index into 4 quartiles, with the lowest quartile representing the least deprived group.

Nine age classes were assessed: younger than 18, 18-30, 31-40, 41-50, 51-60, 61-70, 71-80, 81-90 and >90. For patients younger than 18, four subclasses were created: 0-1, 1-5, 6-10 and 11-17. All identified medical conditions were accounted for in relation to the patient. If a patient had at least once one condition during one of the stays for COVID-19 or for influenza, then the patient is considered to have had the condition. Qualitative variables are

provided as frequencies (percentages), and quantitative variables are provided as means \pm standard deviation (SD) and medians [interquartile range (Q1-Q3)].

The different variables studied in the cohort of patients hospitalized for COVID-19 were compared using the Chi-2 test or the Fisher's exact test (for qualitative variables) and Student's t test or Mann-Whitney test (for quantitative variables) when applicable to the variables of the influenza population to see if some populations are more represented among COVID-19 cases. These comparisons were made for all patients and then by age group.

In order to account for a possible age difference between the two populations, we also stratified the results by age. Furthermore, we estimated an age-standardized mortality ratio by calculating a mortality ratio between the observed number of hospital deaths in the COVID-19 population and the number of deaths that would be expected with the same influenza age-specific case fatality rates.

Considering the potential heterogeneity of patients admitted to hospital in the three stages of the epidemic, we performed a sensitivity analysis restricted to Stage 3 of the epidemic (March 14th onwards).

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

Role of the funding source: The project was funded by the French National Research Agency.

The corresponding author had full access to all of the data and the final responsibility to submit for publication. All authors had access to all the data reported in the study. The funder of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

CQ and JC had access to the raw data. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Nearly twice as many patients were hospitalized for COVID-19 than for seasonal influenza (89,350 over two months vs 45,819 over three months, respectively). The baseline characteristics of these patients are presented in **Table 1**. Patients hospitalized for COVID-19 were more often male. The age distribution also differed, with a median age of 68 for COVID-19 and 71 for influenza, while the proportions in extreme ages (below 18 and above 80) were higher for influenza.

There were differences in the distribution of the social deprivation score, but there was no distinct trend since the 2 extremes (the best and the worst) were both more frequently observed in the COVID-19 group. The deprivation score was significantly lower among COVID patients older than 40 years, including in the oldest age groups. Conversely, it was significantly higher in COVID-19 patients between 18 and 40 years.

The Charlson comorbidity index was slightly higher in the influenza group than in the COVID-19 group, but statistical significance was not reached with the Elixhauser comorbidity score. More specifically, COVID-19 patients were more often obese or overweight, diabetic, hypertensive, and dyslipidemic, whereas the influenza patients suffered more often from chronic heart failure, peripheral vascular disease, chronic respiratory disease, cirrhosis, and deficiency anemia. By contrast, people living with HIV were not over- or under-represented in the COVID-19 group. However, there were fewer immunocompromised patients in the COVID-19 group than in the influenza group. Pulmonary bacterial coinfection was diagnosed

in 6,286 (7.0%) COVID-19 patients and in 3,142 (6.9%) patients with influenza ($p=0.26$). The results are presented by age class in **supplementary Table 1 (pages 1-3)**.

Regarding the clinical evolution following admission (**Table 2**), hospitalized COVID-19 patients were more likely to develop respiratory distress, pulmonary embolism and septic shock, but less likely to develop myocardial infarction and atrial fibrillation. For strokes, we found that only hemorrhagic strokes were more frequent among COVID-19 patients.

COVID-19 patients were more likely to need intensive care, and the median length of stay in the ICU for COVID-19 was twice as long (15 for COVID-19 vs 8 days for influenza, $p<0.01$). A quarter of COVID-19 patients remained in the ICU for more than 3 weeks. COVID-19 patients required more invasive mechanical ventilation (9.7% vs 4.0%, $p<0.01$). When admitted in ICU, COVID-19 patients requested also more frequently mechanical ventilation than influenza patients. Finally, the in-hospital case fatality rate was higher in patients hospitalized for COVID-19 (16.9% vs 5.8%, $p<0.01$), with a relative risk of death of 2.9 [2.8-3.0].

