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Article original

Major interregional differences in France of COVID-19 hospitalization and mortality from January to June 2020

Variabilité de l'incidence des hospitalisations et de la mortalité entre les régions lors de la première vague de COVID-19 entre janvier et juin 2020 en France

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ABSTRACT

Introduction. – Even though France was severely hit by the COVID-19 pandemic, few studies have addressed the dynamics of the first wave on an exhaustive, nationwide basis. We aimed to describe the geographic and temporal distribution of COVID-19 hospitalisations and in-hospital mortality in France during the first epidemic wave, from January to June 2020.
Methods. – This retrospective cohort study used the French national database for all acute care hospital admissions (PMSI). Contiguous stays were assembled into "care sequences" for analysis so as to limit bias when estimating incidence and mortality. The incidence rate and its evolution, mortality and hospitalized case fatality rates (HCFR) were compared between geographic areas. Correlations between incidence, mortality, and HCFR were analyzed.
Results. – During the first epidemic wave, 98,366 COVID-19 patients were hospitalized (incidence rate of 146.7/100,000 inhabitants), of whom 18.8% died. The median age was 71 years, the male/female ratio was 1.16, and 26.2% of patients required critical care. The Paris area and the North-East region were the first and most severely hit areas. A rapid increase of incidence and mortality within 4 weeks was followed by a slow decrease over 10 weeks. HCFRs decreased during the study period, and correlated positively with incidence and mortality rates.
Discussion. – By detailing the geographical and temporal evolution of the COVID-19 epidemic in France, this study revealed major interregional differences, which were otherwise undetectable in global analyses. The precision afforded should help to understand the dynamics of future epidemic waves.

RÉSUMÉ

Introduction. – La France a été fortement touchée par la pandémie de COVID-19, et aucune étude n'a décrit de manière exhaustive son impact sur les hospitalisations. Notre objectif était de décrire la distribution

Abbreviations: SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; PMSI, Programme de médicalisation des systèmes d'information; SIR, Standardised incidence ratios; ATIH, Agence Technique de l'Information sur l'Hospitalisation; ICD, International Classification of Diseases; CCU, Critical care unit; CIR, Crude incidence rates of hospitalisation; CMR, Crude mortality rates; SMR, Standardised mortality ratios; HCFR, Hospitalised case fatality rate; INSEE, Institut national de la statistique et des études économiques

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géographique et l'évolution temporelle des hospitalisations liées à la COVID-19 et la mortalité intrahospitalière en France durant la première vague, de janvier à juin 2020.
Méthodes. – Cette étude de cohorte rétrospective est basée sur les données de la base nationale du PMSI. Les hospitalisations contiguës ont été rassemblées en « séquences de soins » afin de limiter les biais lors des calculs d'incidence et de mortalité. Les taux d'incidence et leur évolution, la mortalité et le taux de létalité ont été comparés selon différents niveaux géographiques. Les corrélations entre incidence, mortalité et taux de létalité ont été analysées.
Résultats. – Durant la première vague épidémique, nous avons dénombré 98 366 patients hospitalisés en France (taux d'incidence 146,7/100 000 habitants), parmi lesquels 18,8 % sont décédés. L'âge médian était de 71 ans, le ratio homme/femme de 1,16 et 26,2 % des patients ont nécessité des soins intensifs. L'Île-de-France et le Grand Est ont été les régions touchées les plus précocement et les plus sévèrement. Une rapide augmentation de l'incidence et de la mortalité sur 4 semaines a été suivie par une lente diminution durant 10 semaines. Le taux de létalité a progressivement diminué durant cette période et était corrélé positivement avec l'incidence et la mortalité.
Discussions. – La description géographique et temporelle de cette première vague épidémique de COVID-19 en France montre d'importantes variations régionales et départementales, qu'une analyse globale n'aurait pas pu mettre en évidence. La précision apportée par ces analyses peut aider à mieux comprendre la dynamique de futures vagues épidémiques.
Mots-clés. – COVID-19 ; France ; étude de cohorte ; hôpital ; mortalité

1. Introduction

On 7 January 2020 the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), responsible for the coronavirus disease 2019 (COVID-19), was isolated in China [1,2]. In February 2020, when the situation seemed to be under control in Wuhan, the epidemic rapidly disseminated worldwide. On January 24, the first three European cases were reported in France, though earlier circulation of the virus has since been evidenced [3–5]. By the end of February, two clusters had been identified ; the first in the Oise department, north of Paris, and the second in the Haute-Savoie department [6,7]. In early March, a new cluster was identified in the Haut-Rhin department, in north-eastern France [8]. Just after the WHO made the assessment that COVID-19 could be characterised as a pandemic, France entered into a strict lockdown, from 17 March to 10 May 2020 [9,10].

Nationwide analyses of the first-wave period have been carried out in several different countries, including England, Germany, and Brazil [11–13]. To date, however, the few studies focused on the impact of the first wave in France on a nationwide level have been based on limited data sources across restricted periods [14–16].

The aim of this study was to describe the geographic and temporal distribution of 1) the incidence of hospital admissions and 2) in-hospital mortality in a nationwide cohort of patients with a diagnosis of COVID-19, admitted to any public or private hospital in France over the period of time corresponding to the first pandemic wave : January to June 2020

2. Methods

2.1. Database

We performed a retrospective cohort analysis on data from the French "*Programme de Médicalisation des Systèmes d'Information"* (PMSI)[17]. The PMSI is a comprehensive nationwide database that gathers hospitalisation data transmitted monthly by all public and private hospitals in France. Diagnoses are coded using the International Classification of Diseases, 10th Revision (ICD-10). After pseudonymisation, the data are uploaded by each hospital on a secure national platform managed by the French National Agency for the Management of Hospitalisation Data (*Agence Technique de l'Information sur l'Hospitalisation*, ATIH), and are integrated into the PMSI national database.

We included data from all patients hospitalised in French hospitals with COVID-19 during the first epidemic wave (January 1—June 30, 2020). Patients without a precise residency zip code or those living in a foreign country were excluded from the computation of these rates (n = 361, 0.4 %). Patients were followed up through death or discharge, up until September 30, 2020. Hospital stays for COVID-19 were identified by the following ICD-10 codes : U07.10, U07.11, U07.12, U07.14 and U07.15 (Table 1), according to the national guidelines [18]. Confirmed cases were defined as patients with ICD codes U07.10, U07.12 and U07.14. All contiguous hospital stays for the same patient were gathered together and considered as a unique "care sequence" as previously detailed in another paper [19]. Two hospital stays were considered as contiguous if the discharge date of the first stay and the admission date of the second stay were separated by one day or less. If a patient was transferred from one hospital to another on the same day or during the night between two days, it was considered as a single care sequence. Each care sequence started with a hospital stay with COVID as defined above, but subsequent contiguous hospital stays were included regardless of COVID status. Counting care sequences instead of hospital stays limits bias when estimating incidence and mortality. The care sequence starting date was that of the first stay, and the end date was the date of death or the date of discharge of the last stay. In case of multiple hospitalisations with more than one day between the two care sequences, only the first sequence per patient was considered. We excluded care sequences having lasted for only a single day, except in the case of death.

The variables extracted for each patient were age, gender, zip code of residence, dates of hospital admission and discharge, in-hospital death, hospital name, hospital identification number, hospital zip code and admission to a critical care unit (CCU). Date of in-hospital death

Table 1
Codification of the International Classification of the diseases (ICD), 10th revision, modified by the ATIH to identify the COVID cases in the PMSI database.

ICD 10 Code	Label	Number of patients with this code* (n = 98,366)
U07.10	COVID-19, respiratory form, confirmed case	64,584 (65.7 %)
U07.11	COVID-19, respiratory form, unconfirmed case	23,356 (23.7 %)
U07.12	COVID-19, without symptoms, confirmed case	4480 (4,6 %)
U07.14	COVID-19, other clinical form, confirmed case	3893 (3.9 %)
U07.15	COVID-19, other clinical form, unconfirmed case	2053 (2.1 %)

Confirmed cases (U07.10, U07.12, U07.14) are based on polymerase chain reaction test or serology ; unconfirmed cases (U07.11, U07.15) are based on clinical evidence associated with chest computed tomography.

