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## SPECIALTY SECTION

This article was submitted to Pulmonary Medicine, a section of the journal Frontiers in Medicine

RECEIVED 15 July 2022

ACCEPTED 17 August 2022

PUBLISHED 16 September 2022

## CITATION

Poucineau J, Delory T, Lapidus N, Hejblum G, Chouaïd C, Le Cœur S and Khat M (2022) Hospital admissions and mortality for acute exacerbations of COPD during the COVID-19 pandemic: A nationwide study in France. *Front. Med.* 9:995016. doi: 10.3389/fmed.2022.995016

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# Hospital admissions and mortality for acute exacerbations of COPD during the COVID-19 pandemic: A nationwide study in France

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**Background:** A global reduction in hospital admissions for acute exacerbations of chronic obstructive pulmonary disease (AECOPD) was observed during the first months of the COVID-19 pandemic. Large-scale studies covering the entire pandemic period are lacking. We investigated hospitalizations for AECOPD and the associated in-hospital mortality at the national level in France during the first 2 years of the pandemic.

**Methods:** We used the French National Hospital Database to analyse the time trends in (1) monthly incidences of hospitalizations for AECOPD, considering intensive care unit (ICU) admission and COVID-19 diagnoses, and (2) the related in-hospital mortality, from January 2016 to November 2021. Pandemic years were compared with the pre-pandemic years using Poisson regressions.

**Results:** The database included 565,890 hospitalizations for AECOPD during the study period. The median age at admission was 74 years (interquartile range 65–83), and 37% of the stays concerned women. We found: (1) a dramatic and sustainable decline in hospitalizations for AECOPD over the pandemic period (from 8,899 to 6,032 monthly admissions, relative risk (RR) 0.65, 95% confidence interval (CI) 0.65–0.66), and (2) a concomitant increase in in-hospital mortality for AECOPD stays (from 6.2 to 7.6% per month, RR 1.24, 95% CI 1.21–1.27). The proportion of stays yielding ICU admission was similar in the pre-pandemic and pandemic years, 21.5 and 21.3%, respectively. In-hospital mortality increased to a greater extent for stays without ICU admission (RR 1.39, 95% CI 1.35–1.43) than for those with ICU admission (RR 1.09, 95% CI 1.05–1.13). Since January 2020, only 1.5% of stays were associated with a diagnosis of COVID-19, and their mortality rate was nearly three-times higher than those without COVID-19 (RR 2.66, 95% CI 2.41–2.93).

**Conclusion:** The decline in admissions for AECOPD during the pandemic could be attributed to a decrease in the incidence of exacerbations for COPD patients and/or to a possible shift from hospital to community care. The rise in in-hospital mortality is partially explained by COVID-19, and could be related to restricted access to ICUs for some patients and/or to greater proportions of severe cases among the patients hospitalized during the pandemic.

#### KEYWORDS

AECOPD, hospitalizations, COVID-19 pandemic, mortality, nationwide study, France

## Introduction

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death and affects over 390 million people worldwide (1, 2). People living with COPD are prone to acute exacerbations of their symptoms, and severe exacerbations require hospital admission. If infected with COVID-19, they are at high risk of severity or mortality (3, 4).

A substantial decrease in the number of hospital admissions for acute exacerbation of COPD (AECOPD) during the first months of the COVID-19 pandemic has been reported in several countries (5–17), ranging from –42 to –48% among nationwide studies (6–8, 15, 17). This observation raises two critical concerns in terms of generalizability. First, whether this downturn pattern persisted over the entire pandemic period remains unknown, as most studies covered the first wave only (6, 7, 12–16), and no study spanning beyond February 2021 has yet been published. Second, to our knowledge, only five of the above-mentioned studies used national data (6–8, 15, 17), and these concerned relatively small countries (Wales, Scotland, Denmark, Slovenia and Norway), with the exception of South Korea, covering the first half of 2020 only (15). Furthermore, findings on in-hospital mortality trends for COPD patients during the pandemic are inconsistent. Two studies found an increased mortality in 2020 compared to pre-pandemic years, of respectively +53 and +130% but both were based on small numbers (8, 16), while others did not find a significant difference (11, 12, 14). To date, time trends in in-hospital mortality have not been analyzed with large-scale and exhaustive data. Finally, while most studies found a stable proportion of AECOPD stays involving intensive care units (ICU) admission in 2020 compared to previous years (11, 14, 16), a cohort study in Denmark found a 36% decrease in the risk of admission to an ICU in COPD patients (7).

France has been heavily affected by the COVID-19 pandemic, with over 31 million confirmed cases and 146,000 deaths as of July 2022 (18). Numerous health measures have been implemented, including stringent lockdowns and travel restrictions, likely to affect care for non-COVID-19 disorders.

During lockdowns, hospitals suspended most ‘non-essential’ activities to focus on managing COVID-19 cases.

Based on exhaustive hospitalization data at the national level, the present study describes how hospitalizations for acute exacerbations of COPD (AECOPD) and the associated in-hospital mortality varied in France throughout the first 2 years of the pandemic. The specific objectives of the study were to (1) study trends in admissions and mortality by demographic characteristics, (2) compare the observed trends with those estimated in the absence of a pandemic, (3) explore possible associations between COVID-19 diagnosis, ICU admission and in-hospital mortality, (4) suggest interpretations of the results based on the literature and the context in France during the pandemic.

