COVID-19: Spatial Analysis of Hospital Case-Fatality Rate in France

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Abstract

When the population risk factors and reporting systems are similar, the assessment of the case-fatality (or lethality) rate (ratio of cases to deaths) represents a perfect tool for analyzing, understanding and improving the overall efficiency of the health system.

The objective of this article is to estimate the influence of the hospital care system on lethality in metropolitan France during the inception of the COVID-19 epidemic, by analyzing the spatial variability of the hospital case-fatality rate between French districts (i.e. French *départements*).

The results show that the higher case-fatality rates observed by districts are mostly related to the level of morbidity, therefore to the overwhelming of the healthcare systems during the acute phases of the epidemic. However, the magnitude of this increase of case-fatality rate represents less than 10 per cent of the average case-fatality rate and cannot explain the magnitude of the variations in case-fatality rate reported per country by international organizations or information sites. These differences can only be explained by the systems for reporting cases and deaths, which, indeed, vary greatly from country to country, and not attributed to the care or treatment of patients, even during hospital stress due to epidemic peaks.

Introduction

Since the beginning of the epidemic, the lethality rate, or case-fatality rate (CFR) of COVID-19 and the differences between countries have been the subject of many questions about national pandemic response policies and patient treatment. Most studies on the lethality of COVID-19 seek to estimate the true lethality of the disease,

an issue that has been addressed since the beginning of the epidemic [MOR 20] [RIN 20] [SPY 20] [BAU 20].

The case-fatality rate is the ratio between the number of closed cases (i.e. recovered or dead) and the number of deaths due to the disease. It is estimated by the healthcare system based on the reporting of these two values. The case-fatality rate should not be confused with the mortality rate, which is the ratio of the number of deaths to the total population, or also with the morbidity rate, which is the ratio of the number of cases to the total population. Mortality and morbidity rates depend on the extent of disease in a population, unlike case-fatality rates, which are normally calculated independently of the number of infected persons [POR 08].

The case-fatality rate of a disease in a population is an index of severity of the disease in that population, and of the capacity of the healthcare system to reduce mortality. In principle, this allows to compare the effectiveness of healthcare systems across regions or countries.

The aim of this article is to analyze the effectiveness of the healthcare system in France in the context of the COVID-19 epidemic. Based on spatial differences in lethality, this study ultimately shows that the case-fatality rates published by the international agency by country (May 2020) do not allow to compare the country one to the others.

Lethality depends on the intrinsic virulence of the virus but, unlike morbidity, it does not depend on its contagiousness. Virulence comes from the reproductive capacity of the virus in the cell, its capacity for cellular degradation, and its ability to induce or not an innate or specific immune response. Virulence is of purely biological origin and once the virus has entered the target cell where it will cause its pathogenic effect does no longer depends on environmental conditions outside the host. Virulence is independent of the host population, but may change over time and space if there is a risk of natural mutation/selection of the pathogen. Contagiousness characterizes the biological capacity of the virus to reach the target cell system of its host, and the ability to be transmitted from one individual to another. The efficiency of transmission depends largely on environmental conditions (e.g., climate, urbanization, population density, mobility), which can vary greatly from one country to another.

In addition to the virulence of the virus, the case-fatality rate depends on biological risk factors and on population vulnerability (age structure, genetic factors, prevalence of co-morbidities, healthcare accessibility, etc.) as well as other factors related to the health system (equipment, capacity, staff, management, care of patients, effectiveness of therapies, patient management in a critical phase of the disease), and factors related to the detection and registration system for cases and deaths (clinical cases definition, detection, surveillance systems, case and death reporting). The evaluation of the case-fatality rate normally requires the detection and counting of all infected persons, irrespective of their level of symptoms (i.e. disease severity).

When the population risk factors and reporting systems are identical, case-fatality rate evaluation represents an excellent tool for analyzing, understanding and improving the overall performance of the health system, particularly at the level of hospital units.

Studying the magnitude of differences in case-fatality rates between units also makes it possible to assess the impact of the quality of the health system on case-fatality.

There are large differences in the case-fatality rates of COVID-19 published by country (Table 1) or calculated directly from WHO data. These rates vary considerably, from less than 0.02 (Thailand, Australia, Chile) to more than 0.15 (France, Belgium, UK), with a mean at 0.04 and a standard deviation of 0.045 (WHO, May 8, 2020, Figure 1).

Country	CFR (%)*	Population > 65-year-old (%)**	Hospital bed number***
France	19.00	20.02	621
Belgium	16.42	18.80	623
UK	14.94	18.40	273
Italy	13.84	22.75	331
Netherlands	12.59	19.20	466
Sweden	12.29	20.10	254
Spain	11.73	19.38	297
Iran	6.31	6.18	150
USA	5.40	15.80	290
Greece	5.52	21.65	424
China	5.50	10.92	420
Switzerland	5.01	18.62	470
Germany	4.28	21.46	823
Portugal	4.15	21.95	332
Austria	3.88	19.02	760
Tanzania	3.75	2.60	70
Japan	3.56	27.58	1340
India	3.36	6.18	70
Czech Republic	3.28	19.42	645
Turkey	2.72	8.48	270
Norway	2.62	17.05	390
Uruguay	2.53	14.81	280
South Korea	2.36	14.42	1150
Thailand	1.83	11.90	210
Slovakia	1.74	15.63	579
Australia	1.41	15.65	380
Chile	1.21	11.53	220

Table 1: Case-fatality rates and characteristics of vulnerability to COVID-19

Caption: *Lethality rate for Covid-19 reported among selected countries from WHO, as for May 8, 2020 [WHO 20]; **population percentage over 65-year-old by World Bank, 2016; ***Hospital beds per 100,000 people by World Bank, 2013, Eurostat, 2014
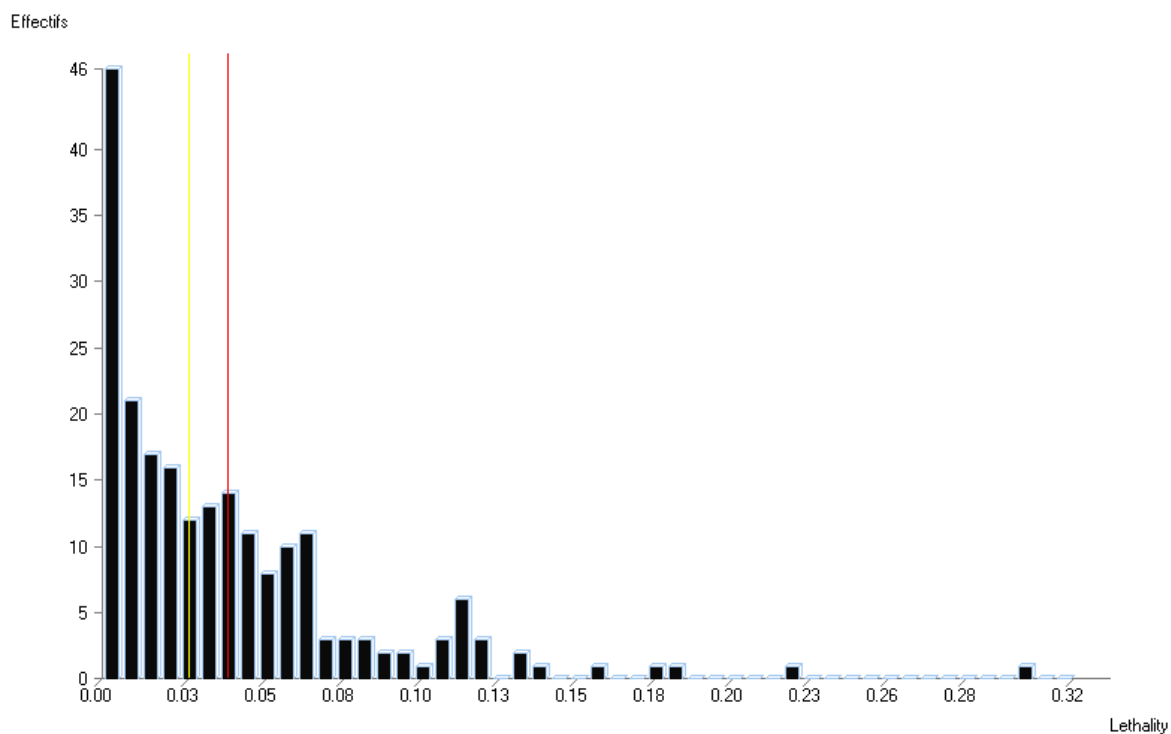
Figure 1. Distribution of case-fatality rates calculated by country, based on case and death data from WHO (WHO, May 8, 2020).