We found a standardized mortality ratio of 2.82. This means that the number of observed deaths was 2.82 times higher than what would be expected if the COVID-19 population had the same probability of dying as the influenza population. The case fatality rate was also higher in COVID-19 patients admitted to the ICU, whether they were mechanically ventilated or not. After stratifying patients according to the main comorbidities, the in-hospital mortality for COVID-19 patients was roughly three times higher than that of patients with influenza, whatever the comorbidity (supplementary Table 2), and roughly two times higher in those with pulmonary bacterial coinfection (case fatality rate of 25.4% for COVID-19 vs 13.9% for influenza).

After stratification on age (**Figure 1, supplementary Table 3 and supplementary Figure 1, pages 5 and 6**), the rates of hospitalization in the ICU in the COVID-19 group were significantly higher for patients younger than 18 years and those 61 to 80 years. On the contrary, this rate tended to be lower in particular for patients older than 80 years. However, in patients older than 50 years and younger than 18 years, the case fatality rates were consistently higher in the COVID-19 group.

We identified 1,227 children hospitalized for COVID-19 and 8,942 children hospitalized for influenza (**Figure 2, supplementary Table 4 and supplementary Figure 2, pages 7 and 8**). The need for intensive care was highest in COVID-19 patients younger than 5 years (14/613 for COVID-19, 2.3% vs 65/6,973 for influenza, 0.9%), but the case fatality rate in this group was not higher than for influenza (3, 0.5% vs 13, 0.2%). However, the case fatality rate was tenfold higher for COVID-19 in children aged 11-17 with COVID-19 than in patients in the same age group with influenza (5/458, 1.1% vs 1/804, 0.1%). The 11-17-year-old children hospitalized for COVID-19 were more likely to be obese (2.0% vs 0.5%, $p<0.01$) or overweight (2.6% vs 1.1%, $p<0.01$) than those hospitalized for influenza. By contrast, they were less likely to be diabetic (1.5% vs 4.1%, $p<0.01$) or to have chronic pulmonary disease (0.7% vs 2.1%, $p<0.01$).

Our sensitivity analysis, which was restricted to Stage 3 of the epidemic (March 14th onwards), provided similar results (**supplementary Tables 5, 6, 7 and 8, pages 9 - 13**).

Discussion

In this nationwide survey comparing the COVID-19 epidemic to seasonal influenza, the most striking result is that nearly twice as many patients were admitted to hospital for COVID-19 over a two-month period than for seasonal influenza over a 3-month period. There is a small possibility that certain patients hospitalized in 2020 were misclassified as COVID-19 when they actually had influenza. However, this risk should be limited because the period studied

in 2020 was at the end of the influenza epidemic in France and because the results of sensitivity analysis limited to Stage 3 of the epidemic were similar to those of the main analysis. The observed difference in admissions is likely underestimated considering that the COVID-19 epidemic peaked in the first week of April, and since universal lockdown measures were already in place in France by March 17th, contributing to a reduction in the rate of transmissions and thus of hospitalization in the following weeks [7]. On the other hand, influenza vaccination coverage against seasonal influenza in France was 29.7% for those under 65 and 51.0% for those over 65 in 2018-2019 according to the National Public Health Agency. The influenza vaccine thus likely contributed modestly to lower rates of hospitalization for seasonal influenza and the associated case fatality rate [8], which suggests that this ratio could be higher in other settings or periods, or if the residual population immunity acquired from previous seasonal influenzas (which cannot be assessed) is lower than usual.

Our second key finding is that the in-hospital case fatality rate associated with COVID-19 was nearly three times higher than for seasonal influenza, with an age standardized mortality ratio of 2.82. In addition, COVID-19 patients were twice as likely to be put under invasive mechanical ventilation, and COVID-19 patients hospitalized in the ICU stayed nearly twice as long as those with influenza. It is worth noting that the 2018-2019 period had the highest case fatality rate for seasonal influenza in France within the past 5 years (12,300 deaths including 8,100 directly attributable to influenza) [8]. This indicates that the excess mortality observed for COVID-19 was not the result of an influenza season that was less severe than usual.