## Materials and methods

This observational study was conducted according to STROBE guidelines (19). The study is based on the French National Hospital Database (*Programme de Médicalisation des Systèmes d’Information*; PMSI) from the National Health Data System (*Système National des Données de Santé*; SNDS), an exhaustive and nationwide administrative health claims database, covering 99% of the French population, i.e., over 66 million people, from birth or immigration until death or emigration. The PMSI covers all private and public medical, obstetric and surgery hospitalizations (20). Patients can be tracked individually with a unique and anonymous identifier. All hospital stays are assigned a primary diagnosis (PD) and possibly one or more associated diagnoses (AD), coded according to the International Classification of Diseases, 10th revision (ICD-10). We identified hospital stays for AECOPD using an algorithm based on ICD-10 codes, validated by the French Institute for Public Health, and adapted by Cavailles et al. (21). This algorithm is based on a narrow definition of AECOPD to avoid overlap with asthma or other chronic pulmonary condition. We included patients aged 40 years or older with compatible ICD-10 codes:

- J44.0 or J44.1 as PD,
- or J96.0 as PD and (J43 or J44) as AD,
- or (J09-18 or J20-22) as PD and (J43 or J44) as AD,
- or (J43 or J44) as PD and (J44.0 or J44.1 or J96.0 or J09-18 or J20-22) as AD.

This algorithm excludes stays lasting fewer than 2 days, unless patients died during hospitalization, in order to eliminate scheduled hospitalizations for check-up examinations.

Among the study population, we identified stays with an associated diagnosis of COVID-19, using the ICD-10 code U07.1. In the PMSI, the code U07.2 has not been created and all COVID-19 diagnoses were grouped within the code U07.1. Stays with a primary diagnosis of COVID-19 – whether they had an associated diagnosis of AECOPD or not – were not included.

The study period extended from January 2016 to November 2021 and was divided into two main periods: one further referred to as the “pre-pandemic years” including data from 2016 to 2019 as the reference, and the other as the “pandemic years” including data from January 2020 to November 2021. During the pandemic years, three sub-periods, representing broadly the first three waves of the pandemic in France, were especially investigated: March to June 2020, September to December 2020, and January to May 2021.

The main outcomes of this study were the time trends in (1) monthly incidences of hospitalizations for AECOPD and (2) the corresponding in-hospital fatality rate. Admissions to intensive care units (ICU), COVID-19 diagnoses and their relation to in-hospital mortality were also investigated. Analyses were stratified by sex and age groups (40–49 years, 50–59, 60–69, 70–79, and 80 or older). Relative risks (RR) were estimated by comparing each sub-period of the pandemic to the same months in 2016–2019, for both outcomes. Poisson regressions of the monthly counts of admissions and in-hospital deaths were performed, adjusting on sex, with random intercepts for month and age group, and using national census data and AECOPD admissions as offsets. Expected numbers of admissions and in-hospital deaths in 2020–2021 in the absence of a pandemic were obtained by Poisson regressions using a similar method, adding a sinusoidal component to account for seasonality. To estimate the expected number of in-hospital deaths in 2020–2021, we applied the in-hospital mortality rates observed in 2016–2019 to the stays observed in 2020–2021. Excess deaths were estimated as the difference between *observed* and *expected* deaths in 2020–2021. The same calculation was applied to the group of patients with AECOPD and COVID-19 diagnoses to obtain the proportion of excess deaths attributable to COVID-19.

Sensitivity analyses were conducted to test the variability of our results according to the inclusion or exclusion of stays lasting fewer than 2 days, and the definition of AECOPD admission (broad vs. narrow). The broad definition of AECOPD was based on an algorithm developed by Fuhman et al. (22), which includes all stays with an ICD-10 code J44 or J43 as primary

diagnosis and those with the same codes or combination of codes as described above, regardless of the type of diagnosis (primary or associated).

No missing data had to be processed, as all variables of interest were correctly filled in. The study was conducted in accordance with relevant international and French regulatory requirements, including the dedicated permanent authorization to use PMSI granted to the French Institute for Demographic Studies (INED) by Decree No. 2016–1871 of December 26, 2016 on the processing of personal data. The study was registered on the European Network of Centers for Pharmacoepidemiology and Pharmacovigilance (ENCePP) registry under the number “EUPAS40492”.

The study was funded by the grant PREPS-20-0163 (*Programme de recherche sur la performance du système des soins*, French Ministry of Solidarity and Health).

## Results

### Hospital admissions

From January 1, 2016 to November 30, 2021, 321,013 individuals were hospitalized for AECOPD, with a total of 565,890 corresponding admissions (Table 1). The median age at admission was 74 years (interquartile range 65–83), and 209,290 (37%) concerned women. There was a seasonal pattern in monthly incidence of hospitalizations for AECOPD during the reference pre-pandemic years, with the highest levels observed from December to March and the lowest levels observed from July to September. Such a pattern did not occur during the pandemic years (Figure 1).