In Europe, the characteristics of populations (in terms of risk factor for COVID-19) and health systems are comparable, but the definition, detection and reporting of cases and causes of death can differ greatly from one country to another. Some countries conducted significantly more detection tests and hospitalizations than others (Table 2), resulting in differences in the protocols for patient management. The rate of testing performed (policy) and mortality rates (reporting) vary mainly according to the geographical extent of the epidemic within each country.

Country	rtPCR Test number per 1,000*	Morbidity rate (cases per million)	Mortality rate (death per million)
Belgium	44	4488	735
Spain	41	5494	558
Italy	39	3570	495
Germany	33	2022	88
Australia	29	271	4
United States	25	3906	232
United Kingdom	22	3045	451
France	21	2678	398
Turkey	15	1586	43
Netherlands	14	2438	309
South Korea	12	211	5
Iran	6	1246	78
Japan	1.5	122	4.5
India	1	41	1.4
Indonesia	0.5	48	3.5

Table 2: SARS-Cov-2 detection, COVID-19 morbidity and mortality rates by selected country.
Source: Worldometer, May 8, 2020

The virulence of the COVID-19 pathogen (SARS-CoV-2 virus) is assumed to be identical in all countries. In order to compare case-fatality rates across regions or countries (and thus analyze the effectiveness of healthcare systems), it is necessary, when calculating rates, to standardize population-related risk factors and to use the same definitions and enumeration methods to record cases and deaths. This is not the case for the current pandemic and discrepancies exist among the country systems.

The objective of this article is not to estimate the actual lethality of COVID-19 in France based on the rates published by the health authorities, but to estimate the influence of the healthcare system on lethality by analyzing the spatial variability of the hospital case-fatality rate (confirmed hospitalized cases and hospital deaths) in metropolitan France between districts (i.e. French *départements*). This analysis, limited to metropolitan France, is possible while it remains within the framework of the same system for defining and counting cases and deaths. We thus assume that this system of definition and enumeration was identical throughout France during the period **(**19 March to 8 May) corresponding to the first wave (inception) of the COVID-19 epidemic in France. Therefore the study focuses on the extent of spatial differences in the case-fatality rate in metropolitan France, and enables to highlight the relative differences between districts, as well as to analyze the causes independently of the system of definition and enumeration of cases and deaths, and also independently of the main biological risk factor of severity (age) after standardization on this factor.

Estimating the variability of the case-fatality rate attributable exclusively to hospital care of patients will then allows us to compare the case-fatality rate observed in metropolitan France with the one calculated for other countries. It will allow us to estimate whether the variability of the case-fatality rate due to the management of

patients in the acute epidemic phase can exclusively explain the significant differences in case-fatality rates observed between countries.

Data and Methods

Data

This study is based on daily hospitalization and death declaration data by district in France and is accessible on the "Santé Publique France" website. (www.data.gouv.fr/fr/datasets/donnees-hospitalieres-relatives-a-lepidemie-de-covid-19) from March 19 to May 8, 2020, corresponding to 50 days lockdown (i.e. quarantine) and the spread of the COVID-19 epidemic in France (Figure 2). We also obtain demographic data by districts (source: population by age, INSEE, 2020), as well as data on the distribution of hospitalized cases according to age group (10-year age group) (Santé Publique France).
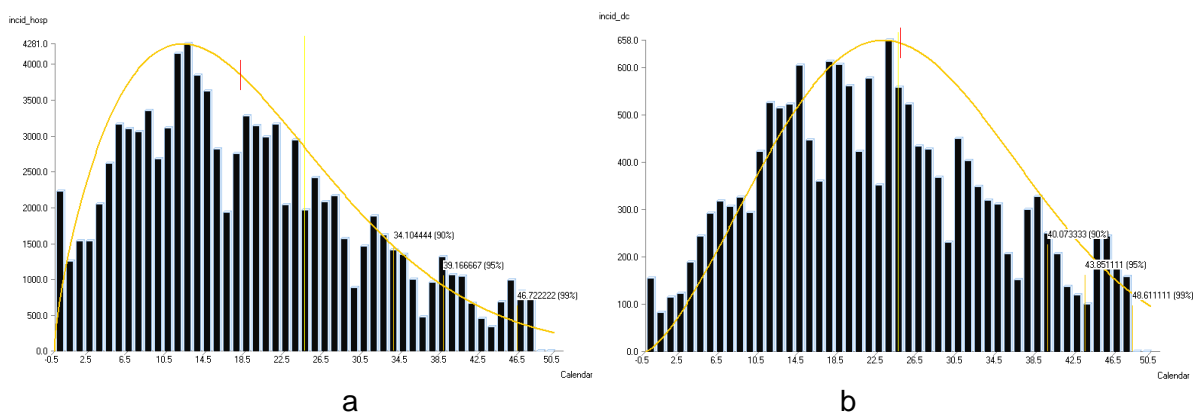

Figure 2. Hospitalizations (a) and death (b) from COVID-19 in France in function of time, from March, 19 to May, 8 2020

