

Comparison of the characteristics, morbidity, and mortality of COVID-19 and seasonal influenza: a nationwide, population-based retrospective cohort study

Lionel Piroth, Jonathan Cottenet, Anne-Sophie Mariet, Philippe Bonniaud, Mathieu Blot, *Pascale Tubert-Bitter, *Catherine Quantin

Summary

Background To date, influenza epidemics have been considered suitable for use as a model for the COVID-19 epidemic, given that they are respiratory diseases with similar modes of transmission. However, data directly comparing the two diseases are scarce.

Methods We did a nationwide retrospective cohort study using the French national administrative database (PMSI), which includes discharge summaries for all hospital admissions in France. All patients hospitalised for COVID-19 from March 1 to April 30, 2020, and all patients hospitalised for influenza between Dec 1, 2018, and Feb 28, 2019, were included. The diagnosis of COVID-19 (International Classification of Diseases [10th edition] codes U07.10, U07.11, U07.12, U07.14, or U07.15) or influenza (J09, J10, or J11) comprised primary, related, or associated diagnosis. Comparisons of risk factors, clinical characteristics, and outcomes between patients hospitalised for COVID-19 and influenza were done, with data also stratified by age group.

Findings 89 530 patients with COVID-19 and 45 819 patients with influenza were hospitalised in France during the respective study periods. The median age of patients was 68 years (IQR 52–82) for COVID-19 and 71 years (34–84) for influenza. Patients with COVID-19 were more frequently obese or overweight, and more frequently had diabetes, hypertension, and dyslipidaemia than patients with influenza, whereas those with influenza more frequently had heart failure, chronic respiratory disease, cirrhosis, and deficiency anaemia. Patients admitted to hospital with COVID-19 more frequently developed acute respiratory failure, pulmonary embolism, septic shock, or haemorrhagic stroke than patients with influenza, but less frequently developed myocardial infarction or atrial fibrillation. In-hospital mortality was higher in patients with COVID-19 than in patients with influenza (15 104 [16.9%] of 89 530 vs 2640 [5.8%] of 45 819), with a relative risk of death of 2.9 (95% CI 2.8–3.0) and an age-standardised mortality ratio of 2.82. Of the patients hospitalised, the proportion of paediatric patients (<18 years) was smaller for COVID-19 than for influenza (1227 [1.4%] vs 8942 [19.5%]), but a larger proportion of patients younger than 5 years needed intensive care support for COVID-19 than for influenza (14 [2.3%] of 613 vs 65 [0.9%] of 6973). In adolescents (11–17 years), the in-hospital mortality was ten-times higher for COVID-19 than for influenza (five [1.1%] of 458 vs one [0.1%] of 804), and patients with COVID-19 were more frequently obese or overweight.

Interpretation The presentation of patients with COVID-19 and seasonal influenza requiring hospitalisation differs considerably. Severe acute respiratory syndrome coronavirus 2 is likely to have a higher potential for respiratory pathogenicity, leading to more respiratory complications and to higher mortality. In children, although the rate of hospitalisation for COVID-19 appears to be lower than for influenza, in-hospital mortality is higher; however, low patient numbers limit this finding. These findings highlight the importance of appropriate preventive measures for COVID-19, as well as the need for a specific vaccine and treatment.

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Introduction

In December, 2019, a new disease now known as COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged as a major world threat. Considering its ability to spread and the relatively low case-fatality rates initially reported in China, SARS-CoV-2 was thought to be more similar to influenza than SARS-CoV-1.¹ The preventive measures for this new infection were based on a comparison with the influenza virus because the viruses have similar modes of

transmission and cause respiratory disease. Patients with COVID-19 were also anticipated to benefit from the clinical knowledge and care management of influenza.

A global pandemic was declared on March 11, 2020. By July 10, 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.² At this point, COVID-19 had developed into a pandemic associated with substantial morbidity and mortality,



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*Contributed equally

Inserm CIC 1432, Clinical Epidemiology/Clinical Trials Unit, Clinical Investigation Centre (Prof L Piroth MD, A-S Mariet MD, Prof C Quantin MD), Infectious Diseases Department (Prof L Piroth, M Blot MD), Biostatistics and Bioinformatics (DIM) (J Cottenet MSc, A-S Mariet, Prof C Quantin), and Reference Centre for Rare Pulmonary Diseases, Pulmonary Medicine and Intensive Care Unit Department (Prof P Bonniaud MD), Dijon University Hospital, Dijon, France; Faculty of Medicine, University of Bourgogne-Franche-Comté, Dijon, France (Prof L Piroth, Prof P Bonniaud, J Cottenet, A-S Mariet, Prof C Quantin); Inserm LNC UMR1231, LipSTIC LabEx Team, Dijon, France (Prof P Bonniaud); and Université Paris-Saclay, UVSQ, Université Paris-Sud, Inserm, High-Dimensional Biostatistics for Drug Safety and Genomics, CESP, Villejuif, France (P Tubert-Bitter PhD, Prof C Quantin)

Correspondence to:
Prof Catherine Quantin,
Biostatistics and Bioinformatics (DIM), Dijon University Hospital, Dijon 21079, France
catherine.quantin@chu-dijon.fr