Another potential explanation for the higher case fatality rate is that the sudden influx of patients over a short period of time created medical structural constraints, and care teams were led to prioritize patients based on clinical status and prognosis. This hypothesis is supported by the lower rate of transfer to ICU in patients older than 80 years with COVID-19, which strongly contrasts with the higher case fatality rate in these same patients.

Considering France's national health insurance system and the lack of association with the social deprivation score as a whole, it seems likely that the drop in intensive care transfers is related to poorer prognoses rather than to socio-economic considerations. Nevertheless, it cannot be excluded that social deprivation may be a significant risk factor in younger adults since the deprivation score was significantly higher in patients aged 18 to 40 years.

The higher in-hospital case fatality rates observed in particular in younger COVID-19 patients also suggests that COVID-19 is intrinsically more severe than influenza. Even though children seemed to have a lower risk of being hospitalized for COVID-19 (as shown here by the very low rate of hospitalization for COVID-19 compared with seasonal influenza in patients younger than 18), the in-hospital death rate in these children was more than 4 times higher than it was for children with influenza. This contrasts sharply with recent reports stating that the clinical manifestations of COVID-19 are very often mild in children [9] [10] [11]. The clinical manifestations of COVID-19 appear to be milder than those of influenza in children under 5 years [12], and did not seem more severe than other CoV or influenza infections in children under one year [13]. If excess in-hospital mortality in our study seemed to be avoided by an increased use of intensive care support for children younger than 5 years, the comparatively higher rate of mortality associated with COVID-19 in children 11 to 17 years old indicates that there is a need to be particularly vigilant in young people with overweight or obesity. The increase in the case fatality rate might be partly linked to pediatric inflammatory multisystem syndrome (PIMS, also Kawasaki-like syndrome). Indeed, an unexpectedly high incidence of this syndrome has been observed recently, including in teenagers with COVID-19 [14] [15], but it remains rare and does not likely explain the increased risk of mortality. In addition, even though this syndrome may sometimes lead to death, no association with overweight has been reported so far.

The third main finding is that severity may be linked to the comorbidities associated with each viral disease. The median age of patients hospitalized for COVID-19 in France was within the range reported in other large international studies [2] [16]. The overall comorbidity scores tended to be lower in COVID-19 patients than in patients with seasonal influenza, and the patients admitted with COVID-19 were more typically male with fewer comorbidities, as previously observed [2]. Whereas diabetes and overweight seem to be particular risk factors for COVID-19 hospitalization [2] [16] [17] [18], major comorbidities such as heart failure, chronic respiratory disease and cirrhosis, albeit frequently associated with COVID-19 [2] [16] [17] [18], were more often observed in the seasonal influenza group. The higher short-term impact of these three conditions when compared with diabetes and obesity [19] is another argument in favour of an intrinsic increased severity of SARS-CoV2. Thus, though the differences in comorbidities might explain the difference in disease severity, these underlying conditions may also be due to an exaggerated immune response in COVID-19, or to the exacerbation of comorbidities in influenza infection. Another point of interest is that people living with HIV in our study did not seem to be more affected by COVID-19 than seasonal influenza. This supports the hypotheses that i) virologically controlled HIV populations do not have a considerably higher risk of developing severe COVID-19 (as sometimes observed in countries with low antiretroviral rates [20]), and, ii) on the contrary, people with HIV should not be considered at a lower risk because of a potential preventive effect of antiretroviral therapy [21].