This analysis was carried out on the 96 districts of metropolitan France (Figure 3), while the French overseas districts and territories were excluded from the analysis for reasons of spatial analysis and mapping. The data were integrated into a geographic information system (SavGIS, ww.savgis.org) for analysis and mapping.
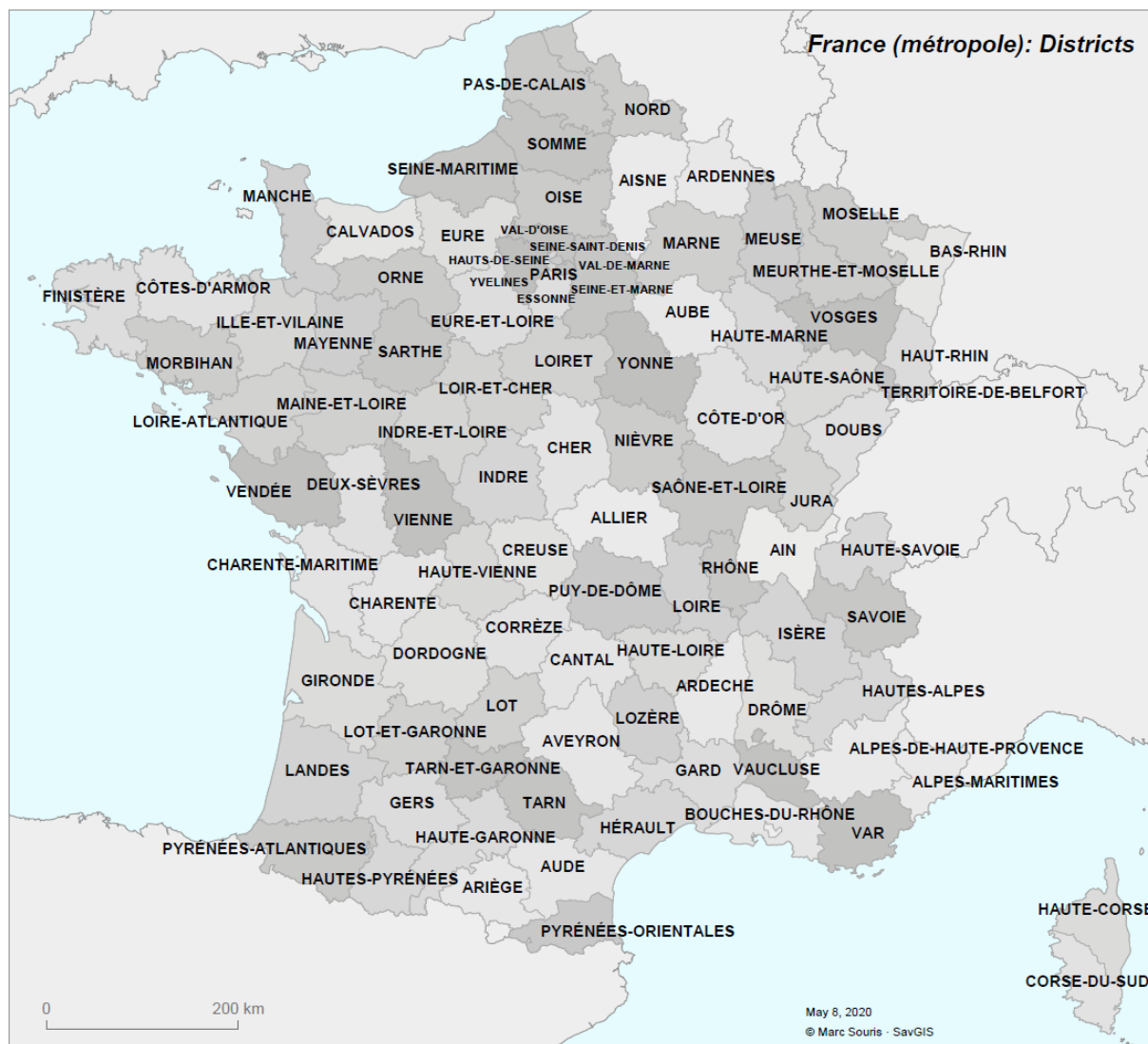
Figure 3. The 96 Districts of Metropolitan France

Focusing only on confirmed hospitalized cases and deaths in hospital, the case-fatality rates calculated in this article for France refer to the hospital case-fatality rates and do not represent the absolute national case-fatality that should include all positive cases and deaths related to COVID-19. Given the estimated high number of non-severe and asymptomatic forms (which a fortiori do not cause deaths) - it is estimated that only 2.6% of infected persons were hospitalized [SAL 20] - this overall lethality is necessarily much lower than hospital lethality, but it will be accurately calculated only at the end of the epidemic when the total number of positive cases (I.e. seroprevalence survey) will be available and the total number of deaths outside hospital due to COVID-19 will be accurately assessed.

All identified and hospitalized cases were tested positive (by rtPCR). All deaths counted were COVID-19 associated. As of May 8, 2020, not all hospitalized cases are closed since the epidemic is still ongoing: deaths counted at the beginning of the study period correspond to cases hospitalized but were not included in the study, and cases counted at the end of the period were not closed and no deaths from these cases were included in the study.

Methods

Age standardization

Since age is a major risk factor for death, age standardization eliminates differences in hospitalization rates, mortality rates, or case-fatality rates between districts due to differences in the age structure of the population of the districts, We performed an indirect standardization by calculating the rate (hospitalization rate and hospital rate) per ten-year age group for the whole of France. Then also lethality rate for the whole of France was calculated but excluding areas that have been under hospital stress (Ile-de-France and Grand-Est). This was done in order to evaluate hospital case-fatality rates per age group independently of possible excess mortality due to the saturation of healthcare systems in certain districts. Classically, E_i (number of deaths expected in district i) is the sum over the different age groups of the district's population in the age group multiplied by the hospital case-fatality rate of the age group:

$$E_i = \sum_{age\ class\ a} P_a \times T_a$$

where P_a is the population of the age group "a" and T_a is the hospital case-fatality rate of the age group calculated over all districts.

Standardized case-fatality rate

The Standardized Lethality Ratio (SLR) is equal to the ratio between the observed death toll Oi and the expected death toll Ei. The standardized hospital case-fatality rate LSi for each district is equal to the average rate for France multiplied by the district's SLR. The significance of the SLR (H0: SLR=1, no statistically significant over - or under-fatality compared to the expected value) is evaluated for each district by a Breslow & Day test [BRE 87] in order to account for the statistical significance of the differences in these ratios between districts. In order to take into account the problem of multiple testing [MIL 96] when the null hypothesis concerns the whole territory ("is there a district for which the H0 hypothesis is rejected?"), the risk of error was set at 0.0005 in order to apply a Bonferonni correction (which is very conservative when data is spatially autocorrelated). When the study is conducted for a single district ("Is the SLR for this district different from 1?"), the risk of error is set at 0.05. All tests are bilateral.

Cartography

The values of morbidity rates, mortality rates, non-standardized case-fatality rates, SLRs and their significance were mapped by districts. In order to map case-fatality rates independently of the rate calculation variability, due to differences in hospitalization numbers between districts, rates adjusted with empirical Bayesian estimator (EBE) were calculated [SOU 19]. All statistical and spatial analysis and mapping were carried out using the SavGIS geographic information system.

Study of statistical correlations

In order to estimate whether possible congestion in the healthcare system influenced hospital case-fatality rate, we studied the correlations between hospitalization and hospital lethality in a global manner over the entire period. Inpatient severity was estimated using the ICU rate (number of patients in intensive care/number of inpatients).

Results

For the whole of France (data from 19 March to 8 May 2020), the hospital case-fatality rate was 0.174. The average hospital case-fatality rates by age group, used in indirect standardization, was calculated from French Public Health data by age class published on 8 May 2020 (Table 3).

Age class	Population (%)	Hospitalization					
		Hospitalized		Death		CFR	
		Total	%	Total	%	CFR (whole country)	CFR without 11 and 44 regions
0-9	11.43	617	0.65	2	0.01	0.0032	0
10-19	12.27	463	0.49	3	0.02	0.0065	0
20-29	11.15	2253	2.4	19	0.11	0.0084	0.0051
30-39	12.36	4325	4.5	72	0.44	0.0166	0.0088
40-49	12.80	7001	7.4	203	1.24	0.0290	0.0183
50-59	13.10	12130	12.9	747	4.56	0.0616	0.0435
60-69	12.01	16115	17.1	1934	11.81	0.1200	0.0988
70-79	8.57	18812	20.0	3723	22.73	0.1979	0.1666
80-89	4.91	21625	22.9	6192	37.80	0.2863	0.2688
90+	1.38	10897	11.5	3485	21.28	0.3198	0.3047
All ages	1	94238	1	16380	1	0.1738	0.1597

Table 3. Hospitalization, mortality and case-fatality rates by age group in metropolitan France (2020). Region 11 is Ile-de-France, region 14 is Grand-Est.

The epidemic in France (data from 19 March to 8 May 2020) presents a very uneven spatial distribution of hospitalizations. It has developed throughout the country at low level, with a mean hospitalization rate of 1.27 per 1,000 (median at 0.88) and a standard deviation of 1.03, except in some regions where transmission has been much more active, such as the Ile-de-France region (mean hospitalization rate 3.01 per 1,000), or the Grand-Est region (mean hospitalization rate 3.2 per 1,000). The mean hospitalization rate varies from 0.19 per 1,000 (Tarn-et-Garonne) to 4.75 (Territoire de Belfort) (Figure 4).

