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Impact of Local Care Environment and Social Characteristics on Aggregated Hospital-Fatality Rate from COVID-19 in France: Nationwide Observational Study.

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Author contribution: Dr Zeitoun had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept, design and acquisition: Zeitoun

Statistical analysis: Faron and Lefevre

Analysis and interpretation of data: Zeitoun, Faron and Lefevre

Drafting the manuscript: Zeitoun

*Critical revision of the manuscript for important intellectual content: Zeitoun,
Faron and Lefevre*

Administrative, technical, or material support: Zeitoun

Abstract

Objectives: We aimed to investigate possible differences in aggregated hospital-fatality rate from COVID-19 in France at the early phase of the outbreak, and to determine whether factors related to population or healthcare supply before the pandemic could be associated with outcome differences.

Study design: Nationwide observational study including all French hospitals from January 24, 2020 to April 11, 2020.

Methods: We analysed aggregated hospital-fatality rate. A Poisson regression was performed to investigate associations between characteristics pertaining to populational health, socioeconomic context and local healthcare supply at baseline, and the chosen outcome.

Results: On April 11, 2020, a total number of 30 960 patients were hospitalized among the 3 046 French healthcare facilities, including 6 832 patients in intensive care unit (ICU). A total of 8 581 deaths due to Covid-19 had been recorded, with a median mortality rate per 10 000 people per department of 0.53 (IQR: 0.29-1.90). There were significant variations between the 95 French departments even after adjusting on outbreak inception ($p < 0.001$). After multivariable analysis, four factors were independently associated with a significantly higher aggregated hospital-fatality rate: a higher ICU capacity at baseline (estimate=1.47; $p=0.00791$), a lower density of general practitioners (estimate=0.95; $p=0.0205$), a higher fraction of activity from the for-profit private sector (estimate=0.99; $p < 0.001$), and the ratio of people over 75 (estimate=0.91; $p=0.0023$).

Conclusions: Aggregated hospital-fatality rate from COVID-19 in France seems to vary among geographic areas, with some factors pertaining to local healthcare supply being associated with outcome.

Key words: COVID-19; aggregated fatality rate; social factors; care environment

Introduction

First cases of coronavirus disease 19 (COVID-19), the viral pneumonia related to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), were officially identified in December 2019 in China and were notified to the World Health Organization (WHO) on December 31, 2020. ¹ Since then, the epidemic has expanded well beyond China and the pandemic has officially been declared by the WHO on March 11, 2020. ² While Italy has been the earliest disease cluster in Europe ³, France has rapidly followed. On February 23, 2020, the French Ministry of Health issued the phase I of the national epidemic. Phases II and III were respectively announced on February 29, 2020 and March 14, 2020. ⁴ Fatality rate, defined as the number of deaths of patients in whom COVID-19 was confirmed, divided by the total number of COVID-19 cases, seems to vary among countries. Italian reports have shown a case-fatality rate ranging from approximately 7% to 10% ⁵, while other countries such as South Korea have observed much lower figures. ⁶ Even if there is uncertainty due to variations in case recording, we lack definitive explanations for possible differences in case-fatality rates between countries. The number of tests that could be made to screen and insulate patients has been raised as a possible factor contributing to differences. Also, it is not known whether this outcome varies within a country. Several factors can likely explain differences such as affected population profile, healthcare environment and quality of care. There has been concern in France regarding critical care capacity with respect to the probable high number of simultaneous severe cases during the outbreak peak. ⁷ It has been estimated by the French Ministry of Health that there were approximately 5,000 intensive care unit (ICU) beds in France yet with differences between regions. Estimates forecasted that this capacity would be exceeded. ⁷

Therefore, we sought to measure aggregated hospital-fatality rate from COVID-19 in France, and to examine the association between populational and local healthcare supply characteristics, and this outcome.