* In case of more than one U07.X code for a patient, the prioritization order is : U07.10 > U07.14 > U07.12 > U07.11 > U07.15

was the date of discharge for hospital stays with discharge code equal to death. These CCUs included intensive care units, intermediate care units ("*soins intensifs*"), and step-down units ("*unité de surveillance continue*").

2.2. Statistical analysis

Two outcomes were considered : Incidence of hospitalisation, and in-hospital mortality. For these two outcomes, we considered temporal and spatial evolution. The time interval used was the week, with Monday being considered as the first day. For spatial descriptions, the zip codes indicating patient municipality of residence were gathered together to provide information at the departmental and regional level.

For continuous variables, the median is described and the interquartile ranges are given [IQR]. Categorical variables are described as number of patients and percentages.

The crude incidence rates of hospitalisation (CIR) were calculated with, in the numerator, the number of patients hospitalised according to their departments of residency, and in the denominator, the number of people in the department. Similarly, the crude mortality rates (CMRs) were calculated using the number of departmental hospital deaths in the numerator. To calculate standardised incidence ratios (SIR) and standardised mortality ratios (SMR), direct standardisation was done, using the official 2020 estimates by age and sex of the populations of the 101 French departments, as published by the National Institute of Statistics and Economic Studies (INSEE) [20]. To compute the weekly incidence of hospitalisation, the starting day of each care sequence determined at which week it would be counted. Patients without a precise residency zip code or those based in a foreign country were excluded from the computation of these rates (n = 361, 0.4 %).

The hospitalised case fatality rate (HCFR) was defined as the number of in-hospital deaths among the discharged COVID-19 patients.

Most of the analyses were performed on the secure ATIH platform. Data extraction and preparation were carried out on 9 January 2021, with SAS Guide Enterprise version 82. Sensitive data analysis was performed with R software 3.5 on ATIH platform, whilst non-sensitive (aggregated) data were downloaded to be computed with R software 4.1, using external packages from the tidyverse collection [21,22].

This study was conducted in accordance with the French legislation concerning reuse of the PMSI database (MR-005 of the Commission nationale de l'informatique et des libertés, CNIL), with inscription on the Health Data Hub public register (N° F20201117130456). Since we used pseudonymised discharge data, patients were not solicited.

3. Results

3.1. Main characteristics

From January to June 2020, a total of 98,366 patients were hospitalised in French healthcare facilities with COVID-19. Among them, 25765 patients (26.2 %) spent at least one day in a critical care unit. The median length of a care sequence was 9 days (IQR = [4;16]). Median age was 71 years (IQR = [56 ; 83], range = [0 ; 108]). Sex ratio was 1.16 males to one female. Males were younger than females, with median ages of 69 (IQR = [56 ; 80]) and 74 (IQR = [57 ; 86]) years old, respectively. Distribution by age and sex is presented in Fig. 1. The cases confirmed by RT-PCR (n=72,957, 74.2 %) and the unconfirmed cases (n=25,409, 25.8 %) had the same median age (71y, IQR= [57 ; 83] vs 71y, IQR= [55 ; 84]), a similar male/female ratio (1.19 vs 1.10) and a higher proportion of cases with at least one day in a CCU (28.0 % vs 21.1 %).

A majority of patients (n = 82,764 ; 84.1 %) had a single hospital stay, while 13.1 % had two consecutive stays, and 2.8 % had three or more consecutive stays. The 98,366 care sequences included a total of 117,291 hospital stays, representing a total of 1,288,688 in-hospital days (Table 2).

Among the 1289 French public and private acute healthcare facilities, 77 % (n = 995) provided care to at least one COVID-19 patient. Amongst them, six public hospitals took care of 20 % of all COVID-19 patients : Assistance Publique — Hôpitaux de Paris (12.9 %), Hospices Civils de Lyon (1.7 %), Groupe Hospitalier de la Région de Mulhouse et Sud Alsace (1.6 %), Hôpitaux Universitaires de Strasbourg (1.6 %), Grand Hôpital de l'Est Francilien (1.5 %),and Assistance Publique-Hôpitaux de Marseille (1.3 %).

3.2. Incidence of hospitalisation

In a French population of 67,063,703, the crude national incidence of hospitalisation with COVID-19 from January to June 2020 was 146.7/100,000. The incidence of cases confirmed by RT-PCR was 108.8/100,000. The number of COVID-19 hospitalisations exceeded the threshold of 1000 hospitalisations per week on March 2 and increased exponentially, reaching a peak of 22,026 admissions/week within 4 weeks (week of March 23, incidence ratio : 32.84/100,000 inhabitants) (Fig. 2A). The decrease phase of this first wave was slower, taking 10 weeks before returning to a level inferior to 1000 admissions (week of June 1).

The demographic characteristics of the patients without a precise residency zip code or living in a foreign country (n = 361, 0.4 %), who were excluded from the by-department computation of rates, were comparable to those of the 98,005 included patients. While they presented with lower mean age (64 vs 68 years), and a lower proportion of probable COVID cases (19.9 % vs 25.9 %) the sex ratio and the death rate were comparable (see Table, Appendix 1).

Incidence varied greatly across French regions and departments (Table 3). The highest crude incidence ratio (CIR) and standardized incidence ratio (SIR) were in the Île-de-France followed by the Grand Est regions. At a departmental level, the highest crude incidence was in the Haut-Rhin (440.4/100,000), but after age and gender standardisation, the highest incidence was in Seine-Saint-Denis (520.7/100,000).

Similar to crude incidence, standardised incidence varied greatly from one department to another and from one week to the next (Fig. 3). We considered two thresholds, 20/100,000 and 60/100,000 inhabitants hospitalised per week, to define two levels of in-hospital alert. The threshold of 20 hospitalisations per 100,000 inhabitants by week was first exceeded in the Haut-Rhin (week of March 2) and then in the Oise (week of March 9). Most of the other departments exceeded this threshold at a later date, during the weeks of March 16 (20 departments) or March 23 (18 departments). Fifty-seven out of the 101 French departments never reached this weekly incidence. As regards the 44 departments with a weekly hospitalisation rate over the threshold of 20/100,000, median duration of the wave was 3.5 weeks (IQR = [2 ; 5]), reaching a maximum of 11 weeks in the overseas department of Mayotte. One overseas department, Guyane (French Guyana), exceeded this threshold during the week of June 8, 3 months after the first department. Only ten departments recorded hospitalisation incidence over 60/100,000 by week, and all with the exception of Guyane were located in the Île-de-France and Grand Est regions.

The peak, defined as the highest weekly standardised incidence rate, was reached for the overwhelming majority of departments (n = 93) during the weeks of March 23 (76 departments) and March 30 (17 departments). The highest weekly incidence rates occurred in Seine-Saint-Denis (119/100,000) and Haut-Rhin (96/100,000).

3.3. In-hospital mortality

Among the 98,366 patients hospitalised, 18,447 (18.75 %) died in hospital before September 30, representing a mortality ratio of 27 in-hospital deaths/100,000 inhabitants. These deceased patients were older than the average hospitalised COVID-19 patients (median age of 82 years, IQR = [72 ; 88]), and a majority were male (sex ratio of 1.47 males to one female).

Table 2
Analysis of hospital stays by the region and department of the healthcare provider.