The hospital mortality rate (not age-standardized) has the same spatial distribution. It varies from 0.01 per 1,000 (Tarn-et-Garonne) to 1.13 per 1,000 (Territoire de Belfort), with a mean of 0.21 (median 0.12) and a standard deviation of 0.21.
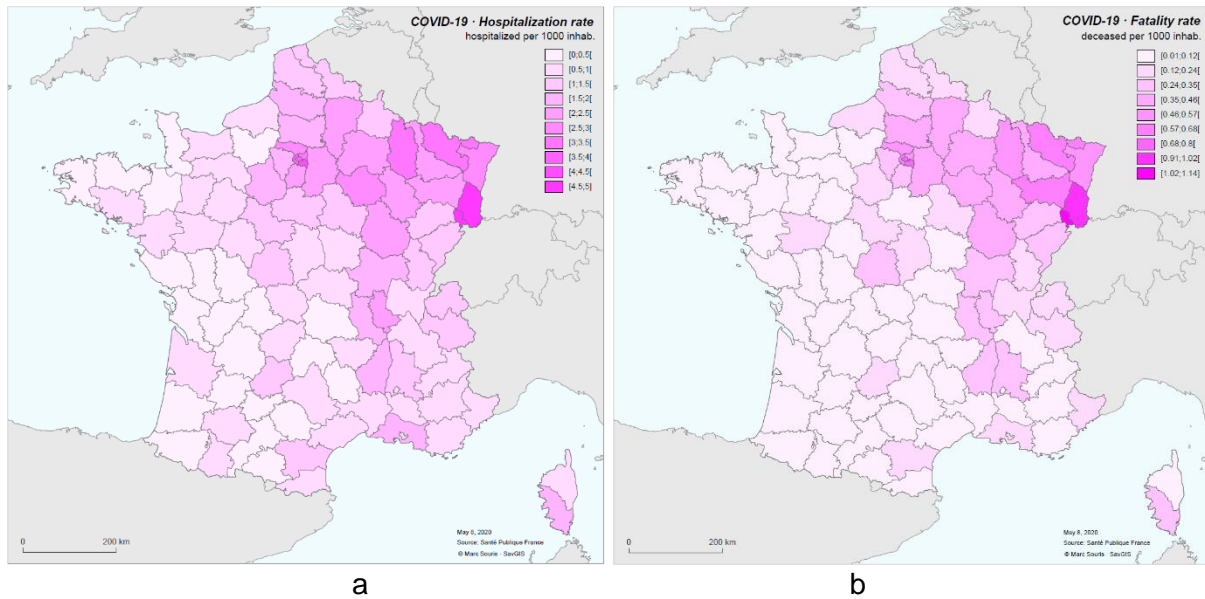
Figure 4: Hospitalization rate (a) and hospital mortality rate (per 1000 inhabitants) (b) for COVID-19 in metropolitan France for the period March 19 to May 8, 2020.

A cartographic representation by cartogram shows the relative differences in the circulation of the disease by districts (Figure 5).
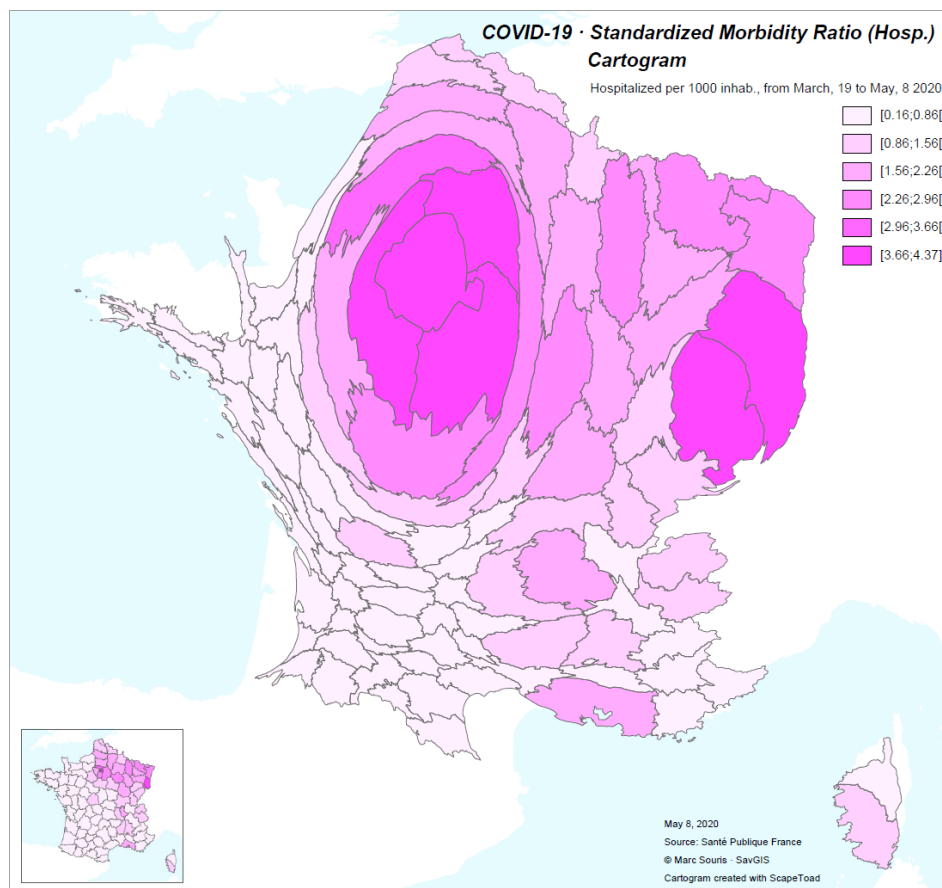

Figure 5. Cartogram of the standardized hospitalization rate for COVID-19 in France from March 19 to May 8, 2020.

Caption: The geometry of the districts in France is shown in the lower left corner.

The observed gross hospital case-fatality rate calculated by district showed a mean of 0.153 with a standard deviation of 0.045. It varies between 0.046 (Ariège) and 0.258 (Vosges). Without the Ile-de-France and Grand-Est regions, the mean gross case-fatality rate per district is 0.149 with a standard deviation of 0.048 (figure 6).
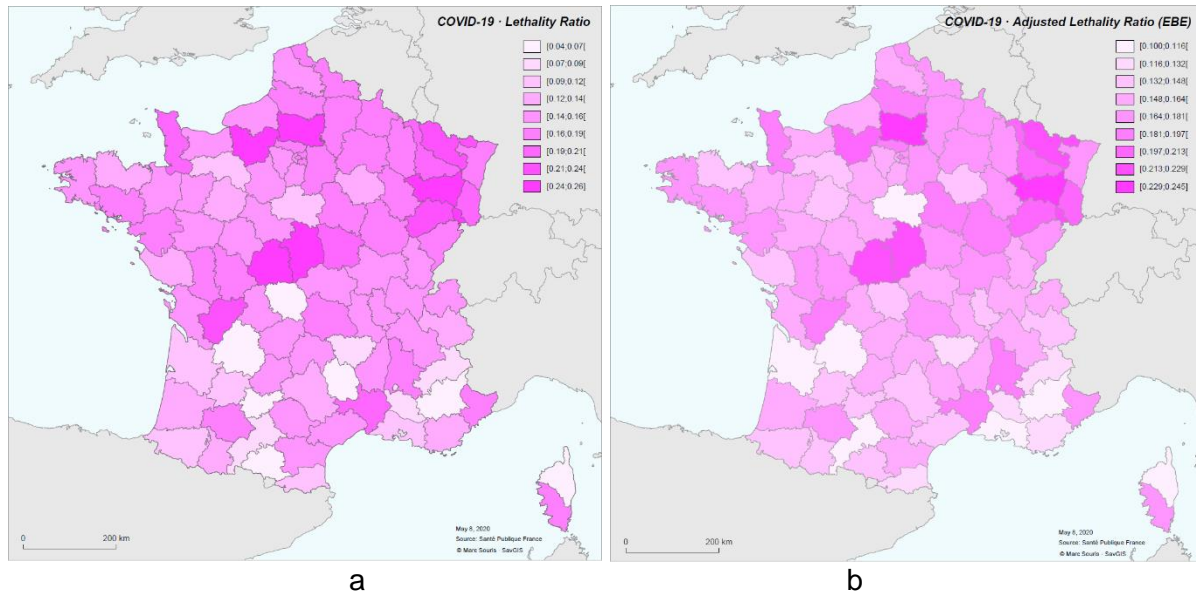

a   b

Figure 6: Case-fatality rate (a) and case-fatality rate adjusted by empirical Bayesian estimator (b) for the COVID-19 epidemic in France from 19 March to 8 May 2020

