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# ORIGINAL ARTICLE

# Impact of the COVID-19 pandemic and a national lockdown on hospitalizations for stroke and related 30-day mortality in France: A nationwide observational study

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# Abstract

**Background and purpose:** The aim of this nationwide study was to assess the impact of the COVID-19 pandemic on stroke hospitalization rates, patient characteristics and 30-day case fatality rates.

**Methods:** All hospitalizations for stroke from January to June of each year from 2017 to 2020 were selected using International Classification of Diseases, 10th revision, codes 160 to 164 in the national hospital discharge database. Patient characteristics and management were described according to three time periods: pre-lockdown, lockdown, and post-lockdown. Weekly incidence rate ratios (IRRs) were computed to compare time trends in the rates of patients hospitalized for stroke as well as in-hospital and 30-day case fatality rates between the years 2017–2019 and 2020.

**Results:** In 2020, between weeks 1 and 24, 55,308 patients were hospitalized for stroke in France. IRRs decreased by up to 30% for all age groups, sex, and stroke types during the lockdown compared to the period 2017–2019. Patients hospitalized during the second and third weeks of the lockdown had higher in-hospital case fatality rates compared to 2017–2019. In-hospital case fatality rates increased by almost 60% in patients aged under 65 years. Out-of-hospital 30-day case fatality rates increased between weeks 11 and 15 among patients who returned home after their hospitalization. Important changes in care management were found, including fewer stroke patients admitted to resuscitation units, more admitted to stroke care units, and a shorter mean length of hospitalization.

**Conclusions:** During the first weeks of the lockdown, rates of patients hospitalized for stroke fell by 30% and there were substantial increases of both in-hospital and out-of-hospital 30-day case fatality rates.

## KEYWORDS

case fatality, COVID-19 pandemic, hospitalisations, lockdown, stroke

# INTRODUCTION

The COVID-19 pandemic greatly overwhelmed healthcare facilities around the world, including France. French hospitals were reorganized at a local level to optimize the management of patients infected by SARS-CoV-2 [1]. France was one of the main European countries where the SARS-CoV-2 virus initially spread, leading to a marked excess mortality in March and April 2020 [1,2]. A national lockdown was implemented from March 17 to May 11, 2020 (weeks 12 to 19), targeting a population of 66 million inhabitants. Lower rates of patients hospitalized for stroke during the COVID-19 pandemic have been described in local areas of France as well as in other countries [1,3-14]. However, the magnitude of this decrease differed among countries, with only a limited decline in stroke admissions in Germany [15] compared with a 39% reduction in the United States [3,4] and a 60% reduction in the Veneto region of Italy [12,16]. By contrast, a study conducted in Brescia, Italy, reported similar rates of stroke admissions and even a higher rate of ischemic stroke admissions during the months of March and April 2020 compared to previous years [17]. The authors hypothesized that the SARS-CoV-2 infection might be associated with a higher risk of ischemic events [17]. Few studies, however, have explored the impact of the COVID-19 pandemic on stroke hospitalization at a whole-country level in Europe or North America (Table S1). As stroke is an emergency condition that requires quick and specific care and represents one of the main causes of disability and death in many countries [18], the impact of the pandemic on this acute disease is a major public health concern.

The first objective of this study was to evaluate the collateral effects of the COVID-19 pandemic on stroke epidemiology, including hospitalizations and outcomes. The secondary objective was to evaluate the impact of the pandemic on stroke care organization and stroke management. Thus, this nationwide study compares the rates of patients hospitalized for stroke in France in the weeks before, during, and after the lockdown in 2020 with the corresponding weeks in the years 2017 to 2019. The study describes changes in patient characteristics and care management during lockdown and analyses the time trends of in-hospital and 30-day out-of-hospital case fatality rates.

# METHODS

#### Data source

For this observational and cross-sectional study, we used data from the national hospital discharge database (*Programme de médicalisation des systèmes d'information* [PMSI]), which comprehensively collects all stays in both private and public hospitals across France, covering a population of approximately 66 million inhabitants [19]. Data collected in the PMSI are linked to the French national health database (*Système National des Données de Santé* [SNDS]), which comprehensively gathers individual outpatient data such as healthcare prescriptions and procedures reimbursed by the French national health insurance system for all individuals living in France and covered by universal medical coverage. The SNDS also records the long-term disease status of patients, which entitles them to 100% reimbursement for all healthcare expenditures related to that particular disease [19].

## Study population

All patients hospitalized for stroke between weeks 1 and 24 from 2017 to 2020 were selected. After week 24, an exhaustive record of hospitalizations could not be ensured. Stroke was defined by codes

I60 to I64 of the International Classification of Diseases, 10th revision (ICD-10), which were registered as the main diagnosis of the entire hospital stay or one of the medical units where the patient stayed [20,21]. For each patient, we selected the first hospitalization for stroke between weeks 1 and 24 of each year.

# **Data collection**

The following patient characteristics were recorded for the hospital stay: age, sex, type of stroke (ischemic [ICD-10 codes I63 or I64] and haemorrhagic [I60 to I62]), obesity (E66), and stroke signs (speech impairment [R47] or paralysis [G81]). We also recorded an infection with SARS-CoV-2 identified with a positive PCR, antigenic or serologic test, or through computed tomography. The weekly number of patients hospitalized with a SARS-CoV-2 infection in France is presented in Figure S1. Using medical data for the 5 years preceding the hospitalization for stroke, cardiovascular and non-cardiovascular comorbidities were recorded. We then calculated a Charlson index score of comorbidities [22], which included congestive heart failure, dementia, chronic pulmonary disease, rheumatologic disease, mild liver disease, diabetes with chronic complications, hemiplegia or paraplegia, renal disease, any malignancy (including leukemia and lymphoma), moderate or severe liver disease, metastatic solid tumor, and AIDS/HIV. Three groups were defined according to the number of comorbidities: scores from 0 to 1, from 2 to 3, and 4 or more. The underlined hypothesis of such analysis was the modification of stroke care access during the COVID-19 pandemic according to the level of comorbidities. Lastly, treatments given for cardiovascular conditions or their risk factors were considered if the patients had at least three drug deliveries in the year preceding the hospitalization for stroke.