Methods

Data sources

We used official and publicly available sources to retrieve and gather the needed data: The Ministry of Health, the National Institute for Statistics and Economic Studies (INSEE, *Institut National de la Statistique et des Etudes Economiques*), the Directorate of Research, Evaluation, and Statistics (DREES, *Direction de la Recherche, des Etudes, des Evaluations et des Statistiques*), the French Public Health Insurance (*Assurance Maladie*) which covers the entire population, Public Health France (*Santé Publique France*), and the National Institute for Demographic Studies (*Institut National d'Etudes Démographiques*). In each data source, the relevant data were collected for the most recent year available as already performed in another study.⁸

France and the French population

France is divided into administrative units, each corresponding to a defined territory. Those administrative units are called departments. There are 95 departments in what is called the metropolitan territory, i.e. excluding overseas departments. Those 95 metropolitan departments were chosen as a unit of analysis because they represent the smallest geographic unit for which the needed data were available. For each

department, data regarding the total population as measured in January 2020 were collected, as well as age and gender characteristics.

Healthcare supply and care environment

Data regarding care providers and local healthcare ecosystems were also collected as follows for each of the 95 departments (year of availability between brackets): total number of physicians (2017), physician rate per 100 000 people (2017), then divided into general practitioner rate per 100 000 people and specialist rate per 100 000 people (2017), dental surgeon rate per 100 000 (2017), nurse rate per 100 000 (2017), physiotherapist rate per 100 000 (2017), pharmacist rate per 100 000 (2017). We also retrieved the number of hospital beds per 10 000 people, including surgery beds, medicine beds, obstetrical beds, physical medicine beds, psychiatry beds and those in long-term care facilities (2017) according to a 2019 report from the French Ministry of Health, ⁹ and the total number of adult intensive care beds in each department at baseline, i.e. before the outbreak (2020). Last, the fraction of hospital care activity as measured by hospital-days, performed by the for-profit private sector was collected (2017).

Health and wealth indicators

For each department, the following health indicators were retrieved: overall mortality (2019), mortality over 65 (2019), infant mortality (2019), prevalence of significant chronic condition as defined and fully covered by the national Public Health Insurance (2017). For this latter indicator, prevalence was collected in an aggregated

manner and by condition. For the purpose of the current study, only chronic conditions that have been reported in the literature to date to be possible risk factors of COVID-19 fatality were included, namely diabetes mellitus, cancer, severe hypertension and chronic obstructive pulmonary disease. We could not retrieve data regarding obesity since it is not recorded as such by the national Public Health Insurance. The complete list of those conditions can be found in the Supplemental Material. Since there is a well-established relationship between wealth and health,¹⁰ we also intended to collect economic variables: unemployment rate (last trimester of 2019), median household income (2017), poverty rate (2017), and Universal Health Coverage (2019), which is provided by the French state to people below a certain threshold of total purchasing power.

Outcome measures

Aggregated hospital-fatality rate was chosen as study outcome (i.e. for each day of the study period, the number of hospital deaths divided by the number of admitted patients). We chose not to analyze case-fatality rate since it would be unreliable in the French case. Indeed, France has not performed systematic or large SARS-CoV-2 testing, and the number of recorded cases has repeatedly been recognized as being orders of magnitude below actual frequency. Conversely, all serious cases of suspected COVID-19 were required to be tested for confirmation. Hospitalized cases, whether in regular wards or intensive care units (ICUs), therefore represent a reliable denominator for calculation. For each day of study period and in each of the 95 French departments, the number of hospitalized COVID-19 patients and the number of COVID-19 patients in ICUs were collected. Also, for each day of study sample, the

cumulative number of COVID-19-related in-hospital deaths over study period was collected.

Statistical analysis

To account for gaps in outbreak start between areas, the time origin for each department was set to the first day where at least 10 deaths due to Covid-19 had been recorded in total. To investigate the relationship between our covariates and the selected outcome, a mixed-effects Poisson generalized linear regression was used. Models were adjusted for the number of people living in the department and the corrected day since the beginning coded as a third order polynomial as fixed effects. To account for the hierarchical structure of our data, the department (grouping variable) was used as a random effect. Both a random intercept and random slope (for the corrected days since the beginning) were used. Any variable achieving a p-value < 0.2 in the univariable analysis was proposed in the multivariable model. In this model a backward selection based on p-values was used with a threshold of 0.2. Poisson's model results are given as exponent coefficient and thus indicate the multiplicative effect of the variable on the death count (e.g. a value of 2 indicates that the variable doubles the death count). All tests were bilateral and a p-value of 0.05 was retained for statistical significance. Issues such as aberrant or missing points were handled by linear interpolation. Analyses were done with the R 3.6.2 software and the lme4 package.