Case-fatality rates have evolved over the period studied. Here we represent non-standardized rates calculated for three periods: March 19 to 31; April 1 to 12; April 13 to 25. Rates are calculated with a 12-day time lag between cases and deaths (Figure 7).
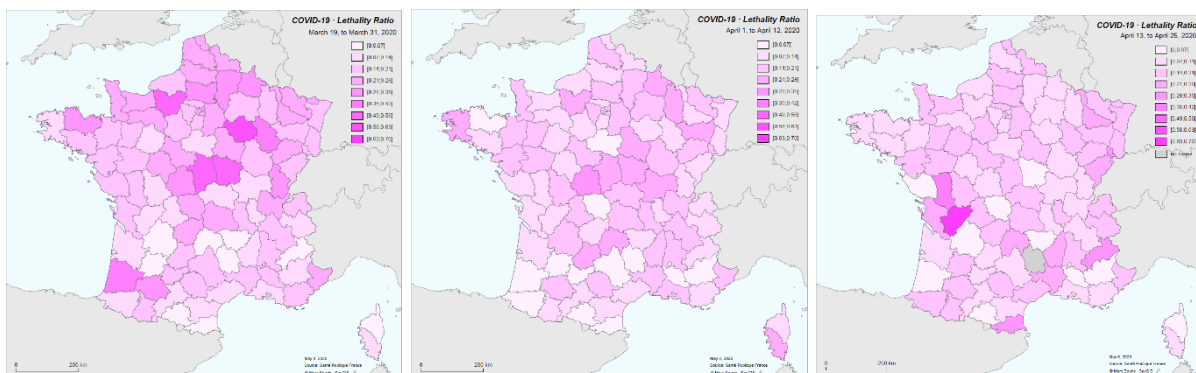

Figure 7: Calculated case-fatality rates by 13-day period.

The standardized case-fatality rate per district is between 0.044 (Ariège, SLR=0.25) and 0.255 (Vosges, SLR=1.48), with the mean at 0.151 and the median at 0.153. If the Ile-de-France and Grand-Est regions are excluded from the calculation of age-specific case-fatality rates, the CFR is between 0.044 and 0.251, with the mean at 0.144 and a median at 0.147 (SLR between 0.28 and 1.67, mean at 0.99 and median at 1) (Figure 8). In the following, we will consider only the standardized case-fatality rates calculated with age-specific case-fatality rates that do not take into account the Ile-de-France and Grand-Est regions.
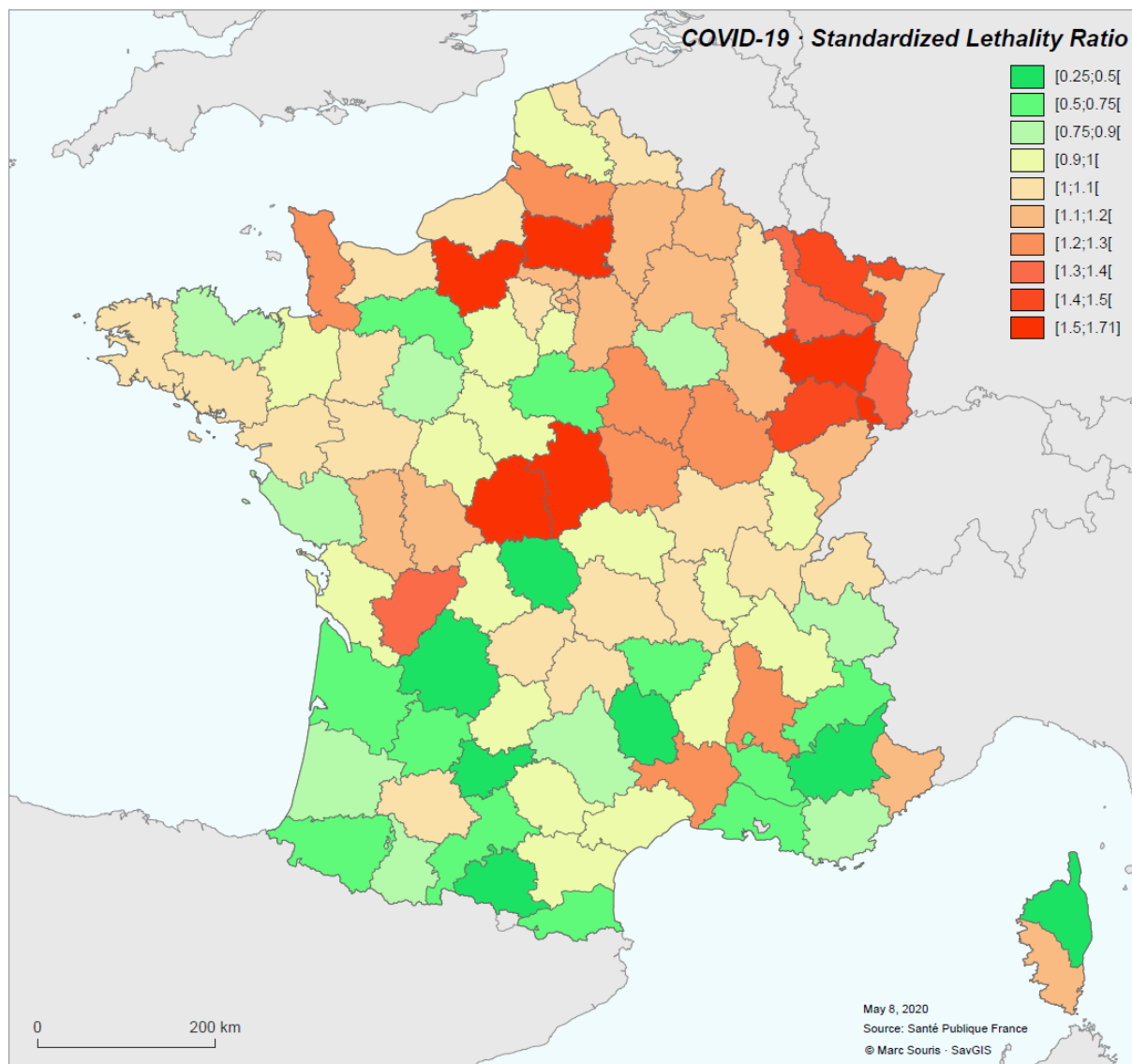
Figure 8. Standardized Lethality Ratio (SLR) for COVID-19 in metropolitan France for the period March 19 to May 8, 2020.

The spatial distribution of standardized morbidity rate (hospitalized cases) shows a significant spatial autocorrelation (Moran index: 1.54, p-value < 10^{-6}), and this is expected for an infectious disease. The case-fatality rate shows also significant spatial autocorrelation (Moran index: 0.29, p-value < 0.000007), and this is no expected. The analysis of the clusters clearly shows a clustering of high case-fatality rate values in regions of high morbidity (particularly the Grand-Est), and shows some cases of districts with high case-fatality rate values isolated in areas with low rates.