Overall, the average monthly incidence of admissions for AECOPD decreased by 35% during the pandemic years compared to pre-pandemic years (from 8,899 to 6,032 admissions per month, RR 0.65, 95% CI 0.65–0.66; Table 2). The gap widened across the three pandemic sub-periods, from a 34% decrease in the first sub-period (RR 0.66, 95% CI 0.65–0.67), to 45% in the second (RR 0.55, 95% CI 0.55–0.56), and 53% in the third (RR 0.47, 95% CI 0.46–0.47). Thereafter, the incidence of hospitalizations for AECOPD remained low until October 2021, when it started to rise slightly again. This downward trend was observed across all age groups, and was enhanced in the group of patients aged 80 or older vs. others (RR 0.84, 95% CI 0.83–0.85). Trends were similar for in men’s and women’s during the pandemic years.

From January 2020 to November 2021, 2,105 hospitalizations for AECOPD also had a COVID-19 associated diagnosis, accounting for 1.5% of total admissions (Table 1). The proportion of AECOPD stays involving an admission to an ICU was similar in the pre-pandemic and pandemic years (21.5 and 21.3%, respectively). Exacerbations associated with COVID-19

TABLE 1 Mortality and ICU admission rates for AECOPD stays (2016–2021).

	Stays	Deaths	Mortality rate	ICU admission rate
Years 2016–2019	427,165	26,562	6.2%	21.5%
Years 2020–2021*	138,725	10,322	7.4%	21.3%
with COVID-19 AD	2,105	424	20.1%	32.4%
without COVID-19 AD	136,620	9,898	7.2%	21.1%

AECOPD, acute exacerbation of chronic obstructive pulmonary disease; ICU, intensive care unit; AD, associated diagnosis.

\* December 2021 data are not included.

more frequently resulted in ICU admission than those without (32.4 vs. 21.1%, RR 1.58, 95% CI 1.46–1.70).

Whereas 158,725 hospital stays for AECOPD were observed during the pandemic years, we estimated that in the absence of a pandemic, a total of 58,691 additional stays would have been expected in the same period (+37%): 27,095 (95% CI 22,093–32,296) stays in addition to the 76,000 stays observed in 2020, and 31,596 (95% CI 25,334–38,325) stays in addition to the 62,725 stays observed in 2021.

## In-hospital mortality

The average monthly in-hospital mortality rate for AECOPD stays increased by 24% during the pandemic years (from 6.2 to 7.6% fatal issues, RR 1.24, 95% CI 1.21–1.27), reaching a peak at 9.8% in December 2020 (see Figure 1; Table 3). The increase in in-hospital mortality was observed across all age groups during the pandemic years. This trend was attenuated in the group of patients aged 80 or older compared with others (RR 0.92, 95% CI 0.88–0.97). Trends in men's and women's in-hospital mortality were similar during the pandemic years, except for the second sub-period, when men had higher excess in-hospital mortality.

Stays associated with a COVID-19 diagnosis had a substantially higher mortality rate than those without (20.1 vs. 7.2%, RR 2.66, 95% CI 2.41–2.93). Yet, stays without COVID-19 still had a significant increase in in-hospital mortality during the pandemic years compared to pre-pandemic years (from 6.2 to 7.2%, RR 1.21 95% CI 1.18–1.24).

In-hospital mortality rates for stays involving an ICU admission increased slightly during the pandemic years in comparison with pre-pandemic years (from 12.9 to 13.8%, RR 1.09, 95% CI 1.05–1.13). In-hospital mortality rates for stays not involving an ICU admission increased to an even greater extent (from 4.4 to 5.8%, RR 1.39, 95% CI 1.35–1.43).

We estimated that, among the 10,322 deaths observed for AECOPD stays during the pandemic years, 1,974 deaths (19%) were in excess: in the absence of a pandemic, 862 (95% CI 681–1,026) fewer deaths would have been expected in 2020 and 1,112 (95% CI 940–1,272) in 2021 compared to the 5,487 and 4,835 deaths observed, respectively. Regarding stays associated with COVID-19, we estimated that among the 424 deaths observed

during the pandemic, 291 occurred in excess, including 151 (95% CI 148–154) in 2020 and 140 (95% CI 137–143) in 2021. Therefore, since the pandemic started, COVID-19 accounted for 14.8% (95% CI 12.9–17.6%) of the estimated excess deaths for AECOPD stays.