Several aspects of acute care management were considered. We focused on patients' admission to a resuscitation unit or a stroke care unit. In France, intensive care units are intended to treat visceral failures related to a single organ specialty. In the case of multi-visceral failure, patients must be transferred to a resuscitation unit which is equipped with invasive ventilation. A severity score was completed by the physicians for patients admitted to a resuscitation unit. This score corresponds to the simplified acute physiology score (SAPSII) [23]. Regarding acute stroke treatment, data on mechanical thrombectomy (MT) were available exhaustively from 2017 onwards, whereas intravenous thrombolysis (IVT) was not. The length of hospital stay was calculated based on the number of nights spent in hospital. At discharge, we collected information about whether the patient returned home, was transferred to another medical unit (i.e., a short-stay medical unit, follow-up and rehabilitation care) or elsewhere (i.e., long-stay facilities, nursing home, or hospitalized at home), or died in hospital.

## **Statistical analyses**

Patient characteristics and acute care management were compared between the period 2017–2019 and 2020 using the chi-squared

Wet         2017-2019         200 <i>p_{sourcestriction</i> 2017-2019         200 <i>p_{sourcestriction</i> N         34.75         27.147         27.147         27.364         35.769         11.356         35.769         11.356           Metententententententententententententen		Weeks 1 to 1	Weeks 1 to 11 (pre-lockdown in	in 2020)	Weeks 12 to 1	Weeks 12 to 19 (lockdown in 2020)	020)	Weeks 20 to 2	Weeks 20 to 24 (post-lockdown in 2020)	vn in 2020)
94,775         27,167         57,990         16,615         35,769         11,52           46.5         48.0         0.082         48.2         47.5         9.076         48.2         7.3           75.4         73.5 (15.4)         73.3 (15.4)         73.4 (15.4)         73.4 (15.4)         73.2 (110.1)         73.3 (110.1)           76.4         75.9         0.082         73.4 (15.4)         73.4 (15.4)         73.2 (110.1)         73.5 (110.1)           76.4         75.9         0.083         74.4         0.003         71.8         73.3 (110.1)           76.4         75.9         0.083         73.4         1.0         0.311         1.0         73.5           8         1.0         0.59         1.1         0.569         1.1         1.0         23.5           8         1.0         0.59         23.1         1.0         0.311         1.0         1.0           8         1.0         0.59         31.1         1.0         0.311         1.0         1.0           8         1.0         1.0         0.001         23.1         23.1         23.1         23.1           9         1.1         1.0         1.0         1.0         1.0 </th <th>Year</th> <th>2017-2019</th> <th>2020</th> <th><b>p</b> 2020 vs 2017-2019</th> <th>2017-2019</th> <th>2020</th> <th><b>p</b>2020 vs 2017-2019</th> <th>2017-2019</th> <th>2020</th> <th><b>p</b>2020 vs 2017-2019</th>	Year	2017-2019	2020	<b>p</b> 2020 vs 2017-2019	2017-2019	2020	<b>p</b> 2020 vs 2017-2019	2017-2019	2020	<b>p</b> 2020 vs 2017-2019
445         480         002         482         775         0025         482         775         771 <th>z</th> <th>84,775</th> <th>27,167</th> <th></th> <th>57,998</th> <th>16,615</th> <th></th> <th>35,769</th> <th>11,526</th> <th></th>	z	84,775	27,167		57,998	16,615		35,769	11,526	
445         48.0         0.082         48.2         47.5         0.076         48.2         7.3           735 (15.4)         735 (15.3)         0.408         734 (15.4)         734 (15.5)         0.448         73.2 (15.6)         731 (10.1)           73.4         7.4         7.5         0.088         744 (15.5)         0.448         73.2 (15.6)         731 (10.1)           7.4         7.4         0.08         7.4 (15.2)         0.049         7.3         10.1           8         1.0         1.1         0.569         1.1         1.0         1.0         1.0           7.8         2.82         0.003         1.1         1.0         0.311         1.0         1.0           7.8         2.82         2.83         0.0001         37.8         2.000         39.1         2.0           7.15         50.7         60.001         37.8         4.0         4.0         2.0         2.0           8.10         6.07         6.01         6.01         6.0         6.01         4.1         4.7           8.11         6.07         6.01         6.01         6.01         6.01         6.0         6.0           8.12         6.02         6.001<	Patient characteristics									
735 (154)         735 (153)         0.08         734 (154)         735 (153)         0.018         734 (152)         0.018         731 (153)         731 (101)           74         769         0.083         733         734         734         734         734           74         75         0.083         743         734         733         735           8         10         11         0.569         11         0.539         231         735           8         10         11         0.569         14         233         231         233           8         10         10         0.03         240         2000         231         310         233           8         10         405         405         311         10         310         310           9         203         318         223         240         311         310         323           9         30         318         27         20001         370         310         323           9         203         310         27         231         310         310           9         203         201         201         211 <t< td=""><td>Women, %</td><td>48.5</td><td>48.0</td><td>0.082</td><td>48.2</td><td>47.5</td><td>0.076</td><td>48.2</td><td>47.3</td><td>0.116</td></t<>	Women, %	48.5	48.0	0.082	48.2	47.5	0.076	48.2	47.3	0.116
764         769         008         7.3         7.7         003         7.7         7.7           24.7         24.2         0.083         24.4         23.3         0.03         23.1         23.5           8         1.0         1.1         0.569         1.1         1.0         550         1.1         23.5           8.8         1.0         1.1         0.569         1.1         1.0         23.1         23.5           8.8         28.2         2.0         3.03         2.0         3.10         2.10         2.3           3.03         3.18         -0.001         3.7         3.2         0.001         3.1         3.10           47.6         50.7         -0.001         3.7         4.0         3.10         2.1         4.0           47.6         50.7         -0.001         3.7         -0.001         3.1         4.0           47.6         50.7         -0.001         4.7         5.7         -0.001         4.1         4.7           50.7         50.0         6.0         4.0         0.001         4.1         4.7         4.7           50.7         50.0         6.0         4.7         5.7	Age, mean (SD)	73.5 (15.4)	73.5 (15.3)	0.408	73.4 (15.4)	73.4 (15.2)	0.448	73.2 (15.6)	73.1 (10.1)	0.198