The Breslow & Day significance test shows districts where the SLR is statistically significantly different from 1, corresponding to districts with abnormally high (SLR > 1, red) or abnormally low (SLR < 1, green) standardized case-fatality rates. The individual significance threshold is set at 0.05, and for all districts at 0.0005 to account for multi-testing (Figure 9).
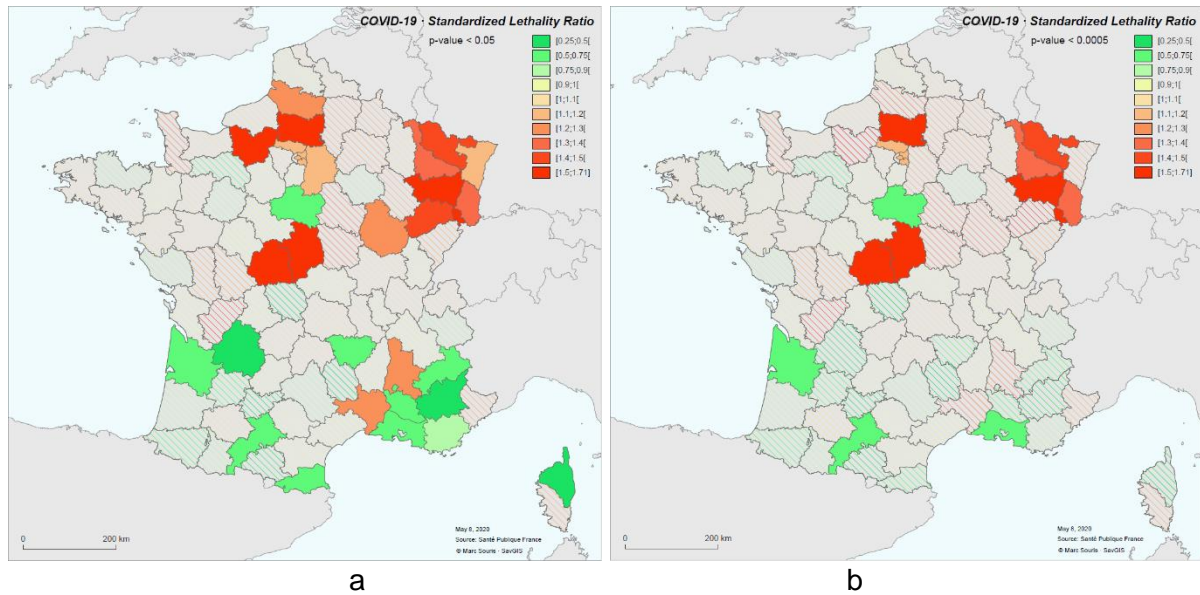
<center>a   b</center>

Figure 9. Geographical units (districts) with SLR significance.

Legend: p-value <0.05 (a), p-value < 0.0005 (b)

There is a correlation between the standardized hospitalization rate and the standardized case-fatality rate (Bravais-Pearson index=0.40) (Figure 10), a correlation which increases (0.48) if we limit the calculation to districts whose SLR is significantly different from 1 (p-value < 0.05).
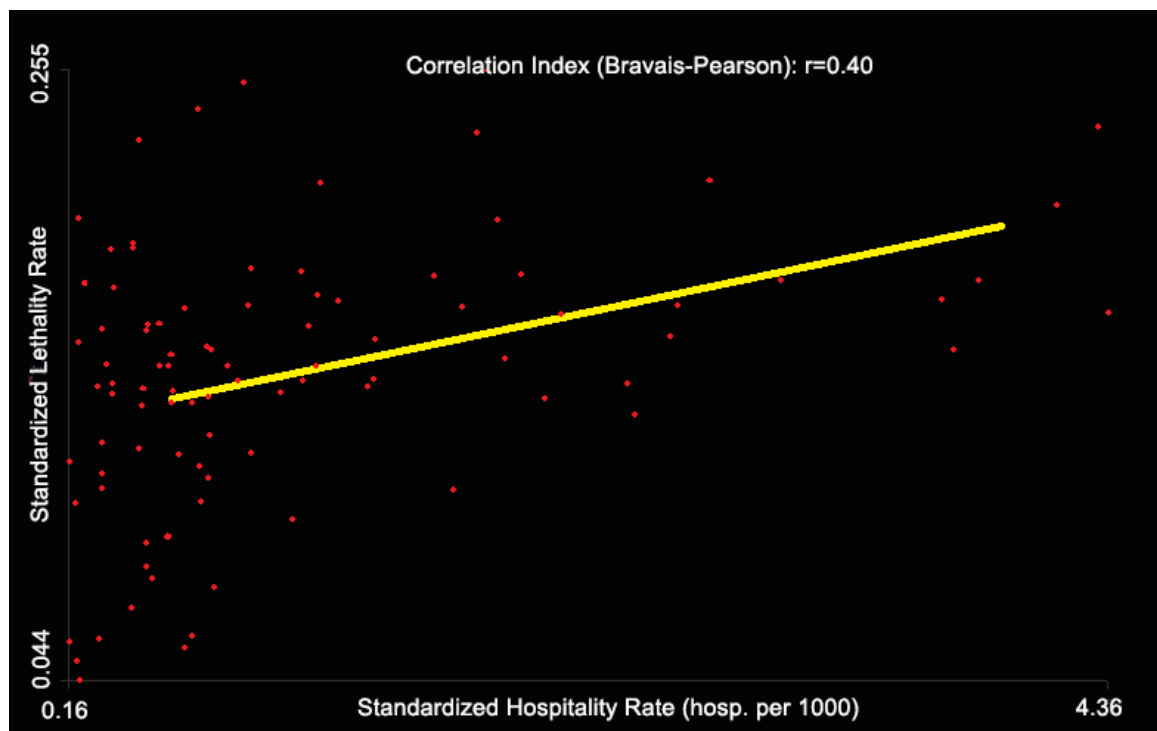

Figure 10. Correlation between Hospitalization rate and CFR during the COVID-19 epidemic in France for the period of time between March 19 to May 8, 2020.

To illustrate the increase of case-fatality rate with hospitalization rate, Table 4 gives the mean of the standardized case-fatality rate over the districts according to their

standardized hospitalization rate. The average case-fatality rate varies from 0.134 for districts with a low hospitalization rate (less than 0.5 per 1000) to 0.152 for all districts. If only districts with high hospitalization rates (above 2 per 1000) are considered, the average case-fatality rate is 0.183. For the eight districts with the highest hospitalization rates (> 3 per 1,000), and considered as district under hospital stress, the average case-fatality rate is 0.191 (Meuse, Moselle, Seine-St-Denis, Hauts-de-Seine, Paris, Val-de-Marne, Haut-Rhin, Territoire de Belfort), while it is 0.149 for all other districts.

Hospitalization rate (per 1000)	Districts number	Standardized CFR (mean)	p-value of T-test with international mean of CFR
< 0.5	31	0.134	$< 10^{-6}$
< 1	59	0.138	$< 10^{-6}$
< 1.5	72	0.142	$< 10^{-6}$
< 2	80	0.146	$< 10^{-6}$
< 2.5	86	0.147	$< 10^{-6}$
< 3	89	0.149	$< 10^{-6}$
< 3.5	90	0.149	$< 10^{-6}$
< 4	93	0.150	$< 10^{-6}$
all	96	0.152	$< 10^{-6}$

Table 4. Average standardized CFR as a function of hospitalization rate during the COVID-19 epidemic in France for the period of time between March 19 to May 8, 2020.

The mapping of the hospitalization rate and the hospital mortality rate with the SLR shows the spatial correspondence of these values (Figure 11).