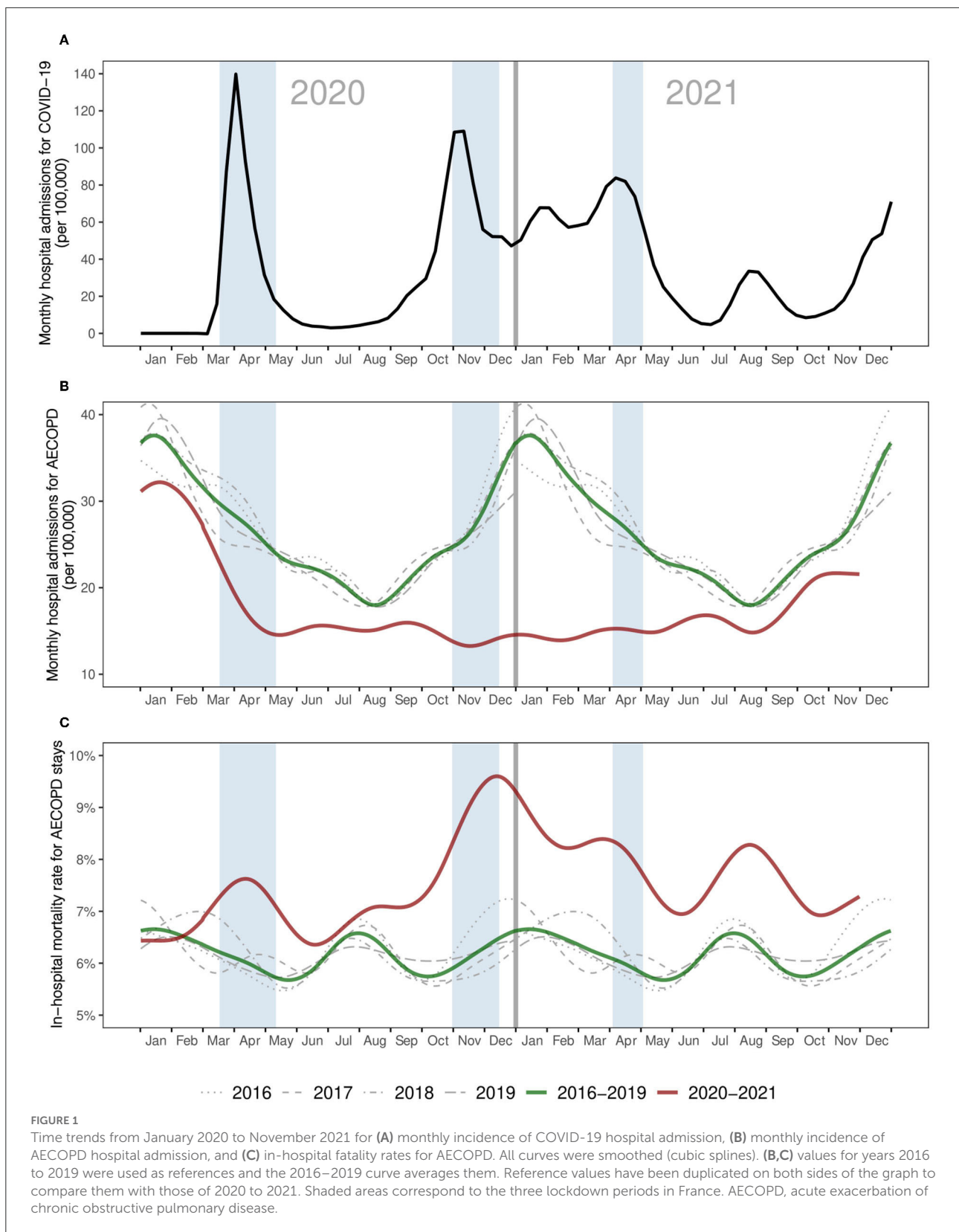
## Sensitivity analysis

There was a greater proportion of stays shorter than 2 days among AECOPD stays during the pandemic years compared to pre-pandemic years (14 and 10%, respectively). Nevertheless, similar trends in AECOPD admissions and in-hospital mortality were obtained when stays shorter than 2 days were included in the analyses. Likewise, results based on the broad definition of AECOPD were very similar to those reported above (data not shown).

## Discussion

The present study is, to our knowledge, the largest study to investigate in detail AECOPD hospitalizations during the 2020 and 2021 pandemic years, compared with the 2016–2019 pre-pandemic years. To date, the largest study in the literature contained fewer than 17,000 hospitalisations (7). Based on the corresponding 565,890 hospital stays for AECOPD, the major findings of this study are (1) a sharp decline in the number of AECOPD hospitalizations during the 2020–2021 period, and concomitantly, (2) a substantial increase in in-hospital mortality.

A reduction in hospitalizations for AECOPD during the first months of the pandemic has been documented in the literature, with estimates ranging from –42 to –48% among nationwide studies (6–8, 15, 17). In this study, we show that this phenomenon persisted far beyond the first pandemic wave, with a global decline of –35% hospital admissions when considering the whole 2020–2021 pandemic years, and nearly 60,000 fewer stays than expected in the absence of a pandemic. In contrast, hospitalizations for causes other than COVID-19 reduced by only 13% in France in 2020 compared to 2019



**TABLE 2** Relative risk of hospital admission for AECOPD for different pandemic periods, compared with the same months over the reference years, by age group and sex.

	Mar–Jun 2020	Sep–Dec 2020	Jan–May 2021	2020–2021 (total)
<b>Age group (years)</b>				
40–49	0.74 (0.68–0.81)	0.61 (0.56–0.66)	0.51 (0.47–0.55)	0.71 (0.68–0.73)
50–59	0.71 (0.69–0.74)	0.55 (0.53–0.58)	0.49 (0.47–0.51)	0.68 (0.67–0.70)
60–69	0.74 (0.72–0.76)	0.60 (0.58–0.62)	0.52 (0.51–0.54)	0.72 (0.72–0.73)
70–79	0.67 (0.66–0.69)	0.58 (0.56–0.59)	0.48 (0.47–0.49)	0.66 (0.66–0.67)
≥ 80	0.58 (0.57–0.59)	0.50 (0.48–0.51)	0.41 (0.40–0.42)	0.58 (0.57–0.58)
<b>Sex</b>				
Men	0.68 (0.67–0.70)	0.57 (0.56–0.58)	0.47 (0.46–0.48)	0.66 (0.65–0.66)
Women	0.63 (0.61–0.64)	0.52 (0.51–0.53)	0.46 (0.45–0.47)	0.64 (0.64–0.65)
<b>Total</b>	0.66 (0.65–0.67)	0.55 (0.55–0.56)	0.47 (0.46–0.47)	0.65 (0.65–0.66)

Relative risks (95% confidence intervals). AECOPD, acute exacerbation of chronic obstructive pulmonary disease.