3/1         24,2         0.03         24,4         23,3         0.03         23,1         23,5           8         1.0         1.1         0.56%         1.1         1.0         6.03         2.1         1.0           1         0.03         1.1         0.56%         1.1         1.0         5.5%         1.0         1.0           1         0.03         1.0         2.33         28.0         2.00         2.31         2.31         2.31           2.88         3.08         3.18         2.00         2.00         2.1         2.01         2.31         2.31           3.82         40.6          40.6         2.31         2.21         2.31         2.31         2.31           47.6         50.7          40001         3.78         4.20         2.31         4.0           6.02         6.03         4.10         2.21         2.1         2.1         2.1         2.1           6.03         1.10         1.2         2.1         2.1         2.1         2.1         2.1           6.02         6.03         2.1         2.1         2.1         2.1         2.1         2.1           6.02 <td>Ischemic stroke, %</td> <td>76.4</td> <td>76.9</td> <td>0.088</td> <td>76.3</td> <td>77.7</td> <td>0.005</td> <td>77.8</td> <td>77.5</td> <td>0.484</td>	Ischemic stroke, %	76.4	76.9	0.088	76.3	77.7	0.005	77.8	77.5	0.484
%         10         11         0.569         11         10         10         10         10           288         28.2         0019         2.33         28.0         29.1         31.0         31.0           288         28.2         20.3         20.3         20.3         20.3         31.0         31.0         31.0           308         31.8         40.0         37.8         40.2         31.1         31.0         29.3         33.2           308         31.8         40.0         37.8         40.2         31.1         31.0         29.3         32.2           301         6.0001         37.8         42.0         60.001         37.1         40.0         29.1         40.0           41.6         50.7         60.001         64.7         60.001         63.1         40.0           21.6         0.3         -         21.1         -         21.0         50.7         50.7           -         0.3         64.7         60.001         60.0         60.0         60.3         61.5           -         0.3         -         21.1         -         -         0.7         0.7           -         0.3	Hemorrhagic stroke, %	24.7	24.2	0.083	24.4	23.3	0.003	23.1	23.5	0.401
0019         0016         311         310           28.8         28.2         29.3         28.0         29.1         31.0           40.4         40.0         31.8         31.1         31.0         32.2           30.8         31.8         31.8         31.1         31.0         32.2           30.8         31.8         31.8         31.1         31.0         32.2           30.8         31.8         30.2         31.1         31.0         23.9           31.7         50.7         6.0001         37.8         30.0         39.1         40.0           47.6         50.7         6.0001         37.8         42.0         60.001         39.1         40.0           41.6         5.0.7         6.0001         37.9         5.1         5.0         0.1         41.0           21.6         20.1         6.00         4.1         5.1         5.0         6.1         6.1           21.6         20.1         20.1         20.1         20.0         6.1         6.1           21.6         20.1         20.1         21.1         2.1         2.1         0.1           21.6         20.1         20.1         <	lschemic and hemorrhagic stroke, %	1.0	1.1	0.569	1.1	1.0	0.311	1.0	1.0	0.520
28.8         28.2         28.3         28.0         29.1         31.0           40.4         40.0         40.5         40.5         31.1         31.0         39.9         39.2           30.8         31.8         30.2         31.1         31.0         39.9         39.2           38.2         40.6         <0001	Charlson index score, %			0.019			0.006			0.001
404         400         405         409         399         399         392           308         31.8         30.2         31.1         31.0         299         393           38.2         40.6         <0.0001	0-1	28.8	28.2		29.3	28.0		29.1	31.0	
30.8         31.8         30.2         31.1         31.0         299           38.2         40.6         <0.0001	2-3	40.4	40.0		40.5	40.9		39.9	39.2	
38.2         40.6         <0001         378         42.0         <0001         38.1         40.0           47.6         50.7         <0001	4+	30.8	31.8		30.2	31.1		31.0	29.9	
47.6         50.7         <00001         47.7         52.7         <00001         68.7         60.3         64.5           60.2         63.0         <00001	Speech impairment, %	38.2	40.6	<0.0001	37.8	42.0	<0.0001	38.1	40.0	0.001
60.2         63.0         -0001         60.0         64.7         -0001         60.3         615           -         0.2         -         -         -         -         -         0.7         61.5           -         0.2         -         -         2.1         -         -         0.7           -         0.3         -         -         3.0         61.7         -         0.7           -         0.3         -         -         3.0         0.7         -         0.7           status in the 5 years preceding the stroke <sup>4</sup> -         -         3.0         0.79         1.7         1.7           21.6         20.1         -         0.0001         19.9         18.1         -         0.7         1.68           17.9         17.9         0.79         0.39         1.77         0.74         18.0         17.6           13.0         12.8         0.399         1.77         0.724         18.0         17.6           13.0         12.8         0.250         23.9         0.79         13.7         17.6           25.6         25.0         0.087         25.0         23.9         0.76	Paralysis, %	47.6	50.7	<0.0001	47.7	52.7	<0.0001	48.1	48.7	0.223