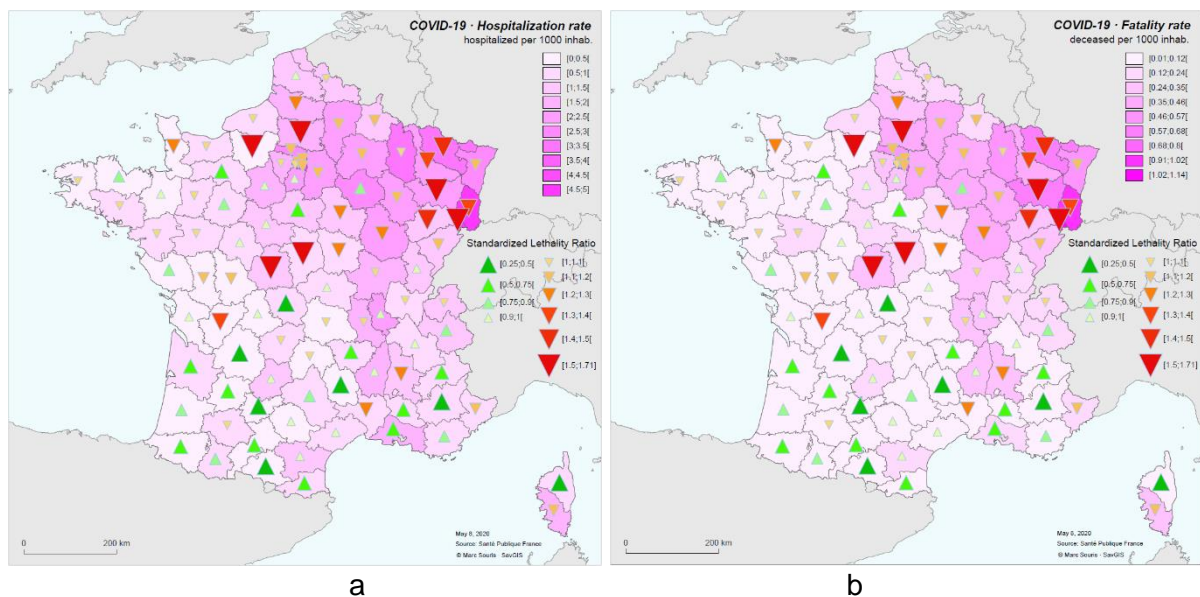a   b

Figure 11. SLR (symbols) and Hospitalization rate (a) and fatality rate (b) during the COVID-19 epidemic in France for the period of time between March 19 to May 8, 2020.

A typology combining hospitalization rates and case-fatality rates is proposed: low rates (values below the mean by less than one standard deviation), high rates (values above the mean by more than one standard deviation), so as to represent five classes (low-low, low-high, high-low, high-high, other) (Figure 12). The "high hospitalization-high case-fatality rate" class is spatially clustered. The "low hospitalization rate-high lethality rate" class is dispersed, and the population density is significantly lower in that class than in all the other districts (p-value < 0.02).
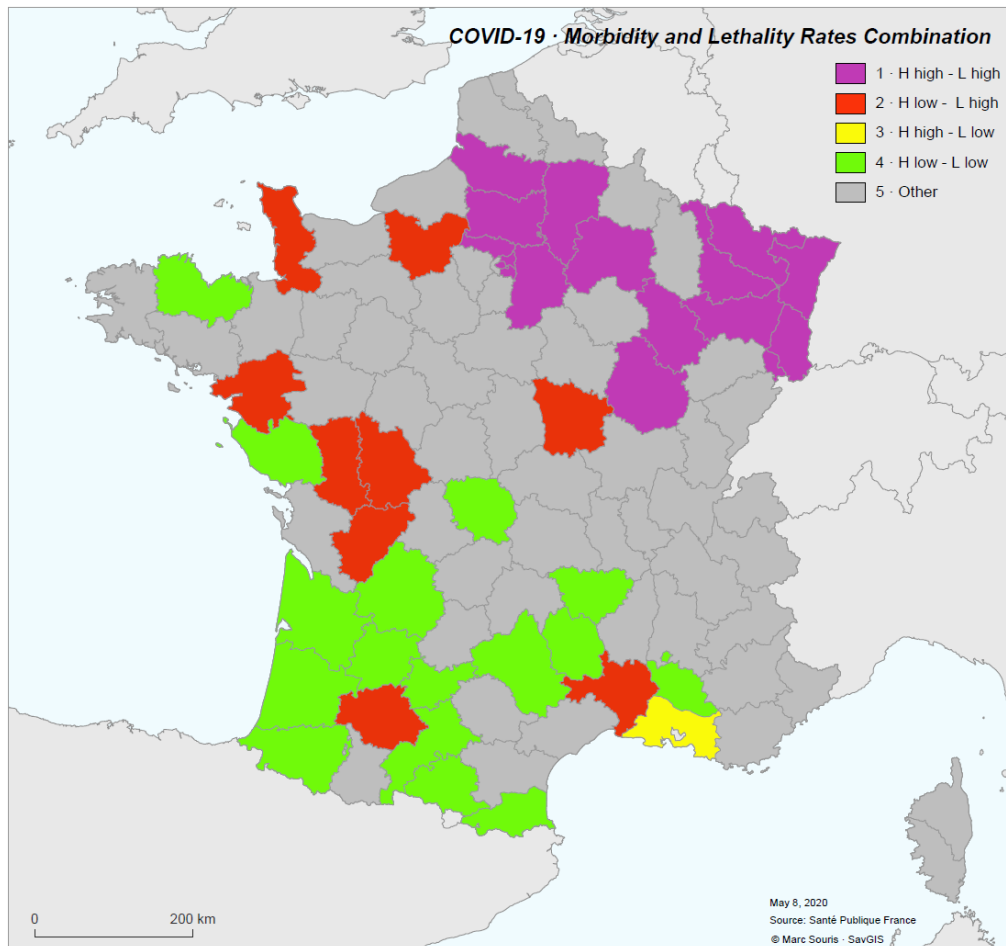

Figure 12. Combination of standardized hospitalization and case-fatality rates in five classes.

The ratio between the rate of patients in intensive care and the rate of hospitalization gives in principle an indication of the severity of the patients in hospital. This hospitalization rate and severity rate show a weak negative correlation (r=-0.22), indicating a decrease in the intensive care rate when the hospitalization rate is high. This trend may be due to the saturation of intensive care units. The relationship between hospitalization and severity could also be interpreted as a decrease in less severe hospitalizations in order to be able to manage more severe cases when the healthcare system is overloaded, which would result in an increase in lethality. Nevertheless, in both cases, there is no correlation between the severity rate and the case-fatality rate (r=-0.1), indicating that globally, the intensity of reanimation does not impact the case-fatality rate. Finally, the severity rate does not have a spatial