**TABLE 3** Relative risk (95% confidence interval) of in-hospital death for AECOPD stays for different pandemic periods, compared with the same months over the reference years, by age group and sex.

	Mar–Jun 2020	Sep–Dec 2020	Jan–May 2021	2020–2021 (total)
<b>Age group (years)</b>				
40–49	2.41 (1.39–4.20)	1.98 (1.06–3.68)	1.42 (0.79–2.56)	1.48 (1.11–1.97)
50–59	1.03 (0.79–1.35)	1.29 (0.98–1.69)	1.20 (0.94–1.53)	1.15 (1.03–1.29)
60–69	1.22 (1.08–1.37)	1.43 (1.26–1.62)	1.42 (1.27–1.59)	1.28 (1.21–1.35)
70–79	1.31 (1.19–1.44)	1.55 (1.41–1.71)	1.45 (1.33–1.58)	1.31 (1.25–1.37)
≥ 80	1.17 (1.08–1.26)	1.34 (1.24–1.45)	1.29 (1.21–1.38)	1.20 (1.16–1.24)
<b>Sex</b>				
Men	1.23 (1.15–1.31)	1.47 (1.38–1.56)	1.37 (1.29–1.45)	1.25 (1.22–1.29)
Women	1.20 (1.09–1.32)	1.31 (1.19–1.45)	1.33 (1.23–1.44)	1.23 (1.18–1.28)
<b>Total</b>	1.22 (1.15–1.28)	1.42 (1.34–1.49)	1.35 (1.29–1.42)	1.24 (1.21–1.27)

Relative risks (95% confidence intervals). AECOPD, acute exacerbation of chronic obstructive pulmonary disease.

(23), indicating that the decline was steeper for AECOPD-related hospitalizations.

Several factors may have contributed to this sharp decline. First, public health measures are likely to have had protective effects on the onset of COPD exacerbations, mainly through a substantial reduction in the circulation of viral respiratory infections (VRI), the most common triggers of AECOPD (24–26). Evidence supports this interpretation. A study in Singapore showed a reduction in VRI-associated AECOPD during the first months of the pandemic (13), while in Hong Kong, an increase in the use of face masks was associated with a decrease in AECOPD (12). Another study in the United States showed a positive correlation between COPD admissions and community viral burden (11). The present study shows that in France, in contrast with what was observed during the pre-pandemic years, the number of hospital admissions for AECOPD did not increase during the winter months of the pandemic, a season when the circulation of VRI is usually high. Furthermore, a considerable increase in flu vaccination coverage was observed in France in 2020 compared with 2019 (27). This suggests a

real reduction in AECOPD due to decreased exposure to VRI, leading to a reduction in this population's need for hospital care (7). Moreover, COPD patients have demonstrated strict compliance with health regulations during the pandemic in some countries, along with greater adherence to their treatments (10, 28, 29). Finally, the reduction of air pollution observed in France in 2020 likely constituted another protective effect on the onset of AECOPD (30, 31).

The pandemic context, however, also had negative effects on COPD patients' health, with a deterioration in their mental health due to isolation (14, 29, 32, 33) and a reduction in their physical activity (14, 29). These aspects represent risk factors for AECOPD and might therefore dampen slightly the above-mentioned protective effects on COPD patients.

On the other hand, changes in health-seeking patterns in COPD patients during the pandemic might have contributed to the decrease in hospital admissions for AECOPD. Several studies have reported hospital avoidance behaviors for fear of becoming infected with COVID-19 (14, 33, 34), and access to hospital care was reduced by overcrowding during the pandemic. These

aspects may have led to a shift from hospital care to ambulatory care. Some patients who would have normally been admitted to hospitals might have instead been treated by ambulatory care. Furthermore, the development of remote care (telemedicine) and of self-medication might also have contributed to a lesser use of hospital care for COPD patients (29, 33). This hypothesis is not supported by a study from Wales in which a reduction in primary care consultations for AECOPD was observed in 2020 compared with previous years (6). In contrast, another study from England reports an increase in community managed exacerbations in 2020 compared with 2019, but this study is limited to a single secondary care clinic (29).

Finally, another hypothesis to explain the reduction in AECOPD-related hospitalizations could be an excess mortality among the patients with prevalent severe COPD. Some of these patients may have died because of COVID-19 or reduced access to health-care. However, this assumption is not supported by nationwide studies from Denmark and Slovenia, where all-cause mortality was reported to decrease in COPD patients, regardless of severity (7, 8).