	Hospital stays	Patients	Mean stay duration (days)	Total days of hospital care	% of national total	Critical care stays	Total days of critical care
France	**117,291**	**98,366**	**10.99**	**1,288,688**	**100.00**	**29,522**	**365,258**
Île-de-France	**42,199**	**35,866**	**11.16**	**470,934**	**36.54**	**11,979**	**148,727**
75 Paris	10,639	9362	11.80	125,538	9.74	3184	42,996
77 Seine-et-Marne	3674	3321	10.68	39,240	3.04	967	11,787
78 Yvelines	3517	3052	11.14	39,183	3.04	1061	12,094
91 Essonne	3444	3120	12.24	42,138	3.27	946	12,594
92 Hauts-de-Seine	5963	5411	11.44	68,246	5.30	1636	22,199
93 Seine-Saint-Denis	5303	4957	10.14	53,779	4.17	1741	17,912
94 Val-de-Marne	6168	5749	10.97	67,655	5.25	1784	20,451
95 Val-d'Oise	3491	3214	10.07	35,155	2.73	660	8694
Centre-Val de Loire	**3650**	**2959**	**11.11**	**40,551**	**3.15**	**713**	**9750**
18 Cher	345	269	12.54	4328	0.34	41	484
28 Eure-et-Loir	776	701	11.90	9235	0.72	124	1847
36 Indre	389	321	11.01	4281	0.33	47	453
37 Indre-et-Loire	986	738	8.66	8535	0.66	226	2890
41 Loir-et-Cher	428	393	12.63	5404	0.42	73	758
45 Loiret	726	633	12.08	8768	0.68	202	3318
Bourgogne-Franche-Comté	**5487**	**4802**	**11.04**	**60,581**	**4.70**	**1446**	**17,793**
21 Côte-d'Or	1257	1100	10.62	13,354	1.04	656	7500
25 Doubs	1060	881	10.02	10,621	0.82	250	3268
39 Jura	327	321	10.88	3559	0.28	62	437
58 Nièvre	140	117	13.45	1883	0.15	22	395
70 Haute-Saône	322	305	10.61	3416	0.27	107	933
71 Saône-et-Loire	1100	917	9.58	10,534	0.82	150	1724
89 Yonne	507	472	13.55	6872	0.53	90	1639
90 Territoire de Belfort	774	766	13.36	10,342	0.80	109	1897
Normandie	**3109**	**2651**	**11.04**	**34,331**	**2.66**	**655**	**8392**
14 Calvados	492	423	11.63	5721	0.44	134	1938
27 Eure	458	398	9.20	4215	0.33	55	642
50 Manche	278	229	10.69	2973	0.23	53	891
61 Orne	432	369	12.51	5403	0.42	63	807
76 Seine-Maritime	1449	1311	11.06	16,019	1.24	350	4114
Hauts-de-France	**11,121**	**9295**	**10.38**	**115,424**	**8.96**	**3117**	**34,587**
02 Aisne	1485	1356	11.26	16,727	1.30	262	3451
59 Nord	4348	3545	9.45	41,074	3.19	1303	14,300
60 Oise	1948	1779	11.37	22,149	1.72	425	5169
62 Pas-de-Calais	1879	1610	9.82	18,459	1.43	829	7564
80 Somme	1461	1193	11.65	17,015	1.32	298	4103
Grand Est	**17,879**	**14,656**	**11.15**	**199,426**	**15.48**	**4090**	**48,623**
08 Ardennes	276	246	10.56	2914	0.23	46	682
10 Aube	504	460	13.24	6671	0.52	85	1073
51 Marne	1308	1148	11.06	14,467	1.12	220	2922
52 Haute-Marne	391	359	12.20	4771	0.37	71	1010
54 Meurthe-et-Moselle	2020	1595	11.12	22,462	1.74	575	7169
55 Meuse	521	415	11.74	6116	0.47	62	848
57 Moselle	3778	3244	10.91	41,209	3.20	736	8283
67 Bas-Rhin	4319	3383	10.66	46,054	3.57	931	13,366
68 Haut-Rhin	3729	3321	11.88	44,314	3.44	1099	11,291
88 Vosges	1033	960	10.11	10,448	0.81	265	1979
Pays de la Loire	**3363**	**2912**	**10.65**	**35,826**	**2.78**	**590**	**7278**
44 Loire-Atlantique	1205	976	9.79	11,796	0.92	238	2735
49 Maine-et-Loire	887	838	11.06	9809	0.76	186	2237
53 Mayenne	230	201	13.62	3132	0.24	26	508
72 Sarthe	574	507	11.65	6687	0.52	61	839
85 Vendée	467	416	9.43	4402	0.34	79	959
Bretagne	**1807**	**1592**	**10.97**	**19,830**	**1.54**	**450**	**5587**
22 Côtes-d'Armor	320	264	10.58	3384	0.26	66	521
29 Finistère	373	335	11.34	4231	0.33	101	1329
35 Ille-et-Vilaine	517	464	11.48	5936	0.46	132	1576
56 Morbihan	597	551	10.52	6279	0.49	151	2161
Nouvelle-Aquitaine	**3766**	**3051**	**10.29**	**38,739**	**3.01**	**969**	**12,028**
16 Charente	142	124	7.87	1117	0.09	35	353
17 Charente-Maritime	280	235	12.02	3366	0.26	56	940
19 Corrèze	251	219	11.14	2795	0.22	38	454
23 Creuse	85	75	13.04	1108	0.09	41	420
24 Dordogne	157	136	11.56	1815	0.14	17	243
33 Gironde	1733	1307	9.70	16,810	1.30	463	5572
40 Landes	108	105	11.71	1265	0.10	32	474
47 Lot-et-Garonne	158	117	10.45	1651	0.13	24	329
64 Pyrénées-Atlantiques	294	258	10.47	3077	0.24	60	784
79 Deux-Sèvres	94	85	9.89	930	0.07	12	233
86 Vienne	251	228	10.59	2657	0.21	69	831

(*continued*)

Table 2 (*Continued*)

	Hospital stays	Patients	Mean stay duration (days)	Total days of hospital care	% of national total	Critical care stays	Total days of critical care
87 Haute-Vienne	213	198	10.08	2148	0.17	122	1395
Occitanie	**4205**	**3588**	**11.17**	**46,952**	**3.64**	**1198**	**15,212**
09 Ariège	37	37	14.30	529	0.04	10	220
11 Aude	384	344	12.00	4608	0.36	70	774
12 Aveyron	207	171	7.29	1509	0.12	20	266
30 Gard	446	411	14.29	6375	0.49	165	2010
31 Haute-Garonne	913	745	11.58	10,571	0.82	372	4937
32 Gers	226	199	12.43	2810	0.22	43	297
34 Hérault	996	833	10.47	10,428	0.81	297	3471
46 Lot	87	73	10.30	896	0.07	17	239
48 Lozère	27	27	9.67	261	0.02	2	42
65 Hautes-Pyrénées	190	171	12.04	2288	0.18	35	646
66 Pyrénées-Orientales	406	379	8.43	3423	0.27	85	1041
81 Tarn	218	193	11.04	2407	0.19	61	876
82 Tarn-et-Garonne	68	64	12.46	847	0.07	21	393
Auvergne-Rhône-Alpes	**12,369**	**10,382**	**11.05**	**136,688**	**10.61**	**2436**	**31,784**
01 Ain	695	620	9.36	6502	0.50	156	1336
03 Allier	270	255	11.75	3173	0.25	49	799
07 Ardèche	606	561	12.84	7784	0.60	74	1123
15 Cantal	80	60	12.36	989	0.08	26	244
26 Drôme	737	664	11.41	8412	0.65	156	2259
38 Isère	1060	968	12.24	12,973	1.01	210	2376
42 Loire	1756	1442	12.37	21,721	1.69	286	5302
43 Haute-Loire	78	72	16.00	1248	0.10	13	256
63 Puy-de-Dôme	460	403	9.33	4291	0.33	91	1314
69 Rhône	4714	3845	10.79	50,872	3.95	1046	12,808
73 Savoie	536	478	9.88	5297	0.41	98	1003
74 Haute-Savoie	1377	1195	9.75	13,426	1.04	231	2964
Provence-Alpes-Côte d'Azur	**6499**	**5529**	**10.80**	**701,92**	**5.45**	**1517**	**20,881**
04 Alpes-de-Haute-Provence	98	94	9.42	923	0.07	13	163
05 Hautes-Alpes	159	147	9.76	1552	0.12	38	530
06 Alpes-Maritimes	1 132	916	9.20	10,411	0.81	213	2835
13 Bouches-du-Rhône	3755	3232	11.39	42,761	3.32	950	13,477
83 Var	961	865	11.69	11,230	0.87	234	3065
84 Vaucluse	394	337	8.41	3315	0.26	69	811
Corse	**327**	**306**	**14.29**	**4673**	**0.36**	**75**	**1125**
2A Corse-du-Sud	229	212	15.92	3645	0.28	59	895
2B Haute-Corse	98	94	10.49	1028	0.08	16	230
DROM (Départements et régions d'outre-mer)	**1510**	**1395**	**9.63**	**14,541**	**1.13**	**287**	**3491**
971 Guadeloupe	238	214	10.27	2444	0.19	65	759
972 Martinique	191	172	11.91	2275	0.18	58	948
973 Guyane	538	521	9.09	4889	0.38	77	789
974 La Réunion	259	236	8.84	2290	0.18	40	349
976 Mayotte	284	282	9.31	2643	0.21	47	646