Ethics

This study used administrative and anonymized data that do not permit any reidentification. Use of such anonymized data complies with the European General Data Protection Regulation and does not require any approval from an ethic committee according to the French law.

Results

Healthcare supply and social indicators in France

There were a total number of 3046 healthcare facilities (including public hospitals, non-for-profit private hospitals and for-profit private hospitals) gathering 399,865 beds. The for-profit private sector represented 96,988 beds (24.3%) and after excluding psychiatry, physical and rehabilitation facilities and long-term care facilities, it gathered 16,543,811 hospital-days out of 75,002,801 in total (22.1%) according to a report pertaining to the whole 2017 year. The details of the social and wealth indicators are presented in Table 1. The median area of the 95 departments was 5 880 km² (IQR: 4 977-6 817 km²).

Covid-19 epidemic

The study included data from January 24, 2020 (first French case) to April 11, 2020. There were 15 missing data out of 3,467 datapoints in total (0.4%). On April 11, 2020, a total number of 30,960 patients were hospitalized, including 6,832 in ICU. A total of 8,581 hospital deaths due to Covid-19 had been reported with a median value of 28 deaths per department (IQR: 10-101). The highest number was observed in the Paris department with a cumulative number of 841 deaths. The median mortality rate per

10,000 people per department was 0.53 (IQR: 0.29-1.90), with significant variations between the departments even after adjusting on the day of the outbreak inception ($p < 0.001$) (Figure 1 and Figure 2).

The course of the outbreak in terms of hospitalizations, whether in regular wards or ICU, as well as mortality, also varied among the departments. Four selected examples are presented in the Figure 3.

Univariate and multivariable analysis

The details of univariate and multivariable analyses are given in Table 1. Following univariate analysis, eleven factors were included in the multivariable analysis. Apart from the population, four factors were independently associated with a significantly higher aggregated hospital-fatality rate from Covid-19: a higher ICU capacity at baseline (estimate=1.47; $p=0.00791$), a lower density of general practitioners (estimate=0.95; $p=0.0205$), a higher fraction of activity from the for-profit private sector (estimate=0.99; $p < 0.001$) and the ratio of people over 75 (estimate=0.91; $p=0.0023$). No health indicator was associated with our outcome in the multivariable analysis.

Discussion

In this nationwide observational study regarding COVID-19 in France, we found significant differences between areas in terms of aggregated hospital-fatality rate. Four factors were associated with our study outcome: a higher density of ICU beds at baseline, a lower fraction of hospital care activity from the for-profit private sector, a

lower density of general practitioners, and a greater proportion of people over 75 were all predictors of higher aggregated hospital-fatality rate in the current model.

Our study has several strengths. First, it is a nationwide analysis gathering exhaustive data from reliable sources. For most of covariates, year of availability was very recent, thereby limiting timeliness issues. In addition, the variables of interest are unlikely to significantly change across a relatively short period of time. Second, we collected a very diverse set of data regarding demographics, populational health, wealth, and also characteristics of care supply and local healthcare ecosystems. Populational health data were in particular critical to incorporate in the model since they are factors likely to influence disease outcome. We had very fine health data beyond age, namely prevalence of chronic conditions that have already been recognized as risk factors for COVID-19 outcome.^{3, 11, 12} Third, we used a robust statistical model to analyse the data, namely a Poisson linear model as the variables were daily counts and a mixed model as the observed data were not independent (repeated measures within a department), which allows separate intercept and slopes for each department. Also, time-adjustment was made so as to align all departments on a similar basis and take into account timeliness issues.