- $2.1$ - $ 0.7$ - $3.0$ -       - $0.7$ - $3.0$ -       - $0.7$ 01 $19.9$ $18.1$ $-0.0001$ $20.0$ $16.8$ 01 $19.9$ $18.1$ $-0.0001$ $20.0$ $16.8$ 01 $19.9$ $18.1$ $-0.0001$ $20.0$ $16.8$ 02 $4.0$ $3.9$ $0.548$ $3.9$ $3.7$ 03 $17.7$ $0.724$ $18.0$ $17.6$ 12.1 $12.1$ $0.724$ $18.0$ $17.6$ 12.2.5 $0.339$ $0.005$ $24.6$ $24.8$ 8.1 $8.0$ $0.651$ $8.0$ $7.9$ 14 $4.3$ $4.6$ $0.112$ $4.3$ $4.4$ $66.1$ $64.8$ $0.002$ $66.2$ $64.3$ $65.2$ $62.9$ $0.627$ $18.2$ $62.4$ $18.1$ $17.9$ $0.627$ $18.2$ $62.4$	Speech impairment or paralysis, %	60.2	63.0	<0.0001	60.0	64.7	<0.0001	60.3	61.5	0.028
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	SARS-CoV-2 identified with a biologic test, %	I	0.2	1	I	2.1	I	I	0.7	I
01     19.9     18.1     <0.0001	SARS-CoV-2 identified with a biologic test or computed tomography, %	I	0.3	I	I	3.0	I	I	0.7	I
20.1 $< 0.0001$ $19.9$ $18.1$ $< 0.0001$ $16.8$ $3.9$ $0.090$ $4.0$ $3.9$ $0.548$ $3.9$ $3.7$ $17.9$ $0.093$ $17.8$ $17.7$ $0.724$ $18.0$ $17.6$ $12.8$ $0.285$ $12.8$ $12.5$ $0.310$ $12.8$ $12.1$ $25.0$ $0.087$ $25.0$ $23.9$ $0.005$ $24.6$ $24.8$ $8.0$ $0.969$ $8.1$ $8.0$ $0.651$ $8.0$ $7.9$ $4.7$ $0.001$ $4.3$ $4.6$ $0.112$ $4.3$ $4.4$ $6.9$ $0.985$ $66.1$ $64.8$ $0.002$ $66.2$ $64.3$ $6.8$ $0.007$ $63.2$ $62.9$ $64.3$ $64.3$ $64.3$ $18.6$ $0.007$ $63.2$ $62.9$ $0.435$ $63.2$ $62.4$ $18.6$ $0.07$ $63.2$ $62.9$ $62.9$ $64.3$ $18.6$ $0.007$ $63.2$ $62.9$ $62.9$ $62.4$ $18.6$ $0.07$ $63.2$ $62.9$ $0.435$ $62.4$	Hospitalization or long-term disease :	status in the 5 ye	ars preceding the	e stroke <sup>a</sup>						
39         0.090         4.0         3.9         0.548         3.9         3.7           17.9         0.939         17.8         17.7         0.724         18.0         17.6           12.8         0.939         12.8         12.5         0.310         12.8         12.1           25.0         0.865         12.8         12.5         0.310         12.8         12.1           25.0         0.969         8.1         8.0         0.0651         8.0         79           8.0         0.969         8.1         8.0         0.651         8.0         79           4.7         0.001         4.3         4.6         0.112         4.3         4.4           65.9         0.985         66.1         64.8         0.002         64.3         64.3           65.8         0.9985         65.1         64.8         0.002         64.3         64.3           65.8         0.9985         65.1         64.8         0.002         64.3         64.3           18.6         0.9985         65.1         64.3         0.002         64.3         64.3           18.6         0.291         18.1         17.9         0.435         63.2	Stroke	21.6	20.1	<0.0001	19.9	18.1	<0.0001	20.0	16.8	<0.0001
17.9       0.939       17.8       17.7       0.724       18.0       17.6         12.8       0.285       12.8       12.5       0.310       12.8       12.1         25.0       0.087       25.0       23.9       0.005       24.6       24.8         8,0       0.969       8.1       8.0       0.651       8.0       79         4.7       0.001       4.3       4.6       0.112       4.3       4.4         66.9       0.985       66.1       64.8       0.002       66.2       64.3         65.8       0.007       63.2       62.9       0.435       65.2       64.3         18.6       0.007       63.2       62.9       0.435       63.2       62.4         18.6       0.291       18.1       17.9       0.627       18.2       18.2	Transient ischemic attack	4.1	3.9	0.090	4.0	3.9	0.548	3.9	3.7	0.387
12.8       0.285       12.8       12.5       0.310       12.8       12.1         25.0       0.087       25.0       23.9 <b>0.005</b> 24.6       24.8         8.0       0.969       8.1       8.0       0.651       8.0       7.9         4.7 <b>0.001</b> 4.3       4.6       0.112       4.3       4.4         66.9       0.985       66.1       64.8 <b>0.002</b> 65.2       64.3         65.8       0.097       63.2       62.9       0.435       65.2       64.3         18.6       0.007       63.2       62.9       0.435       63.2       62.4         18.6       0.291       18.1       17.9       0.627       18.2       18.2	Ischemic heart disease	17.9	17.9	0.939	17.8	17.7	0.724	18.0	17.6	0.356
25.0       0.087       25.0       23.9       0.005       24.6       24.8         8,0       0.969       8.1       8.0       0.651       8.0       7.9         4.7       0.001       4.3       4.6       0.112       4.3       4.4         66.9       0.985       66.1       64.8       0.002       66.2       64.3         65.8       0.985       66.1       64.8       0.002       66.2       64.3         18.6       0.007       63.2       62.9       0.435       62.4       18.2         18.6       0.291       18.1       17.9       0.627       18.2       18.2	Heart failure	13.0	12.8	0.285	12.8	12.5	0.310	12.8	12.1	0.052
8.0         0.969         8.1         8.0         0.651         8.0         79           4.7 <b>0.001</b> 4.3         4.6         0.112         4.3         4.4           66.9         0.985         66.1         64.8         0.002         66.2         64.3           65.8         0.007         63.2         62.9         0.435         63.4         62.4           18.6         0.007         63.2         62.9         0.435         63.2         62.4           18.6         0.291         18.1         17.9         0.627         18.2         18.2	Arrhythmia	25.6	25.0	0.087	25.0	23.9	0.005	24.6	24.8	0.727
4.7       0.001       4.3       4.6       0.112       4.3       4.4         66.9       0.985       66.1       64.8       0.002       66.2       64.3         62.8       0.007       63.2       62.9       0.435       63.4       62.4         18.6       0.291       18.1       17.9       0.627       18.2       18.2	Valvulopathy	8.0	8,0	0.969	8.1	8.0	0.651	8.0	7.9	0.700
669         0.985         66.1         64.8         0.002         66.2         64.3           628         0.007         63.2         62.9         0.435         63.2         62.4           18.6         0.291         18.1         17.9         0.627         18.2         18.2	Venous thromboembolism	4.2	4.7	0.001	4.3	4.6	0.112	4.3	4.4	0.660
62.8 0.007 63.2 62.9 0.435 63.2 62.4 18.6 0.291 18.1 17.9 0.627 18.2 18.2	<b>Circulatory diseases</b>	66.9	66.9	0.985	66.1	64.8	0.002	66.2	64.3	0.001
63.7         62.8         0.007         63.2         62.9         0.435         63.2         62.4           18.3         18.6         0.291         18.1         17.9         0.627         18.2         18.2	Treatment delivery in the year preced	ding the stroke <sup>a</sup>								
18.3 18.6 0.291 18.1 17.9 0.627 18.2 18.2	Antihypertensive	63.7	62.8	0.007	63.2	62.9	0.435	63.2	62.4	0.150
	Oral antidiabetic or insulin	18.3	18.6	0.291	18.1	17.9	0.627	18.2	18.2	0.972