The COVID-19 crude mortality ratio (CMR) varied significantly across French regions and departments (Table 3), with the Grand Est region reporting the highest (57.91/100,000 inhabitants), and the overseas departments (DROM) the lowest (5.45/100,000). After standardisation for age and gender, the highest mortality rate (SMR) occurred in the Île-de-France region (72.80/100 000).

If the maximum weekly number of discharged patients was recorded in the week of April 6 (n = 15,653), the highest number of hospital deaths had occurred one week prior : March 30, with 3582 deaths (Fig. 2B). The weekly hospitalised case fatality rate (HCFR) ranged during the first wave from 12.8 % (35 deaths) during the week of March 2, to a maximum of 26.3 % (942 deaths) during the week of March 16, and was as low as 7.5 % (56 deaths) during the week of June 29 (Fig. 2C). The hospital case fatality rate (HCFR) rate throughout the study period likewise varied among French departments (Table 3,) with a maximum of 29.3 % (84 deaths out of 287 cases) in Cher and 25.9 % in Moselle (817 deaths out of 3155 cases), and a minimum of 3.4 % in La Reunion, albeit among a very low number of cases (7 deaths out of 206 cases).

Although mortality and incidence rates are highly correlated (Fig. 4A and B, r = 0.969 and r = 0.973), in one department, Moselle, the mortality rate was higher than what would be expected based on this correlation, whereas in Guyane and Mayotte, the standardised mortality rate was lower than expected. While the HCFR tends to increase with CIR and CMR, the relationship is not linear, with a ceiling effect approximating 20 % (Fig. 4C and D). The Cher department, which exhibited the highest HCFR, nevertheless presented incidence rates below the national level and mortality rates within the range of the latter. In contrast, some departments (la Réunion, Guyane, Mayotte, Hautes-Alpes) had a lower HCFR than would have been expected based on their incidence rates.

4. Discussion

To our knowledge, this report is the first to detail the spatial and temporal distribution of COVID-19 hospitalisations in France from January to June 2020, period covering the first pandemic wave, on a nationwide level. Following the appearance of initial clusters in the east of France and north of Paris, the epidemic spread throughout the country, with different departments undergoing different epidemic progressions, as illustrated in this work. The nationwide lockdown, which began on March 17, slowed the epidemic, of which the

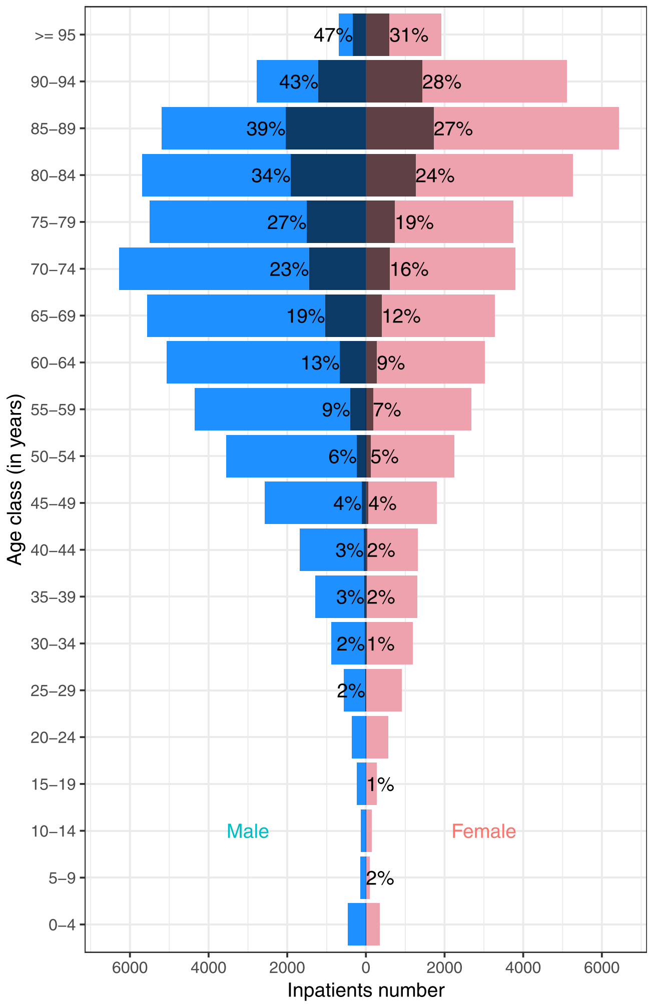

Fig. 1. Population age pyramids of COVID-19 hospitalisations from January to June 2020 in France. Hospitalized case fatality rates (HCFR) are given as percentages, and represented as grey shadows.

hospitalisation peak for almost all departments was reached during the week of March 23. Unfortunately, in some departments at the start of the national lockdown, the incidence rate of hospitalisation was already extremely high. Due to overwhelmed critical care capacities, some patients were transferred to other hospitals in France or even abroad. This was rendered possible by interregional cooperation and a lesser impact of the epidemic in some departments. Throughout the study period, 57 % of French departments never reached the threshold of a weekly rate of 20 hospitalisations per 100,000 inhabitants. The slower progression of the epidemic in those departments may have been due to their geographical location, far removed from the first clusters, and also to their lower density of population, which ranged in France from 3 (Guyane) to 1022 inhabitants per square kilometre (Île de France) [23].

The global dynamic of the first wave can be characterized as a four-week exponential increase, followed by a less rapid decrease over the course of ten weeks. One department, Guyane, had a limited number of cases from January to June 2020 whilst only in July did the epidemic peak arrive. The overseas location of this department (between Suriname and Brazil) could explain the belated occurrence of the first wave.

Among hospitalised patients, a greater number of deaths were observed at the beginning of the epidemic, which may be explained by initial lack of knowledge about the disease and the most appropriate care modalities ; limited CCU capacities may also have had an influence at the early stages [24], as did testing capacity, which was limited at the onset of the pandemic. Conversely, decreased in-hospital mortality of COVID-19 patients throughout the study period may have been due to increased screening of patients, resulting in an increased number of cases detected before it was too late. As for the proportion of unconfirmed cases, it was higher among patients who spent at least one day in a CCU than among those who did not (28.0 % vs 21.1 %). Due to low availability of PCR tests until May 2020, a sizable proportion of severe symptomatic cases may have been diagnosed based only on clinical and TDM evidence.

While the mortality rate of in-hospital COVID-19 cases was strongly correlated with the incidence rate, case fatality rates in hospitals displayed a ceiling effect approximating 20 to 25 %. This may have been due to effective hospital organisation, and more specifically, to flexibility ; when necessary, CCU capacities were scaled up, and medical evacuations to less affected departments were carried out ; these responses may have limited case fatality rates in hospitals. While the correlation between mortality and incidence was very strong, a few exceptions were highlighted, including Moselle, in which, given the level of incidence, mortality was higher than would have been expected. Excess mortality could have been due to level of vulnerability, particularly with regard to the pre-existing state of health of the population. Other determinants (socioeconomic, population density, overall health status, healthcare access...), which were not evaluated in our study, may partially account for the geographical differences in mortality [25]. They may also reflect the difficulty of providing patients with adequate treatment, at a time when, as in other countries, the French healthcare system was at saturation.