Our findings have implications. Critical care capacity has been a matter of concern regarding COVID-19 outbreak. It has been predicted that France did not have enough ICU beds to absorb all of the patients in need along several days or weeks. Yet we found no evidence that less ICU beds at baseline in a given area were associated with a worst outcome. Conversely, we found that areas with an initial higher density of ICU beds were associated with a higher aggregated hospital-fatality rate. We do not have any certain explanation for those unexpected findings. It may be that critically ill patients were more often transferred from rural areas or smaller facilities to more

comprehensive facilities. It also should be underlined that hospitals have anticipated the outbreak progression by resetting their organization and creating new ICU capacity in other wards. We could not measure actual ICU beds at a given time since those data were not consistently reported. This will need further investigation. We also found that areas in which the density of general practitioners was higher were associated with a better outcome. Even though this should be interpreted with caution, one may hypothesize that general practitioners played a critical role in the epidemic, through adequate orientation of COVID-19 patients to hospitals while maintaining others at home. Last, it is remarkable that social and wealth factors were not associated with the chosen outcome. The relationship between wealth and health has been consistently documented by a huge body of literature. Again, we cannot certainly explain why herein departments with more deprivation were not associated with a higher aggregated hospital-fatality rate yet it should be recalled that France has a very protective social system with a great safety net. Perhaps it helped to attenuate the social risk in the case of the epidemic.

This study has limitations. Firstly, as an observational study, it cannot establish definitive causality. We cannot exclude the possibility that our results might be confounded by factors that were not measured. In particular, we cannot rule out that criteria for admitting patients were different among areas and that some hospitals had more serious cases than others, whether in regular wards or ICUs. **Also, we did not have access to age- and gender-structure of hospitalized patients. Last, we did not take into account control measures implemented in the different departments even though those measures were thought to be very similar.** Secondly, the follow-up was intentionally limited. However, given the high urgency that many healthcare systems are currently facing worldwide, we aimed at rapidly providing a first evaluation of

hospital-fatality rates from COVID-19 in a markedly affected country. Subsequent work over the outbreak course will say whether local differences and their associated factors persist. Thirdly, we did not have access to hospital data or patient data. Thus, we could not calculate individual hospital-fatality rate and had to deal with aggregate measures which have been updated on a daily basis at the department level over the study period. Fourth, we intentionally excluded nursing home since the related data were not available across the whole study period. This represents a selection bias. Last, as of March 28, 2020, the French government decided to implement targeted transfers of seriously ill patients by medicalized trains or helicopters in order to improve resource allocation within the whole territory. Those transfers may have interfered with our results even though we believe it is unlikely. Indeed, reported counts of those transfers showed it involved very few patients as compared to the magnitude of the epidemic. It seems implausible that it significantly influenced the findings from the regression analysis, which were otherwise consistent over time.

In conclusion, we found significant differences in aggregated hospital-fatality rate across French areas over the early period of the COVID-19 outbreak. Several factors pertaining to local healthcare supply were associated with a worst outcome, such as a higher ICU capacity at baseline and a lower involvement from the private sector as well as a lower density of general practitioners. Those findings clearly deserve further investigation with hospital- or patient-level data and over a longer follow-up.