(Continues)

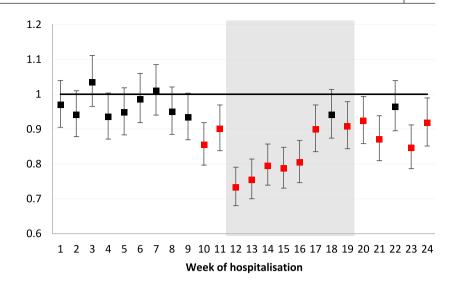
	Weeks 1 to 11	Weeks 1 to 11 (pre-lockdown in	n 2020)	Weeks 12 to :	Weeks 12 to 19 (lockdown in 2020)	020)	Weeks 20 to 2	Weeks 20 to 24 (post-lockdown in 2020)	n in 2020)
Year	2017-2019	2020	<b>p</b> 2020 vs 2017-2019	2017-2019	2020	<b>p</b> 2020 vs 2017-2019	2017-2019	2020	<b>p</b> 2020 vs 2017-2019
Lipid-lowering	32.2	30.9	0.001	31.8	30.7	0.010	31.9	31.0	0.098
Oral anticoagulant	16.2	16.5	0.146	15.9	15.8	0.868	15.9	15.9	0.985
Antiplatelet	31.7	30.0	<0.0001	31.8	29.7	<0.0001	31.3	30.0	0.015
Antiarrhythmic	11.2	10.0	<0.0001	11.1	9.9	<0.0001	10.6	10.3	0.469
Management and hospital stay									
Length of stay, mean (SD)	12.4 (14.4)	12.0 (12.6)	0.053	12.4 (13.8)	10.9 (11.5)	<0.0001	12.1 (13.1)	10.9 (10.1)	<0.0001
At discharge, %			0.173			<0.0001			0.141
Returned home	48.7	49.4		50.0	48.1		49.8	50.7	
Transferred	37.3	37.6		37.2	38.3		37.5	37.2	
Type of medical units for transfer			0.675			<0.0001			0.023
Other acute stay units	40.1	40.1		40.9	37.2		40.8	38.7	
Follow-up and rehabilitation facilities	56.3	56.5		56.0	60.0		55.9	57.9	
Others <sup>b</sup>	3.6	3.4		3.1	2.8		3.3	3.4	
Died	13.9	13.5		12.8	13.6		12.7	12.1	
Admitted to stroke unit, %	49.6	52.4	<0.0001	50.4	55.8	<0.0001	50.8	53.6	<.0001
Admitted to resuscitation unit, %	8.4	8.2	0.241	8.5	7.5	<0.0001	8.4	8.2	0.451
SAPSII, mean (SD), N <sup>c</sup>	46.8 (20.9) 7,150	47.2 (21.6) 2,231	0.207	46.6 (20.7) 4,902	42.1 (22.1) 1,237	<0.0001	46.2 (20.8) 3,000	43.4 (22.9) 941	0.002
MT <sup>d</sup> , %	7.1	5.9	<0.0001 <sup>°</sup>	6.2	6.6	0.160*	6.4	5.3	<0.0001 <sup>°</sup>
p-value < 0.05 (in bold). Abbreviations: MT, mechanical thrombectomy; SAPSII, simplified acute phy	ectomy; SAPSII, s	implified acute p	hysiology score; SD, standard deviation;	tandard deviatio	:				

Abbreviations. Mrt, inscrimination perconny, 3Mr201, simplified active physiology score, 90, standard deviation, <sup>a</sup> Available for patients without linkage error (i.e., 97% of patients): <sup>b</sup> Patients transferred to long-stay units, psychiatric units, nursing homes, or hospitalized at home; <sup>c</sup> Available for patients admitted to resuscitation units; <sup>d</sup> Performed in ischemic stroke patients hospitalized in 2019 or 2020; \*  $p_{2020 \text{ vs}} 2019$ .