Several previously published nationwide studies have focused on the impact on hospitalisation of the first wave of the COVID-19 epidemic in France. They were rendered possible by the accessibility to research teams of the French healthcare system's two centralized databases : (1) the PMSI database, described in our studies, and (2) the SI-VIC system, which is used by health agencies to follow exceptional health crises in real time [26].

A recent study analysed COVID hospitalisation based on the SNDS database, which includes the PMSI [16]. Although this work has some similarities with ours, its main objective was to estimate risk of COVID-19 hospitalisation and mortality among different populations, but without focusing on the temporal and geographical evolution of the first wave. The number of inpatients was 11 % lower (87,809 vs 98,366), probably due to four factors : the inclusion period was shorter, data extraction was made earlier (September 2020 vs January 2021), patients with missing demographic data were discarded, and they only included patients whose COVID codes were considered as principal, whereas we took also associated diagnosis into account.

We found three analyses drawn from the SI-VIC database on French COVID hospitalisations during the first wave [14,15,27]. The main results were similar to ours. However, direct comparison is difficult due to several key differences. Our study included data of inpatients over a longer period, from January to June 2020, while these studies dealt only with the lockdown period (March 17 – May 10). They did not consider the DROM departments, which experienced a much different epidemic dynamic compared to mainland France, as shown in the present study. Furthermore, due to the real-time functioning of the SI-VIC database [28], there were few retrospective corrections (e.g., adding missing cases having occurred prior to March). By contrast, in the PMSI database each hospital was asked to retrospectively review possible COVID cases and to add the appropriate CIM-10 identification codes. In addition, the definition of probable COVID-19 cases was different. To be registered as a probable case in the PMSI, and thereby counted as a COVID-19 case, a positive chest computed tomography (CT) result had to be corroborated with specific clinical features. In the SI-VIC database, the CT result alone was sufficient. This definition may have overestimated the number of cases measured in the SI-VIC, as the specificity of the chest CT has been shown not to be optimal, with varying predictive values across time [29,30].

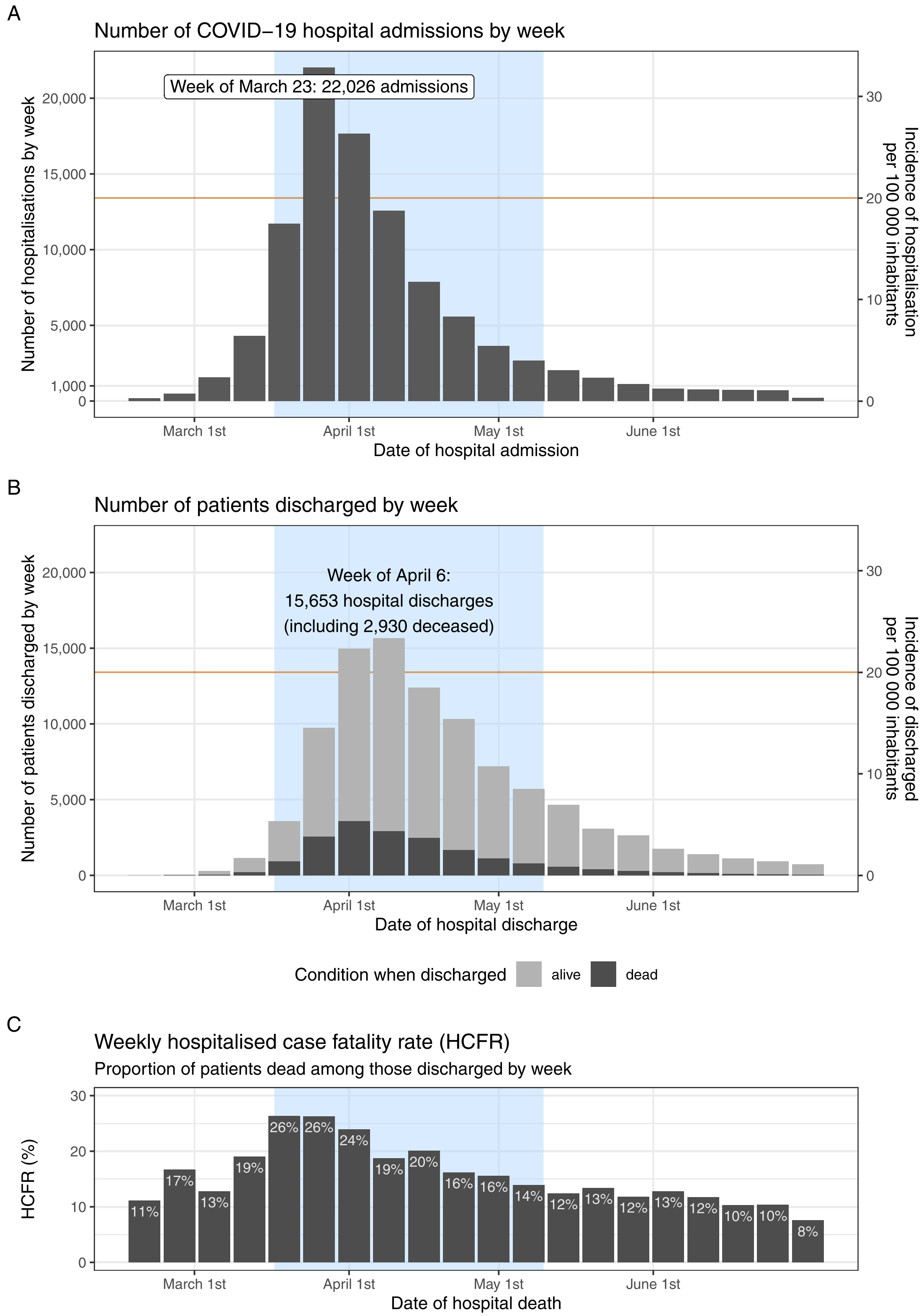

Fig. 2. Evolution by week of (A) the number and the incidence of COVID-19 hospitalisations (B) the number and incidence of COVID-19 patients discharged alive (grey) or deceased (black) and (C) the weekly hospitalised case fatality rates, calculated as the proportion of deaths among all discharged COVID-19 patients. The shaded blue area represents the lockdown period, from March 17 to May 10.

Table 3
Incidence, mortality and fatality for patients hospitalised with COVID-19 in France from January to June 2020, according to region of residency.