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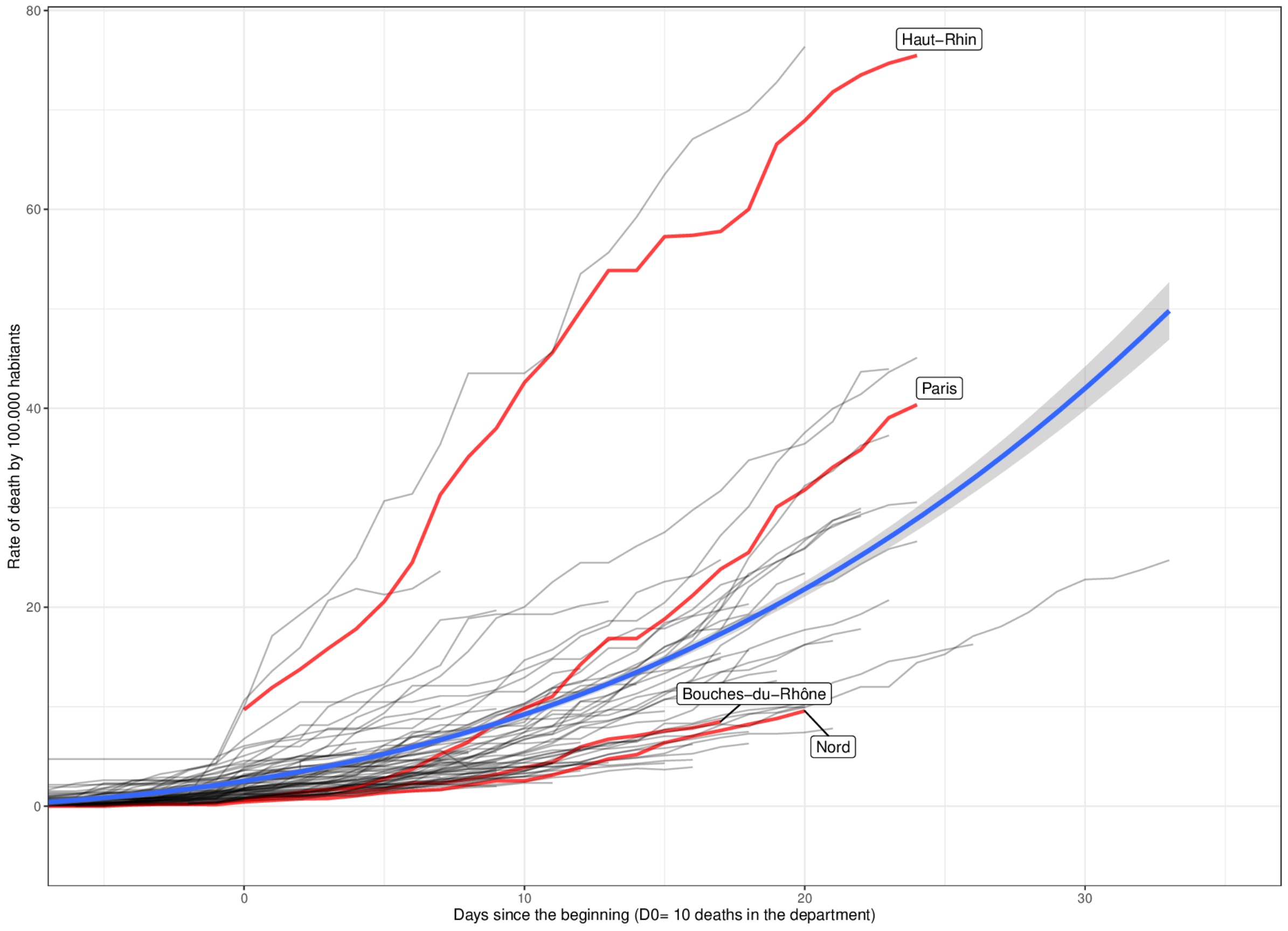
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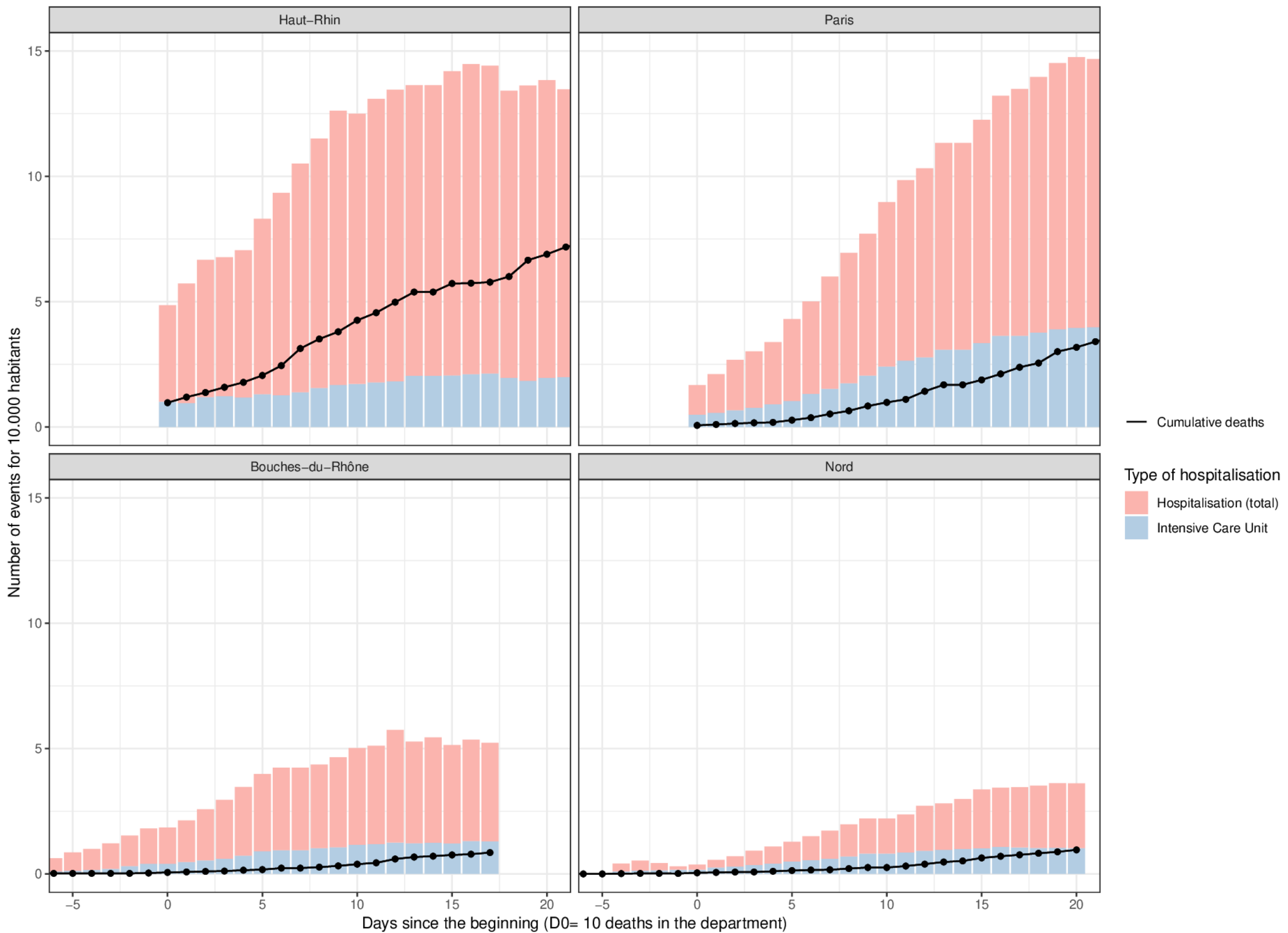