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TABLE 1 (Continued)

FIGURE 1 Weekly incidence rate ratios\* of patients hospitalized for stroke in 2020 compared to 2017-2019. \*Adjusted for potential time trends from 2017 to 2020. Grey zone corresponds to the French national lockdown from weeks 12 to 19 [Colour figure can be viewed at wileyonlinelibrary.com]



test for categorical variables and the Wilcoxon-Mann-Whitney test for quantitative variables. Characteristics were described according to three time periods for each year: weeks 1-11 (prelockdown), weeks 12-19 (lockdown), and weeks 20-24 (postlockdown). We assumed the Poisson distribution for the weekly number of patients hospitalized for stroke and the weekly number of deaths. For each week, regression models were then used to assess changes between 2017-2019 and 2020 in terms of (1) the rates of patients hospitalized for stroke and (2) in-hospital case fatality rates. Rates of patients hospitalized for stroke were computed using yearly population estimates provided by the French National Institute of Statistics as the denominator. The case fatality rate was defined as the ratio of the number of discharged patients who subsequently died to the number of patients hospitalized for stroke. When the linear time trend from years 2017 to 2020 was significant, the incidence rate ratio (IRR) was adjusted for this trend. Weekly IRRs of 30-day out-of-hospital case fatality rates in patients who returned home at the end of their hospital stay were computed for patients affiliated with the French general health insurance scheme (health insurance covering approximately 76% of the population), a subpopulation for which the data on outof-hospital vital status and date of death are rapidly and exhaustively completed.

To study time trends in patient characteristics and acute care management, we computed the weekly odds ratios (ORs) for 2020 as compared to the control years (2017–2019). ORs were also adjusted for potential time trends for 2017–2020. Sensitivity analyses were performed. Firstly, we studied the rates of patients hospitalized for a transient ischemic attack (TIA) (ICD-10 code G45) to verify whether changes in the rates of patients hospitalized for stroke could be linked to a possible over- or under-coding of TIA, which might have occurred when access to imaging was unavailable due to overwhelmed hospitals. Secondly, we excluded stroke patients found to be infected with SARS-CoV-2. Thirdly, we excluded stroke patients with a history of stroke in the 7 months prior to their inclusion in the study. Analyses were performed using SAS Enterprise Guide 7.1

## **Ethics approval**

In line with the French governmental regulations and the National Ethics Committee, no patient consent was required. The databases used in the study contained pseudonymized patient information.

## RESULTS

In 2020, between weeks 1 and 24, 55,308 patients were hospitalized for stroke in France (Table 1), which was a lower number than in the same time period in previous years when more than 59,000 patients were hospitalized annually for acute stroke. The prevalence of comorbidities defined by the Charlson index and the prevalence of circulatory diseases was lower in stroke patients hospitalized during the lockdown (p = 0.006 and p = 0.002, respectively) and in the following weeks (p = 0.0001 and p = 0.001, respectively).

When looking at the time trends week by week, we observed significantly lower rates of patients hospitalized for stroke from weeks 10 to 17 in 2020 compared to 2017–2019 (Figure 1). IRRs decreased by almost 30% in week 12 (Figure 1), corresponding to 600 fewer patients hospitalized for stroke (i.e., approximately 25% less) for this week in 2020 compared to 2017–2019 (Figure S2). Similar results were found by age, sex, and stroke type, except in week 12 when there was a significantly greater decrease in patients hospitalized for strokes among individuals aged 85 years or over (Figure S3). Lower rates of patients hospitalized for stroke were still observed after the end of the lockdown in week 19 (Figure 1). Concomitantly, a decrease in patients hospitalized for TIA was observed from weeks 11 to 17 in 2020, with up to a 40% decrease for week 12 (Figure S4).

Important and significant differences in acute care management were observed between weeks 1 and 24 in 2020 compared to the corresponding weeks in the control years 2017–2019. A significant decrease was observed for the mean length of stay (starting in week 9, i.e., 3 weeks before the lockdown, Figure 2a) as well as the proportion of stroke patients admitted to resuscitation units (Figure 2c). Instead, there was a significant increase in the proportion of stroke patients admitted to stroke care units and the proportion of stroke patients transferred at the end of the hospital stay (Figure 2b,d), particularly those transferred to follow-up and rehabilitation facilities (Table 1). In patients admitted to resuscitation units, the mean SAPSII declined from week 12 onwards (Figure S5). The same observation was made after excluding stroke patients who died (data not shown).