Region/Department		Population	Cases	CIR	SIR	Deaths	CMR	SMR	HCFR (%)
France*		67,063,703	98,005	146.14		18,387	27.42		18.76
Île-de-France		12,278,210	35,618	290.09	349.67	6790	55.30	72.80	19.06
75	Paris	2,148,271	6891	320.77	363.61	1337	62.24	73.42	19.40
77	Seine-et-Marne	1,423,607	3391	238.20	290.82	634	44.53	61.10	18.70
78	Yvelines	1,448,625	3084	212.89	239.02	588	40.59	47.60	19.07
91	Essonne	1,319,401	3404	258.00	307.22	612	46.38	60.52	17.98
92	Hauts-de-Seine	1 ,613,762	4520	280.09	331.36	845	52.36	65.85	18.69
93	Seine-Saint-Denis	1,670,149	6250	374.22	520.74	1192	71.37	119.28	19.07
94	Val-de-Marne	1,406,041	4568	324.88	388.22	886	63.01	81.52	19.40
95	Val-d'Oise	1,248,354	3510	281.17	354.75	696	55.75	79.05	19.83
Centre-Val de Loire		2,559,073	2937	114.77	104.33	517	20.20	17.42	17.60
18	Cher	296,404	287	96.83	77.89	84	28.34	21.53	29.27
28	Eure-et-Loir	429,425	682	158.82	151.90	116	27.01	24.75	17.01
36	Indre	217,139	336	154.74	120.01	86	39.61	27.44	25.60
37	Indre-et-Loire	605,380	597	98.62	91.43	81	13.38	11.87	13.57
41	Loir-et-Cher	327,835	410	125.06	103.36	71	21.66	16.56	17.32
45	Loiret	682,890	625	91.52	91.87	79	11.57	11.49	12.64
Bourgogne-Franche-Comté		2,783,039	4706	169.10	151.33	965	34.67	29.66	20.51
21	Côte-d'Or	532,886	1031	193.47	185.84	213	39.97	37.61	20.66
25	Doubs	539,449	1144	212.07	215.31	221	40.97	41.52	19.32
39	Jura	257,849	345	133.80	115.78	59	22.88	18.73	17.10
58	Nièvre	199,596	142	71.14	54.89	27	13.53	8.98	19.01
70	Haute-Saône	233,194	456	195.55	173.48	98	42.03	36.53	21.49
71	Saône-et-Loire	547,824	828	151.14	124.53	175	31.94	24.01	21.14
89	Yonne	332,096	474	142.73	124.13	101	30.41	25.04	21.31
90	Territoire de Belfort	140,145	286	204.07	203.02	71	50.66	50.40	24.83
Normandie		3,303,500	2604	78.83	75.11	453	13.71	12.75	17.40
14	Calvados	691,453	345	49.89	47.40	58	8.39	7.75	16.81
27	Eure	600,687	575	95.72	98.53	113	18.81	19.86	19.65
50	Manche	490,669	236	48.10	40.40	45	9.17	7.08	19.07
61	Orne	276,903	315	113.76	91.20	46	16.61	12.44	14.60
76	Seine-Maritime	1,243,788	1,133	91.09	91.76	191	15.36	15.60	16.86
Hauts-de-France		5,962,662	9364	157.04	172.96	1981	33.22	38.69	21.16
02	Aisne	526,050	1332	253.21	250.50	324	61.59	60.95	24.32
59	Nord	2,588,988	3332	128.70	147.16	628	24.26	29.92	18.85
60	Oise	825,077	1931	234.04	266.03	433	52.48	64.79	22.42
62	Pas-de-Calais	1,452,778	1663	114.47	122.61	338	23.27	26.45	20.32
80	Somme	569,769	1106	194.11	199.86	258	45.28	47.42	23.33
Grand Est		5,511,747	14,640	265.61	262.39	3192	57.91	57.98	21.80
08	Ardennes	265,531	256	96.41	89.65	55	20.71	19.21	21.48
10	Aube	309,907	463	149.40	143.07	101	32.59	30.48	21.81
51	Marne	563,823	1092	193.68	200.88	245	43.45	45.97	22.44
52	Haute-Marne	169,250	314	185.52	153.19	79	46.68	36.93	25.16
54	Meurthe-et-Moselle	730,398	1330	182.09	186.83	262	35.87	37.34	19.70
55	Meuse	181,641	473	260.40	234.92	90	49.55	43.82	19.03
57	Moselle	1,035,866	3155	304.58	304.72	817	78.87	81.06	25.90
67	Bas-Rhin	1,132,607	3209	283.33	295.60	579	51.12	55.76	18.04
68	Haut-Rhin	763,204	3361	440.38	437.02	727	95.26	96.07	21.63
88	Vosges	359,520	987	274.53	232.45	237	65.92	54.38	24.01
Pays de la Loire		3,801,797	2830	74.44	72.22	459	12.07	11.40	16.22
44	Loire-Atlantique	1,437,137	875	60.88	66.20	157	10.92	12.38	17.94
49	Maine-et-Loire	815,881	831	101.85	96.22	138	16.91	15.02	16.61
53	Mayenne	305,365	204	66.81	59.55	40	13.10	10.78	19.61
72	Sarthe	560,227	507	90.50	82.74	78	13.92	11.94	15.38
85	Vendée	683,187	413	60.45	54.42	46	6.73	5.77	11.14
Bretagne		3,340,379	1501	44.94	42.15	258	7.72	7.01	17.19
22	Côtes-d'Armor	596,186	311	52.16	44.22	48	8.05	6.20	15.43
29	Finistère	906,554	295	32.54	30.25	52	5.74	5.08	17.63
35	Ille-et-Vilaine	1,082,073	395	36.50	38.90	71	6.56	7.18	17.97
56	Morbihan	755,566	500	66.18	57.94	87	11.51	9.71	17.40
Nouvelle-Aquitaine		5,999,982	2893	48.22	42.63	481	8.02	6.61	16.63
16	Charente	348,180	116	33.32	27.09	18	5.17	4.01	15.52
17	Charente-Maritime	647,080	242	37.40	30.02	55	8.50	6.28	22.73
19	Corrèze	240,336	201	83.63	67.34	37	15.40	11.21	18.41
23	Creuse	116,270	56	48.16	38.31	8	6.88	4.10	14.29
24	Dordogne	408,393	167	40.89	32.29	25	6.12	4.16	14.97
33	Gironde	1,633,440	1168	71.51	74.25	186	11.39	12.04	15.92
40	Landes	411,979	130	31.56	27.50	18	4.37	3.76	13.85
47	Lot-et-Garonne	330,336	115	34.81	28.69	16	4.84	3.54	13.91
64	Pyrénées-Atlantiques	683,169	234	34.25	29.53	31	4.54	3.66	13.25
79	Deux-Sèvres	372,627	104	27.91	24.54	21	5.64	4.55	20.19
86	Vienne	437,398	187	42.75	39.37	35	8.00	6.82	18.72
87	Haute-Vienne	370,774	173	46.66	39.89	31	8.36	6.45	17.92

(*continued*)

Table 3 (*Continued*)

Region/Department		Population	Cases	CIR	SIR	Deaths	CMR	SMR	HCFR (%)
Occitanie		5,924,858	3556	60.02	55.45	540	9.11	7.96	15.19
09	Ariège	152,398	41	26.90	22.82	3	1.97	1.51	7.32
11	Aude	372,705	358	96.05	77.91	72	19.32	14.36	20.11
12	Aveyron	278,360	178	63.95	50.66	26	9.34	6.43	14.61
30	Gard	748,468	459	61.33	55.75	84	11.22	9.90	18.30
31	Haute-Garonne	1,400,935	658	46.97	52.47	79	5.64	6.73	12.01
32	Gers	190,040	212	111.56	85.79	34	17.89	11.65	16.04
34	Hérault	1,176,145	753	64.02	62.59	124	10.54	9.99	16.47
46	Lot	173,166	72	41.58	32.27	12	6.93	4.42	16.67
48	Lozère	76,286	29	38.01	31.20	3	3.93	2.95	10.34
65	Hautes-Pyrénées	226,839	161	70.98	57.42	24	10.58	7.88	14.91
66	Pyrénées-Orientales	479,000	368	76.83	69.97	40	8.35	6.68	10.87
81	Tarn	387,898	199	51.30	41.79	30	7.73	5.68	15.08
82	Tarn-et-Garonne	262,618	68	25.89	24.37	9	3.43	3.00	13.24
Auvergne-Rhône-Alpes		8,032,377	10,353	128.89	129.14	1743	21.70	21.69	16.84
01	Ain	656,955	898	136.69	148.40	156	23.75	26.92	17.37
03	Allier	331,315	250	75.46	61.40	47	14.19	10.18	18.80
07	Ardèche	326,875	572	174.99	146.04	117	35.79	28.83	20.45
15	Cantal	142,811	57	39.91	30.42	9	6.30	4.29	15.79
26	Drôme	520,560	614	117.95	110.26	126	24.20	22.17	20.52
38	Isère	1,264,979	1013	80.08	85.43	175	13.83	15.26	17.28
42	Loire	764,737	1353	176.92	163.99	240	31.38	28.09	17.74
43	Haute-Loire	226,901	125	55.09	46.89	18	7.93	6.58	14.40
63	Puy-de-Dôme	660,240	359	54.37	51.99	46	6.97	6.51	12.81
69	Rhône	1,876,051	3571	190.35	214.31	581	30.97	35.10	16.27
73	Savoie	432,548	436	100.80	96.29	65	15.03	14.09	14.91
74	Haute-Savoie	828,405	1105	133.39	150.34	163	19.68	24.01	14.75
Provence-Alpes-Côte d'Azur		5,055,651	5426	107.33	98.35	852	16.85	14.53	15.70
04	Alpes-de-Haute-Provence	165,197	108	65.38	54.17	20	12.11	9.36	18.52
05	Hautes-Alpes	141,756	130	91.71	81.18	11	7.76	6.13	8.46
06	Alpes-Maritimes	1,079,396	886	82.08	70.55	154	14.27	10.94	17.38
13	Bouches-du-Rhône	2,034,469	3041	149.47	147.84	474	23.30	22.70	15.59
83	Var	1,073,836	917	85.39	73.19	136	12.66	10.05	14.83
84	Vaucluse	560,997	344	61.32	57.93	57	10.16	9.28	16.57
Corse		344,679	206	59.77	52.75	38	11.02	9.21	18.45
2A	Corse-du-Sud	162,421	109	67.11	57.34	23	14.16	11.46	21.10
2B	Haute-Corse	182,258	97	53.22	48.43	15	8.23	7.08	15.46
DROM		2,165,749	1371	63.30	74.68	118	5.45	7.96	8.61
971	Guadeloupe	376,879	214	56.78	55.22	33	8.76	8.60	15.42
972	Martinique	358,749	162	45.16	40.77	22	6.13	5.48	13.58
973	Guyane	290,691	521	179.23	310.19	35	12.04	35.06	6.72
974	La Réunion	859,959	206	23.95	27.34	7	0.81	1.50	3.40
976	Mayotte	279,471	268	95.90	351.82	21	7.51	50.82	7.84