Our second major finding is a 24% increase in the proportion of in-hospital deaths for AECOPD stays during the pandemic, with nearly 2,000 estimated excess deaths. There could be several reasons for this observation. First, stays with a COVID-19 diagnosis had significantly higher in-hospital mortality and ICU admission rates compared to those without COVID-19. These findings are in line with several studies in the literature showing higher severity and mortality for COPD patients when infected with COVID-19 (3, 4). Given that the proportion of stays with a COVID-19 diagnosis was low (1.5%), the contribution of COVID-19 to the excess mortality observed for AECOPD stays was limited (15%). Second, a number of stays that would have required ICU admission may not have benefited from it due to overcrowding during the critical phases of the pandemic, thereby contributing to the excess in-hospital mortality. Indeed, the increase in in-hospital mortality was significantly lower for stays with ICU admission compared to stays without ICU admission. Yet, the proportion of stays involving an admission to ICU remained stable from 2016 to 2021 (~21%). Third, there might have been a shift of the clinical profile of the admitted cases, with a higher proportion of severe cases in 2020 and 2021 compared with previous years. This could be due to some mild or moderate cases resorting to ambulatory care to avoid COVID-19 infection in hospital settings, and/or to delays in healthcare for some patients during the first wave, leading to increased severity. In other contexts, though, the decrease in admissions during the pandemic was greater for severe AECOPD compared with mild or moderate disease (8, 10).

Finally, the case of patients aged 80 years or older seems paradoxical. While they exhibited a greater decrease in hospitalizations for AECOPD during the pandemic period compared with other age groups, they did not experience greater excess in-hospital mortality. One explanation could be excess out-of-hospital mortality for

this subpopulation, with some severe cases dying without seeking hospital care.

This study has several limitations. The interpretation of the findings is limited, as we lacked information in order to establish causal links between the observed trends and the suggested explanatory factors. Further explorations of the issues at stake would necessitate granulated information on clinical presentation at admission, prevention measures and prevailing air pollution. As the database does not contain detailed clinical information on the patients, we were not able to validate the diagnosis of AECOPD. However, this is a general limitation for analyzing medico-administrative databases. To address this issue we used two validated algorithms to identify AECOPDs and both led to consistent results. As regards to hospital deaths attributable to COVID-19, although the database is very robust, there could have been an underestimation of COVID-19 cases due to the lack of access to PCR testing at the beginning of the pandemic. Besides, the causes of death were not available and we are therefore unable to know the exact proportion of deaths related to COVID-19.

In conclusion, our findings provide reliable long-term trends in AECOPD hospital admissions and in-hospital mortality at a national level, reflecting sustained direct and indirect effects of the pandemic. Further analyses on individual-level data are needed to explore the trajectories of COPD patients at risk of hospitalization. Several crucial questions remain open regarding patterns of AECOPD, out-of-hospital mortality in COPD patients, and possible shifts in out-of-hospital health-care use.

## Data availability statement

The data analyzed in this study is subject to the following licenses/restrictions: the analysis described in this article was performed in a national database (*Programme de Médicalisation des Systèmes d'Information*; PMSI) belonging to a third-party, namely the French Ministry of Health. Access to this database is available to researchers on reasonable demand, after proper training and upon request to the relevant agency, the *Caisse Nationale d'Assurance Maladie* (CNAM), on condition that the analyses envisaged have been authorized by the French Data Protection Agency (*Commission nationale de l'Informatique et des Libertés*, CNIL). Requests to access these datasets should be directed to [snds.cnam@assurance-maladie.fr](mailto:snds.cnam@assurance-maladie.fr).

## Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the Local Legislation and Institutional Requirements. Written informed consent for participation was not required for this study in accordance with the National Legislation and the Institutional Requirements. In accordance with European and French regulations on data

protection and Ethics, the French Institute for Demographic Studies (INED) has carried out the required compliance formalities for access to administrative health databases. The French decree no. 2016-1871 of December 26, 2016 on the processing of personal data known as the “Système National des Données de Santé” (SNDS) has granted INED permanent access to the SNDS databases. All data of the SNDS are pseudonymized. Researchers and engineers affiliated with INED benefit from simplified access to data, on the condition that they follow the necessary training, respect the security measures outlined in the order of March 22, 2017 on the security framework applicable to the SNDS and accomplish any necessary procedures related to data protection compliance. JP received authorization to access SNDS databases in 2021. The research was approved by INED’s Data Protection Officer and registered in INED’s records of processing activities under references 2021-DPD-0007. JP’s processing of SNDS data is considered compliant in terms of personal data protection and ethical research.

## The COVID-HOSP working group

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## Author contributions

NL, TD, and GH initiated the study. JP performed data extraction, management, and preparation of the first draft. JP, NL, TD, and GH contributed to data analysis and conception of figure and table. JP, NL, TD, GH, CC, SL, and MK reviewed the

manuscript. All authors contributed to the concept and design of the study, critical revision of the manuscript, and approved the final version. Members of the working group participated in interpreting and discussing the results.

## Funding

The study was funded by a grant from the French Ministry of Solidarity and Health (PREPS-20-0163). The funder had no role in study design, collection, analysis, and interpretation of the data, writing of the study report, decision to submit the report for publication.