Fourth, regarding the outcomes of hospitalized patients, respiratory complications were more frequent in COVID-19 than in seasonal influenza. Similar to other studies, we found that bacterial superinfections were infrequent in COVID-19 [16] [22], conversely to what has been reported for influenza epidemics [23]. It therefore seems that SARS-CoV2 has a superior potential for respiratory pathogenicity, potentially by inducing an upregulation of a small number of inflammatory mediators (including IL-6) [24], and that respiratory complications are mainly responsible for the excess mortality observed in COVID-19. As previously reported, COVID-19 patients have a higher risk of pulmonary embolism [25]. A higher risk of haemorrhagic strokes (but not ischemic strokes, as more often observed [26] [27]) has also been described, not only because of specific COVID-19-induced cerebral vasculitis, but also because of the high doses of anticoagulants used to prevent or reduce the risk of thromboembolism. And, more surprisingly, we found that COVID-19 patients, who are often considered to have higher cardiac risks (including for acute coronary syndrome, myocarditis, arrhythmias, and cardiogenic shock) [28], actually had lower cardiac risk than seasonal influenza patients. Patients with influenza were more likely to have chronic heart failure at baseline, but the question of whether the incidence and the impact of seasonal-influenza-related myocarditis is underestimated requires further investigation [29].

Although this study includes data collected on a national level from more than 100,000 hospitalized patients of all ages, we recognize that there are several limitations. First of all, the comparison between COVID-19 and seasonal influenza may seem difficult given possible testing biases and differences between viruses. It is likely that more patients were being tested for COVID-19 than influenza during the 2018-19 season, but we included in our study only hospitalized patients. Tests systematically carried out in an ambulatory care setting for COVID-19 should have a limited influence on the number of patients hospitalized, particularly in intensive care units. However, testing practices for influenza are likely to be highly variable across hospitals, whereas practices for COVID-19 may be more standardized (eg. all hospitalized patients require testing). The comparison between COVID-19 and seasonal influenza may also be not direct since the study periods are roughly one year apart. It also cannot be ascertained that the 2018-2019 seasonal influenza is representative of all seasonal influenzas, even though it was the most severe season in the past 5 years in France. It is also possible that some COVID-19 patients were suffering from influenza at the same time, but such a possibility seems unlikely since influenza diagnostic procedures were

accessible throughout the study period, and moreover because the 2019-2020 influenza epidemic was ending at the start of the COVID-19 epidemic. In addition, we found no differences between the sensitivity analyses restricted to Stage 3 of the COVID-19 epidemic and the main analyses. In the Stage 3 period (March 14th onward), it is very unlikely that COVID-19 patients were suffering from influenza. . The characteristics of patients who died from COVID-19 in places outside of the hospital setting, in a nursing home for example, could be different than the 15,104 deaths identified in our study. Another limitation concerns a potential for misclassification-related or under-detection-related bias, especially for comorbidities since they were only identified during the stays for COVID-19 or for influenza. Even so, this misclassification bias is likely to be non-differential for the majority of the comorbidities. We cannot always distinguish between acute and chronic conditions, for example in heart failure where the same code is used for chronic heart failure and for cardiac decompensation. Moreover, the PMSI inpatient database for COVID-19, with accelerated transmission of COVID-19-related patient data, was only recently developed on the request of the government (following the decree of April 21), and these data are still pending consolidation. This is, in particular, the consequence of the strain on our health care system and its mobilization to care for the sick, and the willingness to act quickly. Information relative to do-not-resuscitate orders was not available in our database, nor was ethnicity data since its collection is not authorised in France. We were also lacking detailed data for some potentially relevant findings such as the higher frequency of septic shock in COVID-19 patients or the underlying reasons for mortality in teenagers. We acknowledge that, despite the collection of nationwide data, the conclusions about ICU support and deaths in children are based on small numbers (e.g. in children under 5 years, 3 deaths were associated with COVID-19 and 13 with influenza). Whether genetic characteristics could be associated with severity could not be assessed in these cases [30]. Finally, we did not have to deal with incomplete data. For some variables, information is not completed in the discharge abstract when there is no impact on patient care during hospitalisation. It is often the case for day-care hospitalisations but this situation does not apply for the considered hospitalisations.