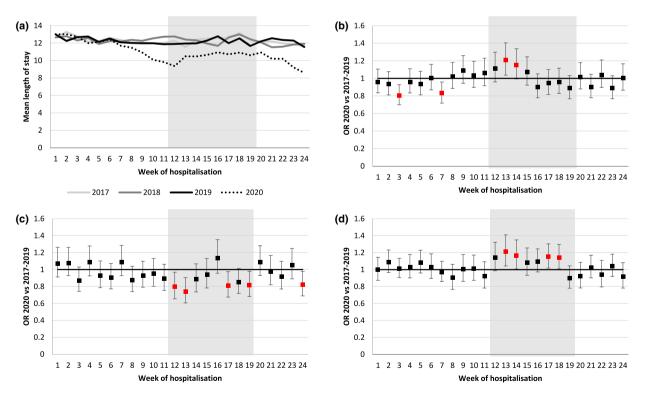
Regarding comorbidities, no significant change in the proportion of patients with a Charlson index score  $\geq 2$  was observed in the weekly analysis (Figure 3). However, a higher proportion of patients presenting speech impairment or paralysis was found in weeks 9–13 in 2020 compared to 2017–2019 (Figure 3). The increase in the proportion of patients with these symptoms reached 10% in week 13. The weekly ORs for MT increased significantly over the weeks of the lockdown (Figure S6).

In-hospital case fatality rates increased by 30% at the beginning of the lockdown in France compared to previous years (Figure 4). This observation occurred in all age groups and types of stroke, although a greater increase in in-hospital case fatality rates (approximately 60%) was found in stroke patients aged under 65 years (Figure S7). Concomitantly, patients hospitalized for ischemic stroke in week 13 were 15% more likely to have atrial fibrillation in 2020 compared to 2017-2019 (Figure S8). In weeks 11–15, an increase in 30-day case fatality rates after hospital admission was also observed among patients affiliated to the general health insurance scheme who returned home at the end of their hospitalization for stroke (Figure 4). All the results remained unchanged when excluding stroke patients with a history of stroke or those infected by SARS-CoV-2.

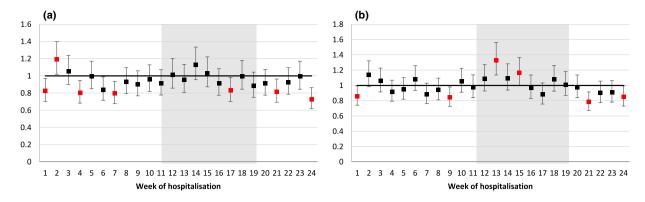
# DISCUSSION

To the best of our knowledge, this is the first study to investigate the nationwide impact of the COVID-19 pandemic and the lockdown on hospitalizations for stroke in France. We observed a 30% decrease in hospitalization rates for stroke during the lockdown, with a concomitant 30% increase in in-hospital case fatality rates during the early weeks of the lockdown and an almost 60% increase in case fatality rates among stroke patients aged under 65 years. In addition, 30-day out-of-hospital case fatality rates after hospital admission increased by up to 70%. Stroke patients hospitalized during the lockdown were more likely to have major stroke symptoms. Finally, important changes in stroke patient management were observed, as patients were less likely to be admitted to resuscitation units, more likely to be admitted to resuscitation units, more likely to stroke care units, and more likely to be quickly transferred to rehabilitation units after the acute stage of stroke care.

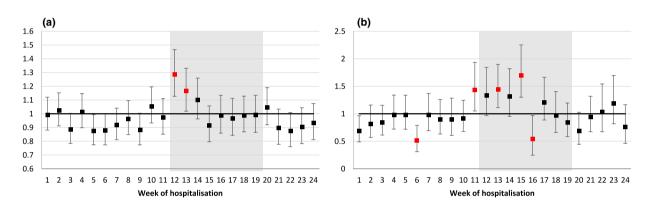
According to our findings, the decrease in hospitalization rates for stroke started 2 weeks before the beginning of the lockdown in weeks 10 and 11 and persisted after the lockdown. International comparisons are limited because of the differences in the spread



**FIGURE 2** Weekly comparison of stroke acute care management in 2020 compared to 2017–2019. (a) Mean length of stay. (b) Odds ratio (OR)\* for stroke patients admitted to a stroke care unit in 2020 vs. 2017–2019. (c) OR\* for stroke patients admitted to a resuscitation unit in 2020 vs. 2017–2019. (d) OR\* for stroke patients transferred at the end of the hospital stay in 2020 vs. 2017–2019. \*ORs adjusted for potential time trends from 2017 to 2019. Grey zone corresponds to the French national lockdown from weeks 12 to 19 [Colour figure can be viewed at wileyonlinelibrary.com]



**FIGURE 3** Weekly comparison of stroke patient characteristics in 2020 compared to 2017–2019. (a) Odds ratio (OR)\* for stroke patients with a Charlson score  $\geq 2$ . (b) OR\* for stroke patients with speech impairment or paralysis. \*ORs adjusted for potential time trends from 2017 to 2020. Grey zone corresponds to the French national lockdown from weeks 12 to 19 [Colour figure can be viewed at wileyonlinelibrary. com]



**FIGURE 4** Weekly incidence rate ratios (IRRs) of case fatality rates in 2020 compared to 2017–2019. (a) Weekly IRRs<sup>\*</sup> of in-hospital case fatality rates. (b) Weekly IRRs<sup>\*</sup> of 30-day case fatality rates among patients who returned home at the end of their hospitalization and were affiliated to the general health insurance scheme (n = 32,443 patients for 2020 and n = 105,060 for 2017–2019). \*Adjusted for potential time trends from 2017 to 2020. Grey zone corresponds to the French national lockdown from weeks 12 to 19 [Colour figure can be viewed at wileyonlinelibrary.com]

of the COVID-19 epidemic (Table S1). In a Danish nationwide study, stroke admissions rates after the lockdown returned to similar levels during the time period prior to the COVID-19 pandemic [7]. Although we observed similar declines in patients hospitalized for both ischemic and haemorrhagic strokes, the Danish study showed different time trends according to the type of stroke, with no decline in admissions for haemorrhagic strokes [7], which are more severe than ischemic strokes. In our study, however, the lower hospitalization rates in 2020 compared to 2017-2019 also impacted the most severe strokes. A similar decrease in hospitalization for TIA was also observed, which raises concerns about the possible increase in related strokes in the future. The decline in hospitalization rates for stroke might have been attributable to patients' fear of being infected with SARS-CoV-2, causing them not to seek medical attention. A decline in stroke triggers such as stress and air pollution during the lockdown might also partly explain the decline in hospitalization rates for stroke [24,25]. Finally, the lower incidence of stroke hospitalizations might be explained by the high mortality of the SARS-CoV-2 infection, mechanically reducing the number of inhabitants at risk of stroke. In England and Wales, cerebrovascular

mortality rates declined by 18% in March 2020 compared to the previous years [26].