distribution corresponding to the spatial distribution of the hospitalization rate (Figure 13).
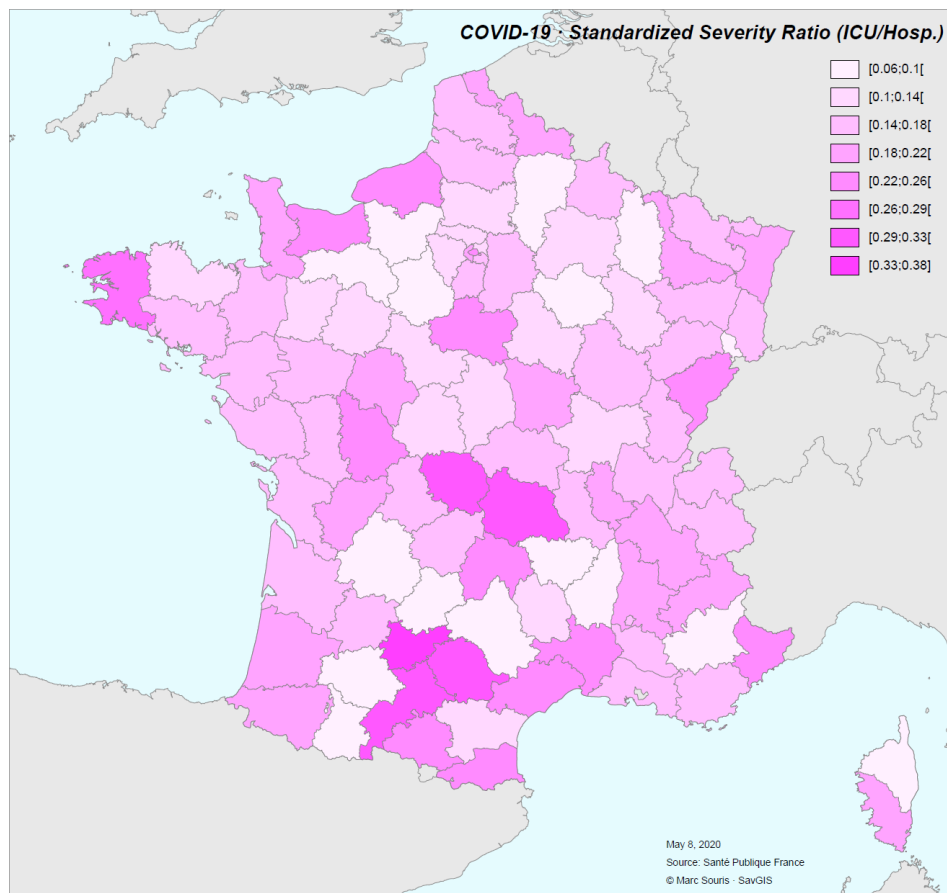

Figure 13. Severity ratio during the COVID-19 epidemic in France for the period of time between March 19 to May 8, 2020.

Discussion

The standardized case-fatality rates of the districts in France (0.04 for Tarn-et-Garonne to 0.26 for the Vosges district) remain in a ratio of 0.3 to 1.6 compared with the national average (mean 0.14, calculated by excluding districts under hospital stress in order not to take account of possible overloading of the healthcare systems). The relationships between morbidity rates and standardized case-fatality rates in France show a correlation between these two indices, the average case-fatality rate for all districts being about 15% higher than the average rate calculated in the 20% of districts with the lowest hospitalization rates. It is therefore very likely that the increase in hospital tension over the period under consideration has increased the hospital case-fatality rate: for the 20 districts with the highest hospitalization rates (essentially located in the Grand-Est and Ile-de-France regions), the average case-fatality rate is 20 per cent higher than the average for all districts, and 25 per cent higher than the average for all other districts alone. It is therefore likely that pressure on hospitals have increased the national average case-fatality rate by district from 0.145 to 0.153. It can thus be estimated that 2,425 deaths (out of the 16,732 deaths due to COVID-19 in hospital in France from 19 March to 8 May 2020, i.e. 15% of the total number of deaths)

are due to the overload of the health system in the Grand-Est and Ile-de-France regions.

There are clearly two risk profiles:

1/ the districts where a high rate of hospitalization is coupled with a high case-fatality rate. These districts correspond to the epicenters of the epidemic, are clustered, and include the densely populated areas of Ile-de-France.

2/ the districts where a low rate of hospitalization is coupled with a high case-fatality rate. These districts are geographically dispersed, sparsely populated and mainly located in rural areas.

The first profile accounts for 60% of the patients (59,878 over 99,970). The case-fatality average for this profile is significantly higher (0.187) as compared with the other districts case-fatality average (0.138). The profile displays a 33% excess mortality, corresponding to 2,716 deaths (11,003 observed vs. 8,287 expected with the CFR 0.138). This excess mortality, corresponding to 16 % of all deaths, is likely to be the result of increased lethality due to overloading of the healthcare system.

The second profile (more rural) accounts for only 12.5% of the patients (12,514 over 99,970), with an average case-fatality rate significantly high (0.178) corresponding to a 25% excess mortality (2,170 observed vs. 1,731 expected deaths), but of low magnitude. It is possible that this excess mortality is due to a lack of care (medical desert, poor hospital response), which would have led to an increase in hospital lethality.

Some districts in the south of France have both a very low rate of hospitalization and a very low case-fatality rate (Gironde, Dordogne, Gers, Pyrénées Orientales), as a result of the low circulation of the virus and the effective response of the health system. Another particular case, is the one of the Bouches-du-Rhône, which appears with a high hospitalization rate (1.96 per 1,000, for a national average of 1.27) and a low case-fatality rate (0.11 for the Bouches-du-Rhône for a national average per district of 0.15). This situation could be due to a medical policy of more active screening and earlier hospitalization of the infected in the district, particularly in Marseille metropolitan area. The high value of the hospitalization rate would then be more the result of a non-severe treatment of the infected than of a more active circulation of the virus in the region, as for the lower hospitalization rates in neighboring districts (0.9 for Var, 0.56 for Vaucluse, 0.52 for Gars, 0.86 for Alpes-de-Haute-Provence, 0.81 for Alpes-Maritimes, 0.68 for Hérault). However, patient severity profile (expressed as the ratio between the number of patients admitted to intensive care and the total number of patients hospitalized) is not particularly low in the Bouches-Du-Rhône (0.163 for a mean of 0.156 and a standard deviation of 0.06 for all the districts), and this hospitalization policy is therefore not proven to be the primary factor in the low observed case-fatality rate.

Time analysis shows that the case-fatality rate has decreased over time, globally and in almost all districts, showing an improvement in the management of severe patients during the epidemic. This decrease stabilized rapidly and no longer evolved in a steady manner. However, this result is limited by the difficulty of calculating a case-fatality rate on aggregated data over a short period of time, with eventual death

occurring several days after hospitalization. We chose to delay the calculation of the number of deaths by 12 days compared to the calculation of the number of hospitalizations, since 85% of deaths occur on an average of 13 days after hospitalization [SAL 20].

WHO data from 219 countries (WHO 20) show a mean case-fatality rate of 0.041 (median 0.029, standard deviation 0.045) with values between 0.31 (Nicaragua) and 0.00 (for countries that did not report deaths, like Vietnam). A T-test shows that the French average is therefore very significantly higher than the world average (p-value < 10-6). Even if we consider only the average case-fatality rate calculated only for the French districts with the lowest hospitalization rates (thus not causing saturation of the health care system), this average is still very significantly higher than the international average (and the rates of most European countries, such as Spain, 11.73, Greece, 5.52, Germany, 4.28, etc.) (table 4). Taking into account the quality of the healthcare system in France (table 1), it can be concluded that the difference between the case-fatality rate calculated for France and the case-fatality rates presented using international WHO data is highly probably the result of a difference in the registration of cases and/or deaths and not due to the quality of health care. These differences in the counting of cases and/or deaths may be due to the hospitalization and screening policy specific to each country as well as the ability or willingness to hospitalize more non-severe forms, to the differences in case definition, or to insufficient quality of the system for detecting and reporting cases and deaths.

Conclusion

This study shows that the higher case-fatality rates observed in France in some districts during the first wave of the COVID-19 epidemic (data from 19 March to 8 May 2020) are mostly linked to the level of morbidity in the district, and therefore likely to the congestion of the healthcare systems during the acute phases of the epidemic. When the hospitalization rate is low, high case-fatality rates concern rural districts with low population density and could be linked to healthcare access in these districts.

However, the increase in the standardized case-fatality rate due to exceptional situations during epidemic peaks represents less than 10% of the average case-fatality rate per district in France, and the hospital case-fatality rate without these districts would be reduced from 0.151 to 0.138. This increase cannot therefore explain the extent of the difference observed between the average case-fatality rate in France and the average of the rates reported for all countries by international organizations or information sites (WHO, Wordometer, etc.). These differences probably stem from the reporting of cases and deaths, which is uneven from one country to another, and not from the care or treatment of patients during hospital stress due to epidemic peaks.

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