## Acknowledgments

We thank Christopher Leichtnam for his Editorial work.

## Conflict of interest

Author CC received payments from: AZ, BI, GSK, Roche, Sanofi Aventis, BMS, MSD, Lilly, Novartis, Pfizer, Takeda, Bayer, Janssen, and Amgen.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## References

- Adeloye D, Song P, Zhu Y, Campbell H, Sheikh A, Rudan I. Global, regional, and national prevalence of, and risk factors for, chronic obstructive pulmonary disease (COPD) in 2019: a systematic review and modelling analysis. *Lancet Respir Med.* (2022). doi: 10.1016/S2213-2600(21)00511-7
- World Health Organization. *The Top 10 Causes of Death*. Available online at: <https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death> (accessed July 13, 2022).
- Gerayeli FV, Milne S, Cheung C, Li X, Yang CW, Tam A, et al. COPD and the risk of poor outcomes in COVID-19: A systematic review and meta-analysis. *EClin Med.* (2021) 33:100789. doi: 10.1016/j.eclinm.2021.100789
- Pranata R, Soeroto AY, Huang I, Lim MA, Santoso P, Permana H, Lukito AA. Effect of chronic obstructive pulmonary disease and smoking on the outcome of COVID-19. *Int J Tuberc Lung Dis.* (2020) 24:838–43. doi: 10.5588/ijtld.20.0278
- Alqahtani JS, Oyelade T, Aldhahir AM, Mendes RG, Alghamdi SM, Miravittles M, et al. Reduction in hospitalized COPD exacerbations during COVID-19: a systematic review and meta-analysis. *PLoS ONE.* (2021) 16:e0255659. doi: 10.1371/journal.pone.0255659
- Alsallakh MA, Sivakumaran S, Kennedy S, Vasileiou E, Lyons RA, Robertson C, et al. Impact of COVID-19 lockdown on the incidence and mortality of acute exacerbations of chronic obstructive pulmonary disease: national interrupted time series analyses for Scotland and Wales. *BMC Med.* (2021) 19:124. doi: 10.1186/s12916-021-02000-w
- Saeed MI, Sivapalan P, Eklöf J, Ulrik CS, Browatzki A, Weinreich UM, et al. Social distancing in relation to severe exacerbations of chronic obstructive pulmonary disease: a nationwide semi-experimental study during the COVID-19 pandemic. *Am J Epidemiol.* (2022) 0:1–12. doi: 10.1093/aje/kwab292
- Sarc I, Lotric Dolinar A, Morgan T, Sambt J, Zihler K, Gavric D, et al. Mortality, seasonal variation, and susceptibility to acute exacerbation of COPD in



the pandemic year: a nationwide population study. *Ther Adv Respir Dis.* (2022) 16:1–15. doi: 10.1177/17534666221081047

9. Lawless M, Burgess M, Bourke S. Impact of COVID-19 on hospital admissions for COPD exacerbation: lessons for future care. *Medicina.* (2022) 58:66. doi: 10.3390/medicina58010066

10. Trujillo C, Garnet B, Zadeh AV, Urdaneta G, Campos M. Decrease in exacerbations during the coronavirus disease 2019 pandemic in a cohort of veterans with COPD. *Chronic Obstr Pulm Dis.* (2021) 8:572–9. doi: 10.15326/jcopdf.2021.0234

11. So JY, O'Hara NN, Kenaa B, Williams JG, deBorja CL, Slejko JF, et al. Population decline in COPD admissions during the COVID-19 pandemic associated with lower burden of community respiratory viral infections. *Am J Med.* (2021) 134:1252–9. doi: 10.1016/j.amjmed.2021.05.008

12. Chan KP, Ma TF, Kwok WC, Leung JK, Chiang KY, Ho JC, et al. Significant reduction in hospital admissions for acute exacerbation of chronic obstructive pulmonary disease in Hong Kong during coronavirus disease 2019 pandemic. *Respir Med.* (2020) 171:106085. doi: 10.1016/j.rmed.2020.10.6085

13. Tan JY, Conceicao EP, Wee LE, Sim XY, Venkatachalam I. COVID-19 public health measures: a reduction in hospital admissions for COPD exacerbations. *Thorax.* (2020) 76:512–3. doi: 10.1136/thoraxjnl-2020-216083

14. Sykes DL, Faruqi S, Holdsworth L, Crooks MG. Impact of COVID-19 on COPD and asthma admissions, and the pandemic from a patient's perspective. *ERJ Open Res.* (2021) 7:00822. doi: 10.1183/23120541.00822-2020

15. Huh K, Kim YE, Ji W, Kim DW, Lee EJ, Kim JH, Kang JM, et al. Decrease in hospital admissions for respiratory diseases during the COVID-19 pandemic: a nationwide claims study. *Thorax.* (2021) 76:939–41. doi: 10.1136/thoraxjnl-2020-216526

16. Farrugia Y, Spiteri Meilak BP, Grech N, Asciak R, Camilleri L, Montefort S, et al. The impact of COVID-19 on Hospitalized COPD exacerbations in Malta. *Pulm Med.* (2021) 2021:1–7. doi: 10.1155/2021/5533123

17. Helgeland J, Telle KE, Grøslund M, Huseby BM, Håberg S, Lindman ASE. Admissions to Norwegian hospitals during the COVID-19 pandemic. *Scand J Public Health.* (2021) 49:681–8. doi: 10.1177/14034948211000813

18. World Health Organization. *WHO Coronavirus (COVID-19) Dashboard.* (2022). Available online at: <https://covid19.who.int/table> (accessed July 11, 2022).