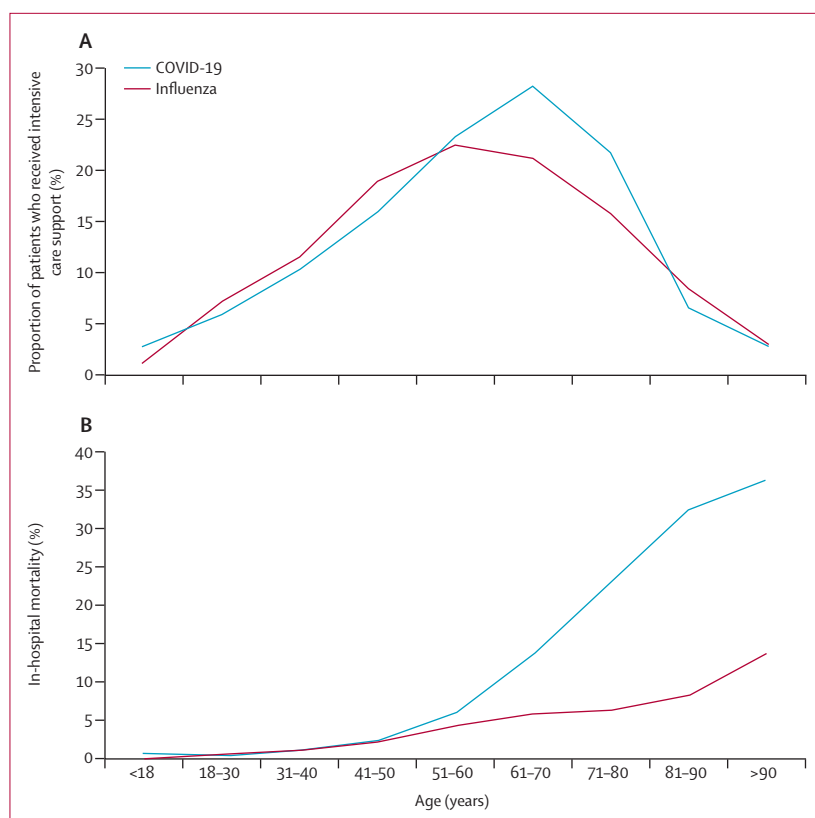


Figure 1: Intensive care support and mortality of patients hospitalised in France for COVID-19 or seasonal influenza, by age at admission

Date are for patients who were hospitalised for COVID-19 between March 1 and April 30, 2020, and for patients who were hospitalised for seasonal influenza between Dec 1, 2018, and Feb 28, 2019.

COVID-19 than influenza (14 [2.3%] of 613 for COVID-19 vs 65 [0.9%] of 6973 for influenza), but in-hospital mortality in this age group was did not significantly differ between the two diseases (three [0.5%] vs 13 [0.2%]). In patients aged 11–17 years, in-hospital mortality was ten-times higher for patients with COVID-19 than those with influenza (five [1.1%] of 458 vs one [0.1%] of 804). Patients aged 11–17 years who were hospitalised for COVID-19 were more likely to be obese (12 [2.6%] of 458 vs four [0.5%] of 804, $p < 0.0001$) or overweight (16 [3.5%] vs nine [1.1%], $p = 0.0036$) than those hospitalised for influenza. By contrast, they were less likely to have diabetes (seven [1.5%] vs 33 [4.1%], $p = 0.012$) or chronic respiratory disease (three [0.7%] vs 17 [2.1%], $p = 0.046$; appendix p 9).

Our sensitivity analysis, which was restricted to stage 3 of the COVID-19 epidemic (March 14, 2020, onwards), provided similar results (appendix pp 10–14).

Discussion

In this nationwide cohort study comparing the COVID-19 epidemic to seasonal influenza, almost twice as many patients were admitted to hospital for COVID-19 over a 2-month period than were admitted for seasonal influenza over a 3-month period. There is a small possibility that some patients hospitalised in 2020 were

misclassified as COVID-19 when they actually had influenza. However, the risk of misclassification is low because the period studied in 2020 was at the end of the influenza epidemic in France. In addition, the results of the sensitivity analysis, which was limited to stage 3 of the epidemic, were similar to those of the main analysis. The observed difference in admissions is likely to be an underestimation, considering that the COVID-19 epidemic peaked in the first week of April, 2020, and universal lockdown measures were already in place in France by March 17, contributing to a reduction in the rate of hospitalisation in the following weeks.¹¹ However, influenza vaccination coverage against seasonal influenza in France was 29.7% for those under 65 years and 51.0% for those over 65 years in 2018–19, according to the National Public Health Agency.¹² Therefore, the influenza vaccine probably contributed to lower rates of hospitalisation for seasonal influenza and associated mortality.¹³ These factors suggest that the difference in numbers of COVID-19 and seasonal influenza cases 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.

We found that the in-hospital mortality for COVID-19 was nearly three-times higher than for seasonal influenza, with an age-standardised mortality ratio of 2.82. In addition, patients with COVID-19 were twice as likely to receive invasive mechanical ventilation, and COVID-19 patients hospitalised in the ICU stayed nearly twice as long as those with influenza. Of note, the 2018–19 period had the highest case-fatality rate for seasonal influenza in France within the past 5 years (12 300 deaths, including 8100 directly attributable to influenza).¹³ Therefore, 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 mortality of COVID-19 is that the sudden influx of patients over a short period of time created medical structural constraints, and care teams were led to prioritise 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 mortality in these same patients.

We did not identify strong associations between disease outcomes and social deprivation score. Considering France's national health insurance system does not require individuals to pay upfront for health care, the lower proportion of patients being admitted to the ICU with COVID-19 than influenza is likely to be related to poorer prognoses rather than socioeconomic considerations. Nevertheless, we cannot exclude the possibility that social deprivation is a risk factor in younger adults because deprivation score was significantly higher in patients with COVID-19 aged