* Patients without a valid zip code (*n* = 361, 0.4 %) were excluded from this analysis. CIR = crude incidence ratio, SIR = standardized (by age and sex) incidence ratio, CMR = crude in-hospital mortality ratio, SMR = standardized (by age and sex) mortality ratio, HCFR = hospitalized case fatality rate, DROM = Départements et régions d'outre-mer.

Other works have also used data drawn from the PMSI to assess the impact of the first wave in France. However, they were focused on highly specific topics, such as the evolution of hospitalisations for myocardial infarctions, stroke and self-harm ; hospitalised case fatality rate in ICUs ; and comparison to the influenza epidemic [31–36].

In a German study based on nationwide administrative healthcare data, the number of hospitalisations for COVID-19 was smaller, with an incidence rate of 12/100,000 inhabitants, ten times less than in France[12]. As in our study, care sequences were analysed. However, the inclusion criteria were more restricted : A shorter study period (February 28 to April 19), patients over the age of 18, covered by only one of the healthcare funds in Germany (representing approximately 32 % of the German population) and only patients with positive tests, whilst our study also included probable cases (representing 25.8 % of the patients included). On April 19, as the number of cases in the general population was lower in Germany (174/100,000 inhabitants) than in France (225/100,000), it is not surprising that in-hospital incidence in Germany was likewise lower than in France [37]. Despite these differences, median age of hospitalised patients (72 years in Germany, compared to 71 in France) and mean stay duration were similar (10 days in Germany, 9 days in France). However, the case fatality rate was higher in Germany (22 %) than in France (19 %), notwithstanding a higher number of ICU beds in Germany.

In England, a nationwide analysis was performed using the Hospital Episode Statistics (HES) dataset [11]. The number of included patients (91,541 vs 98,366), sex ratio (1.24 vs 1.16) and age distribution were similar to those in our study. However, the number of in-hospital deaths (28,200 vs 18,447) was significantly higher, affecting all age strata. It is worth noting that this paper included each patient's first hospitalisation, and did not consider care sequences.

Outside of Europe, in Brazil, a nationwide study included 254,288 inpatients hospitalised between February and August 2020 [13]. This geographical and temporal analysis was based on a comprehensive database, and focused on cases confirmed by RT-PCR. The results were quite different from those recorded in France. Patients were younger (median 61y vs 71y), the incidence of hospitalised confirmed cases was higher (120 vs 109/100,000 inhabitants), the proportion of hospitalised patients admitted to a CCU was higher (39 % vs 28 %) and the hospitalised case fatality rate was twice as high (38 % vs 20 %).

Some limitations of our study must be addressed. First, the PMSI database has been designed not for epidemiology purposes, but for funding allocation. As a result, the quality of the medical information may vary, according to the relation between coding and funding. However, we remain confident in COVID-19 coding, given that specific, emergency ICD-10 codes for COVID-19 were specially created by

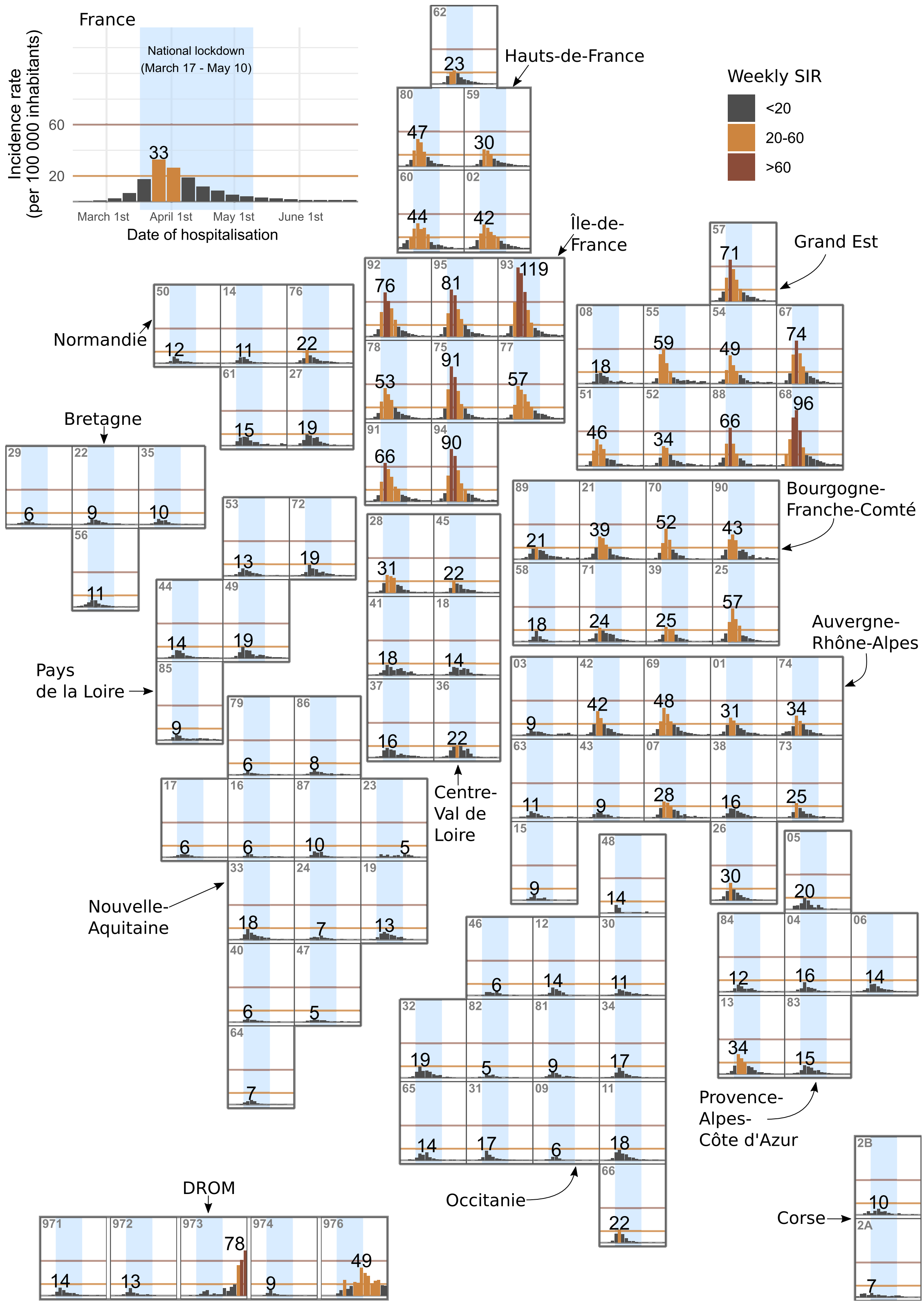

Fig. 3. Map of France with weekly standardised incidence of COVID-19 hospitalisation according to the patient's department of residence. Each small panel represents a French department, and is positioned approximately so as to elucidate the spatial connections between the different departments. The number at the top left corner of each panel is the department number. The shaded blue area represents the lockdown period, from March 17 to May 10. We considered two thresholds to define the beginning and the end of the wave : 20 (orange line) and 60 (red line)/100 000 inhabitants hospitalised per week. The top left panel represents nationwide incidence by week.