In conclusion, despite the initial speculation, there are significant differences between patients with COVID-19 and seasonal influenza requiring hospitalization. SARS-CoV2 appears to have a higher potential for respiratory pathogenicity, leading to more respiratory complications in patients with fewer comorbidities, and it is associated with a higher risk of mortality, particularly in teenagers, but any conclusions for this age group need to be taken with caution considering the small number of deaths. These findings were confirmed even after we took into account the constraints linked to the sudden influx of patients during the epidemic. In future, the possibility of overlapping influenza and COVID-19 epidemics will certainly also increase the complexity of patient management. At a time when no treatment has proven effective for the COVID-19 clinical course, this study highlights – yet again – the importance of all measures of physical prevention and the need for a specific vaccine and treatment for SARS-CoV2.

Contributors

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, LP, CQ and PTB wrote the first draft. JC was in charge of the analysis. JC and CQ accessed and verified the data. PB, LP, CQ, PTB, ASM, JC, MB were involved in the interpretation, critically reviewed the first draft, and approved the final version.

Declaration interests

For Lionel Piroth, since 2017, travel grants from Janssen-Cilag, MSD, Pfizer, and Gilead.

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All other authors declare no competing interests.

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Data sharing:

The PMSI database was transmitted by the national agency for the management of hospitalization data. The use of these data by our department was approved by the National Committee for data protection. We are not allowed to transmit these data.

PMSI data are available for researchers who meet the criteria for access to these French confidential data (this access is submitted to the approval of the National Committee for data protection) from the national agency for the management of hospitalization (ATIH - Agence technique de l'information sur l'hospitalisation).

Address:

Agence technique de l'information sur l'hospitalisation
117 boulevard Marius Vivier Merle
69329 Lyon Cedex 03

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Table 1. Main baseline characteristics of patients hospitalized in France for COVID-19 (from March 1st, 2020, to April 30th, 2020) or seasonal influenza (from December 1st, 2018, to February 28th, 2019)

	COVID-19	2018-2019 seasonal influenza	p-value
Number of patients	89,530	45,819	
Males (n, %)	47,495 (53.1)	22,118 (48.3)	<0.0001
Age			<0.0001
Mean+/-std	65 +/- 20	59 +/- 32	
Med [Q1-Q3]	68 [52-82]	71 [34-84]	
Min-Max	0-106	0-108	
<18	1,227 (1.4)	8,942 (19.5)	
18-30	4,384 (4.9)	1,836 (4.0)	
31-40	6,065 (6.8)	1,568 (3.4)	
41-50	8,892 (9.9)	1,626 (3.6)	
51-60	13,110 (14.6)	3,164 (6.9)	
61-70	15,345 (17.1)	5,624 (12.3)	
71-80	16,265 (18.2)	7,693 (16.8)	
81-90	17,841 (19.9)	11,276 (24.6)	
>90	6,401 (7.2)	4,090 (8.9)	
Social deprivation score			
Mean+/-std	-0.27 +/- 1.78	-0.17 +/- 1.56	<0.0001
Med [Q1-Q3]	-0,15 [-1,23 - 0,92]	-0,01 [-0,96 - 0,87]	
Lowest	22,922 (26.9)	9,195 (21.2)	<0.0001
Second	20,741 (24.4)	11,223 (25.9)	
Third	19,926 (23.4)	12,608 (29.1)	
Highest	21,593 (25.4)	10,256 (23.7)	
Comorbidity scores			
Charlson			
Mean+/-std	1.19 +/- 1.85	1.23 +/- 1.78	<0.0001
Med [Q1-Q3]	0 [0-2]	1 [0-2]	
0	45,237 (50.5)	21,715 (47.4)	<0.0001
1	19,730 (22.0)	10,539 (23.0)	
2	10,654 (11.9)	6,132 (13.4)	
>=3	13,909 (15.5)	7,433 (16.2)	
Elixhauser			
Mean+/-std	2.01 +/- 1.96	2.01 +/- 2.03	0.5906
Med [Q1-Q3]	1 [0-2]	2 [0-3]	
0	25,701 (28.7)	14,080 (30.7)	<0.0001
1	17,497 (19.5)	8,691 (19.0)	
2	15,458 (17.3)	7,280 (15.9)	
>=3	30,874 (34.5)	15,768 (34.4)	
Comorbidities			
Hypertension	29,622 (33.1)	12,921 (28.2)	<0.0001