19. Vandembroucke JP, Poole C, Schlesselman JJ, Egger M. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *PLoS Med.* (2007) 4:27. doi: 10.1371/journal.pmed.0040297

20. Boudemaghe T, Belhadj I. Data resource profile: the French national uniform hospital discharge data set database (PMSI). *Int J Epidemiol.* (2017) 46:392–2d. doi: 10.1093/ije/dyw359

21. Cavailles A, Melloni B, Motola S, Daye F, Laurent M, Le Lay K, et al. Identification of patient profiles with high risk of hospital re-admissions for acute COPD exacerbations (AECOPD) in France using a machine learning model. *Int J Chron Obstruct Pulmon Dis.* (2020) 15:949–62. doi: 10.2147/COPD.S236787

22. Fuhrman C, Roche N, Vergnenègre A, Zureik M, Chouaid C, Delmas M-C. Hospital admissions related to acute exacerbations of chronic obstructive pulmonary disease in France, 1998–2007. *Respir Med.* (2011) 105:595–601. doi: 10.1016/j.rmed.2010.11.014

23. Naouri D. En 2020, le nombre de séjours hospitaliers hors COVID-19 a diminué de 13 % par rapport à. *Direction de la Recherche, des Études, de l'Évaluation et des Statistiques.* (2021) 1204.

24. Papi A, Bellettato CM, Braccioni F, Romagnoli M, Casolari P, Caramori G, et al. Infections and airway inflammation in chronic obstructive pulmonary disease severe exacerbations. *Am J Respir Crit Care Med.* (2006) 173:1114–21. doi: 10.1164/rccm.200506-859OC

25. Launay T, Souty C, Vilcu AM, Turbelin C, Blanchon T, Guerrisi C, et al. Common communicable diseases in the general population in France during the COVID-19 pandemic. *PLoS ONE.* (2021) 16:e0258391. doi: 10.1371/journal.pone.0258391

26. Bosetti P, Huynh BT, Abdou AY, Sanchez M, Eisenhauer C, Courtejoie N, et al. Lockdown impact on age-specific contact patterns and behaviors, France, April 2020. *Euro Surveill.* (2021) 26:2001636. doi: 10.2807/1560-7917.ES.2021.26.48.2001636

27. Santé Publique France. *Bulletin Épidémiologique Grippe, Semaine 50. Saison 2020-2021.* (2022). Available online at: <https://www.santepubliquefrance.fr/maladies-et-traumatismes/maladies-et-infections-respiratoires/grippe/documents/bulletin-national/bulletin-epidemiologique-grippe-semaine-50.-saison-2020-2021> (accessed March 28, 2022).

28. Kaye L, Theye B, Smeenk I, Gondalia R, Barrett MA, Stempel DA. Changes in medication adherence among patients with asthma and COPD during the COVID-19 pandemic. *J Allergy Clin Immunol Pract.* (2020) 8:2384–5. doi: 10.1016/j.jaip.2020.04.053

29. McAuley H, Hadley K, Elneima O, Brightling CE, Evans RA, Steiner MC, et al. COPD in the time of COVID-19: an analysis of acute exacerbations and reported behavioral changes in patients with COPD. *ERJ Open Res.* (2021) 7:00718. doi: 10.1183/23120541.00718-2020

30. Li J, Sun S, Tang R, Qiu H, Huang Q, Mason TG, et al. Major air pollutants and risk of COPD exacerbations: a systematic review and meta-analysis. *Int J Chron Obstruct Pulmon Dis.* (2016) 11:3079–91. doi: 10.2147/COPD.S122282

31. Santé Publique France. *Pollution de l'air Ambiant : Nouvelles Estimations de Son Impact Sur La santé des Français.* (2022). Available online at: <https://www.santepubliquefrance.fr/presse/2021/pollution-de-l-air-ambiant-nouvelles-estimations-de-son-impact-sur-la-sante-des-francais> (accessed May 17, 2022).

32. Pedrozo-Pupo JC, Campo-Arias A. Depression, perceived stress related to COVID, post-traumatic stress, and insomnia among asthma and COPD patients during the COVID-19 pandemic. *Chron Respir Dis.* (2020) 17:1–3. doi: 10.1177/1479973120962800

33. Philip KE, Cumella A, Farrington-Douglas J, Laffan M, Hopkinson NS. Respiratory patient experience of measures to reduce risk of COVID-19: findings from a descriptive cross-sectional UK wide survey. *BMJ Open.* (2020) 10:e040951. doi: 10.1136/bmjopen-2020-040951

34. Liang Y, Chang C, Chen Y, Dong F, Zhang L, Sun Y. Symptoms, management and healthcare utilization of COPD patients during the COVID-19 epidemic in Beijing. *Int J Chron Obstruct Pulmon Dis.* (2020) 15:2487–94. doi: 10.2147/COPD.S270448