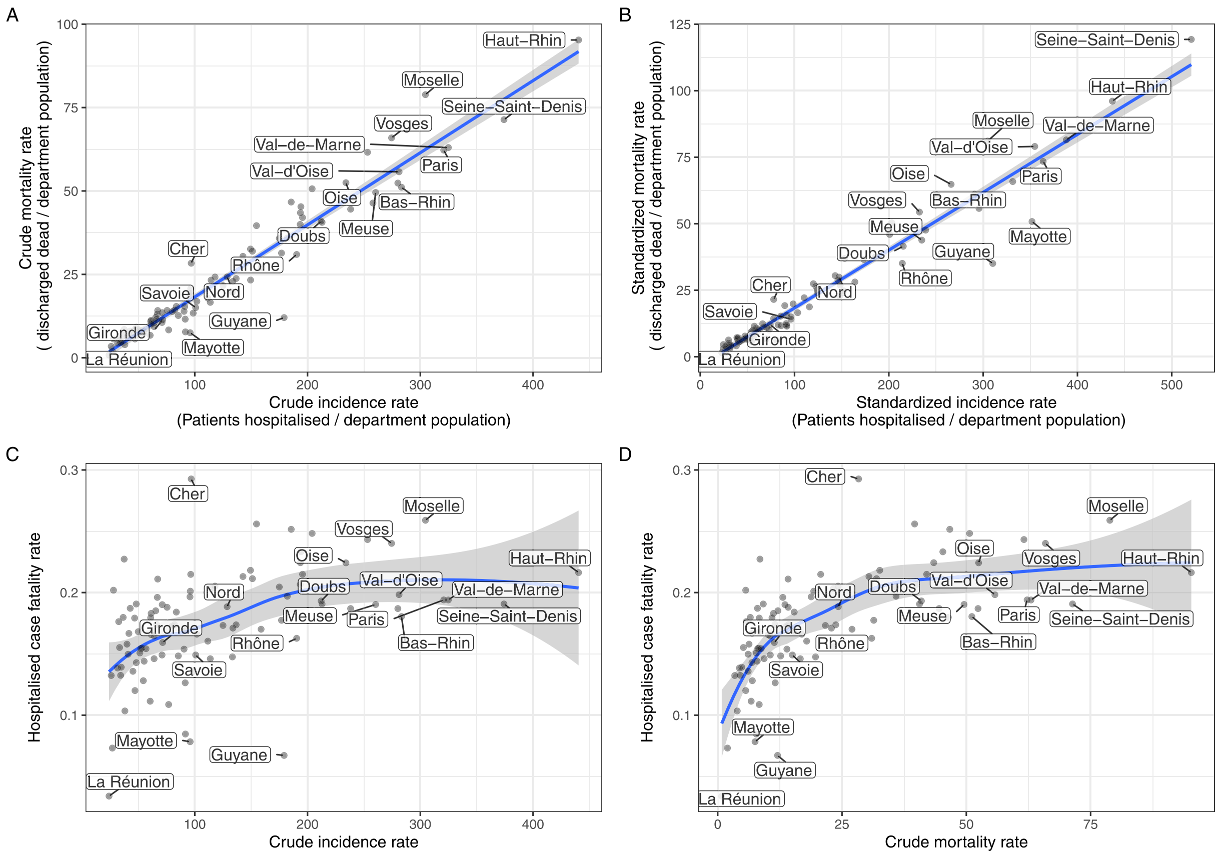

Fig. 4. Correlations between (A) CMR and CIR, (B) SMR and SIR, (C) HCFR and CIR, (D) HCFR and CMR. Each department is represented by a black dot and labelled. For panels (A) and (B), where CIR and SIR are considered, linear regression is represented by a turquoise line, with prediction limits for the individual predicted values shown as blue lines. For panels (C) and (D), where HCFR is considered, penalised B-spline curve is represented by a turquoise line, with prediction limits for the individual predicted values shown as blue lines.

CIR = crude incidence ratio, SIR = standardised (by age and sex) incidence ratio, CMR = crude in-hospital mortality ratio, SMR = standardised (by age and sex) mortality ratio, HCFR = hospitalised case fatality rate.

the WHO [38]. The ATIH circulated the coding rules to all medical information departments, which are responsible in all hospitals for data quality and completeness.

Second, specification of the municipality of residence to locate incident cases of COVID-19 may be imprecise ; some patients hospitalised during the epidemic may have been living outside of their official department of residence, or may have been hospitalised outside of the latter. Moreover, patients residing in a foreign country could not be assigned to a French department, even though they were admitted to a French hospital. That said, they comprise only a limited number of cases (n = 361, 0.4 %), which could barely change the results, and one hospital in the island of Corsica represented 103 (28.5 %) of these cases, which may be due to erroneous data transmission or to a high number of foreigners in this island, which is close to Italy. Despite this exception, municipality of residence remains more appropriate than hospital location as a means of calculating incidence rates, because the reference population at a departmental level is clearly defined, whereas the catchment population of a hospital is not.

Third, this study focuses on hospitalisations in short-stay hospitals, which means that mortality in post-acute and rehabilitation facilities, in retirement homes, or at home was not assessed.

Our study nonetheless has several strengths.

First, it is based on comprehensive national data from all French public and private hospitals. We considered care sequences as opposed to isolated hospital stays. Due to transfers of patients between different hospitals, or between different sites of the same hospital in the case of larger institutions, a simple count of hospital stays would have resulted in overestimation of cases by approximately 19 %, and underestimation of mortality rates, as well. Because the raw data include the date but not the exact time of discharge or hospitalisation, two hospital stays were considered to be contiguous if they were separated by one day or less. This way, it was possible to capture cases of transfers whereby the patient was discharged one day from a given hospital and admitted the next day to a second hospital.

Second, although analysis at a regional and departmental level is difficult to interpret, it more accurately characterizes the spatial and temporal dynamics of the epidemic.

Third, as age and sex were identified as the main risk factors for COVID-19 disease severity and death, we presented both the crude and standardised rates, the objective being to facilitate comparison despite demographic differences between different departments or regions [39].

Given the quality of the PMSI data, which covers all types of hospitals throughout the country, we were able to describe the dynamics of the first wave of COVID-19 hospitalisations in France. Our study highlights major geographical and temporal variability, which would have remained undetected in nationwide global analyses. When data are available, extension of this study by analysis of the second and third waves will contribute to understanding of the subsequent spread of the epidemic.

4.1. Data sharing

The PMSI database was made available by the hospital information technology agency (ATI. The National Commission for Information Technologies and Liberties (Commission Nationale de l'Informatique et des Libertés, CNIL) approved use of this data by our department. While we are not permitted to share these data, PMSI data from ATIH are available to researchers who meet the criteria for access, upon request to the CNIL.

Authors' contributions

All of the authors took part in the design and drafting of the protocol. XL, AB and EO extracted the relevant data from the nationwide PMSI data base. JM, ST, PT and FB carried out data analysis. FS, VG et ML provided advice on the analyses. All of the authors were involved in interpretation of the data and validation of the manuscript.

Ties of interest

The authors have no ties of interest to declare.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi : 10.1016/j.respe.2022.08.008.

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