Dementia	6,742 (7.5)	3,345 (7.3)	0.1274
HIV	432 (0.5)	205 (0.5)	0.3719
Heart failure	7,134 (8.0)	6,266 (13.7)	<0.0001
Chronic respiratory disease	1,433 (1.6)	1,830 (4.0)	<0.0001
Chronic kidney disease	7,458 (8.3)	3,821 (8.3)	0.9540
Cirrhosis	718 (0.8)	489 (1.1)	<0.0001
Diabetes	17,050 (19.0)	7,352 (16.1)	<0.0001
Peripheral vascular disease	2,870 (3.2)	1,614 (3.5)	<0.0021
Overweight	10,116 (11.3)	2,811 (6.1)	<0.0001
Body mass index (BMI)	8,611 (9.6)	2,491 (5.4)	<0.0001
30-40	7,446 (8.3)	2,078 (4.5)	<0.0001
40-50	2,398 (2.7)	706 (1.5)	
>50	1,391 (1.6)	192 (0.4)	
Dyslipidemia	4,489 (5.0)	2,072 (4.5)	<0.0001
Deficiency Anemia	3,501 (3.9)	1,946 (4.3)	<0.0029
Pulmonary bacterial infection	6,286 (7.0)	3,142 (6.9)	0.2629
Immunocompromised	3,395 (3.8)	2,033 (4.4)	<0.0001

Table 2· Main outcomes of patients hospitalized in France for COVID-19 (from March 1st, 2020, to April 30th, 2020) or seasonal influenza (from December 1st, 2018, to February 28th, 2019)

	COVID-19	2018-2019 seasonal influenza	p-value
Number of patients	89,530	45,819	
Acute respiratory failure	24,317 (27·2)	7,977 (17·4)	<0·0001
Pulmonary embolism	3,086 (3·5)	412 (0·9)	<0·0001
Venous thrombosis (including pulmonary embolism)	4,367 (4·9)	766 (1·7)	<0·0001
Septic shock	2,551 (2·9)	918 (2·0)	<0·0001
Myocardial infarction	558 (0·6)	506 (1·1)	<0·0001
Atrial fibrillation	11,129 (12·4)	7,222 (15·8)	<0·0001
Stroke	1,068 (1·2)	569 (1·2)	0·4357
Hemorrhagic stroke	253 (0·3)	93 (0·2)	0·0061
Ischemic stroke	714 (0·8)	405 (0·9)	0·0966
Transient Ischemic Attack	161 (0·2)	92 (0·2)	0·3982
Acute kidney failure	5,761 (6·4)	2,227 (4·9)	<0·0001
Invasive mechanical ventilation	8,684 (9·7)	1,833 (4·0)	<0·0001
Intensive care support	14,585 (16·3)	4,926 (10·8)	<0·0001
Mean stay in ICU (days, +/- SD)	15 +/- 14	8 +/- 9	<0·0001
Median stay in ICU (days, Q1-Q3)	10 [4-21]	5 [2-10]	<0·0001
Mechanical ventilation among ICU patients	10,430 (71·5)	3,004 (61·0)	<0·0001
In-hospital death	15,104 (16·9)	2,640 (5·8)	<0·0001
In hospital death that would be expected with the same influenza age-specific mortality rates	5,355 (6·0)		
Standardized mortality ratio (%)	282		
In-hospital death among ICU patients	3,949 (27·1)	885 (18·0)	<0·0001
Mean stay in ICU (days, +/- SD) non-deceased patients	15 +/- 15	8 +/- 9	<0·0001
Median stay in ICU (days, Q1-Q3) non-deceased patients	10 [3-21]	5 [2-9]	<0·0001
In-hospital death among ICU patients with mechanical ventilation	3,312 (31·8)	780 (26·0)	<0·0001
In-hospital death among ICU patients non ventilated	477 (17·2)	81 (5·4)	<0·0001