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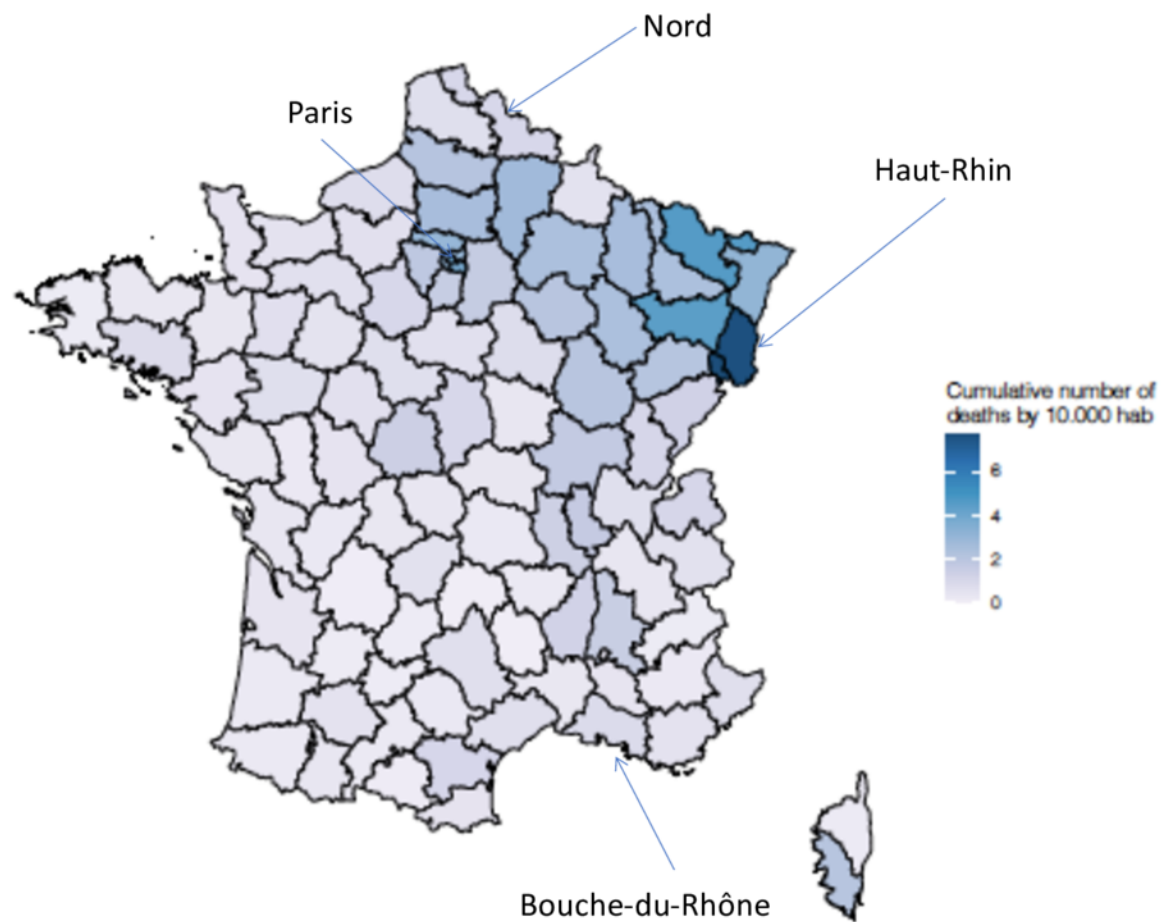
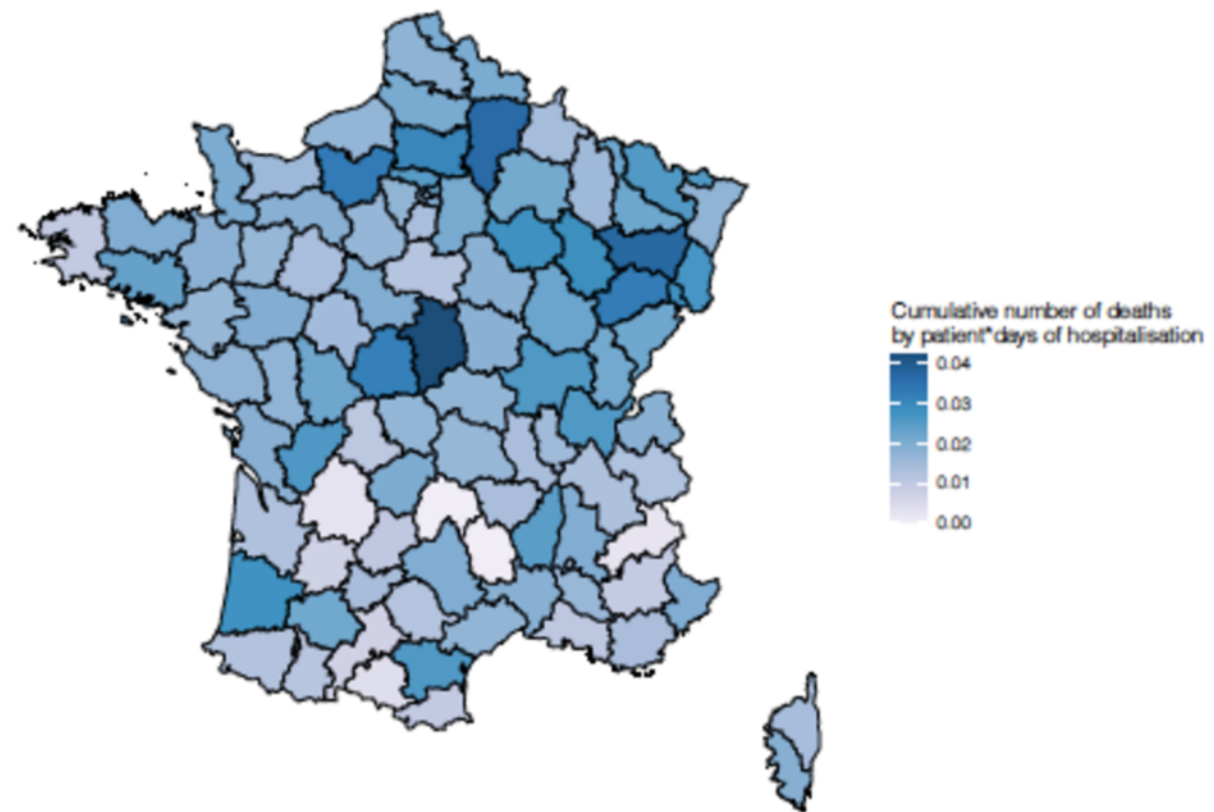
Figure 1. Daily mortality rate per 100 000 habitants due to Covid-19 among the 95 studied departments. (The blue line represents the overall mean with confidence interval in grey coded as a third order polynomic, the 4 red lines represent the selected departments for the Figure 3).