Figure 1: Intensive case support and case fatality rates of patients hospitalized in France for COVID-19 (from March 1st, 2020, to April 30th, 2020) or seasonal influenza (from December 1st, 2018, to February 28th, 2019), according to their age at admission

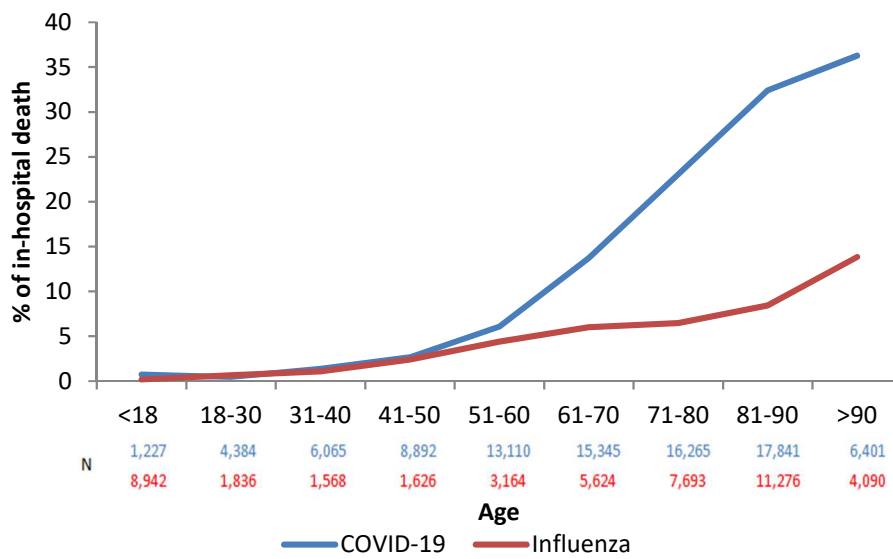
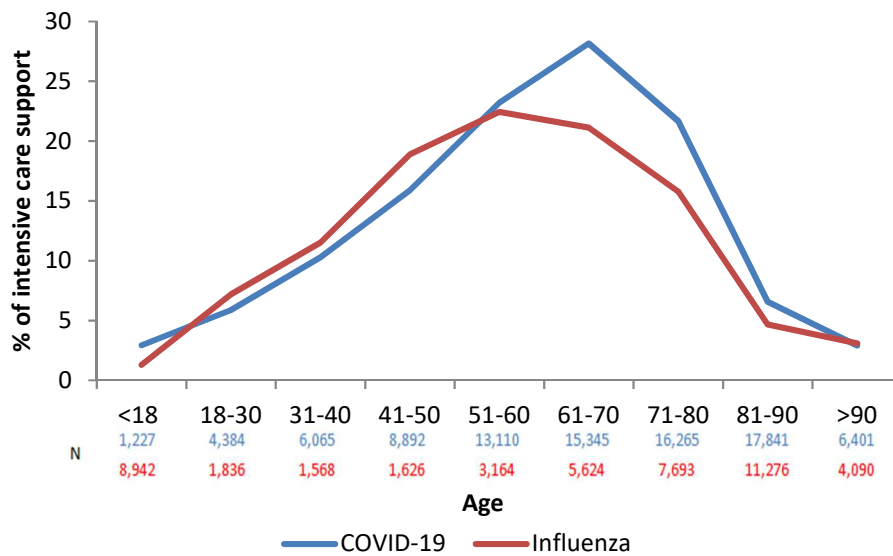


Figure 2: Intensive case support and case fatality rates of children hospitalized in France for COVID-19 (from March 1st, 2020, to April 30th, 2020) or seasonal influenza (from December 1st, 2018, to February 28th, 2019), according to their age at admission