Figure 2. Map of cumulative number of deaths from COVID-19 in each French department according to A: total number of habitants and B: number of patient-days of hospitalisation.

Figure 3. Number of patients admitted in hospital, ICU and reported deaths each day following the Do in four departments in France during the Covid-19 epidemic. Those departments have been chosen to illustrate the heterogeneity of situations across the whole French territory (see Figure 1).





A**B**

Variable	Observed value in France	Univariate analysis			Multivariable analysis		
		Estimate*	95% CI	p	Estimate*	95% CI	p
Healthcare supply							
ICU beds for 10.000 persons	0.6 ± 0.3	1.34	0.99-1.83	0.061	1.47	1.11-1.96	0.0079
Ward beds for 10.000 persons	10.9 ± 2.7	0.99	0.95-1.03	0.72			
Doctors for 10.000 persons	30.5 ± 8.7	1.00	0.98-1.01	0.70			
GP for 10.000 persons	15.0 ± 2.7	0.95	0.91-1.00	0.033	0.95	0.91-0.99	0.0205
Specialists for 10.000 persons	15.4 ± 6.7	1.00	0.98-1.02	0.71			
Private sector (%)	21.9 ± 11.4	0.98	0.97-0.99	<0.001	0.99	0.98-0.99	<0.001
Social variables							
Annual Median income (k€)	20.4 ± 0.2	1.70	0.90-3.19	0.10			
Poverty rate (%)	14.4 ± 3.0	1.01	0.98-1.04	0.57			
Unemployment rate (%)	7.9 ± 1.6	0.99	0.93-1.06	0.76			
Universal medical insurance (%)	1.52±0.75	1.00	1.00-1.00	0.96			
Population (thousands of inhabitants)	520.6 (265.5 – 1079.4)	1.34	1.09-1.64		1.02	1.00-1.05	0.0035
Population older than 75 years (%)	10.8 ± 2.2	0.87	0.82-0.92	<0.001	0.91	0.86-0.97	0.0023
Percent of population aged between 60 and 74	18.8 ± 2.8	0.92	0.87-0.97	0.0012			NS

Population density (inhab/km ²)	565.8 ± 2425.1	1.00	1.00-1.00	0.0256	NS
Health variables					
Departmental mortality rate (%)	10.4 ± 2.3	0.91	0.85-0.97	0.0023	NS
Infant mortality rate	3.4 ± 0.8	1.22	1.07-1.39	0.0031	NS
Mortality rate over 65 (%)	37.3 ± 2.9	1.02	0.99-1.06	0.23	NS
Diabetes mellitus (%)	1.2 ± 0.9	1.24	1.01-1.51	0.036	NS
Severe hypertension (%)	0.2 ± 0.2	1.49	0.64-3.51	0.36	
Chronic Obstructive Pulmonary Disease (%)	0.2 ± 0.2	1.63	0.38-6.99	0.51	
Oncologic disease (%)	1.0 ± 0.8	1.16	0.89-1.51	0.28	

*** estimates are exponent Poisson's model coefficients and thus indicate the multiplicative effect on death counts.**

Table 1. Univariate and multivariable analysis of factors associated with aggregated hospital-fatality rate due to Covid-19 among the 95 departments in France until April 11, 2020. NS stands for “non-significant”