We found greater in-hospital case fatality rates during the first weeks of the lockdown in France and higher out-of-hospital 30day case fatality rates after hospital admission in the subpopulation of patients affiliated to the general health insurance scheme. Several studies have reported higher mortality rates in stroke patients hospitalized during the pandemic [17,27]; however, no study to date has shown such an increase in in-hospital case fatality rates in stroke patients aged under 65 years (Table S1). Several explanations could account for this result. Longer delays in the management of stroke patients have been described during the lockdown in parts of France as well as in other countries, which could have contributed to their greater stroke severity at admission and thus poorer outcomes. However, we did not observe a decrease in the proportion of patients who received MT during the lockdown, which is a proxy of acute stroke management. Therefore, it could be assumed that patients presenting minor or mild strokes were not hospitalized, leading to an increase in the proportion of severe strokes during this period and consequently

higher in-hospital case fatality rates. In line with this observation, several studies have shown an increase in severity scores [8] or in the proportion of severe strokes during the lockdown [28]. A study from the United States showed a rise in the proportion of large vessel occlusion strokes during the COVID-19 pandemic, thus highlighting higher rates of severe stroke [8]. We found a significant increase in the probability of atrial fibrillation in patients hospitalized for ischemic stroke during week 13, the second week of the lockdown. This could reflect the higher rates of cardioembolic strokes, which are generally more severe types of stroke. Moreover, a nationwide Danish study demonstrated a trend towards an increase in ischemic strokes related to atrial fibrillation following the lockdown [29]. The rise in the proportion of patients with speech impairment or paralysis that we observed is consistent with the assumption of higher rates of patients hospitalized for severe stroke during the first weeks of the lockdown in France.

Lower rates of MT, however, were found in our study in 2020 compared to 2019, as previously described in a national multicentre study in France [30]. We observed an increase in the proportion of patients with ischemic strokes who benefitted from this treatment during the lockdown. As mentioned above, this could be attributable to the higher severity of stroke patients hospitalized during the lockdown, mainly characterized by large vessel occlusion. Of note, in another French study based in a single centre in Lyon, rates of MT remained unchanged during the COVID-19 outbreak [31], whereas lower rates of all revascularization treatments were observed in Alsace, one of the centres of the epidemic in France [32]. Local experiences might differ from national observations, as the different French territories were not equally affected by the COVID-19 spread. As data on IVT were not available exhaustively, they were not analysed in our study. This should be addressed in future studies to explore the lower rates of IVT reported in local stroke centres in France [31] and abroad [6,28], and the delay in administering endovascular treatments [4,6,28,33].

Important changes in acute care management during the lockdown in France were evidenced, notably with lower rates of stroke patients admitted to resuscitation units. This was associated with a decrease in the mean SAPSII for patients admitted to resuscitation units. These results could reflect the fact that patients with more severe stroke with lower chances of recovery may not have been admitted to resuscitation units because of the limited number of available beds, which were mainly attributed to patients infected with SARS-CoV-2. In our study, other care management indicators supported the assumption of an effective post-stroke care pathway, as we observed a quicker transfer to follow-up and rehabilitation units during the lockdown. Possible explanations may be that the rehabilitation services had more available beds during this period because of the decrease in admissions due to road accident trauma as well as the reduction in non-urgent scheduled surgeries in French hospitals. As a result, the mean length of stay in acute care during the lockdown was shorter, which may have contributed to an increase in the proportion of patients admitted to stroke care units. This highlights the efficient organization of stroke care networks in France.

Our study provides an exhaustive report on stroke hospitalizations during the COVID-19 pandemic in France for the period before, during and after the lockdown, and compares these data to the same time periods in 2017-2019. Nevertheless, several limitations should be highlighted. We were unable to include certain stroke characteristics such as the formal evaluation of severity using a dedicated scale or the mechanisms of ischemic stroke, thus limiting the interpretation of the results regarding the severity of stroke patients during the COVID-19 pandemic and the higher inhospital case fatality rates during this period. However, our study included in-hospital case fatality rates and 30-day mortality, two major outcomes directly linked to stroke severity. In addition, several aspects relating to care management were not available, such as the time between the onset of stroke symptoms and hospital admission, while others were not fully available, such as IVT. Caution should be taken in the interpretation of results based on one single week.

In conclusion, this nationwide study shows the substantial impact of the COVID-19 pandemic and the lockdown on stroke hospitalizations in France, with an increase in in-hospital case fatality rates, especially in patients aged under 65 years, which was probably related to the hospitalization of more severe stroke patients and the possible delay in hospital admissions. An important increase in 30-day out-of-hospital case fatality rates was also found among patients who returned home at the end of their hospitalization for stroke. Although the impact was limited in time and thus should be interpreted with caution, stroke awareness in the general population should be more intensively promoted during the COVID-19 pandemic to minimize the delay between the onset of stroke symptoms and the admission to hospital. The French stroke care network generally seemed to have effectively handled the first wave of the crisis, although further analyses are required to assess any regional variations in greater detail and to evaluate the cause of death data in France in order to estimate the possible out-of-hospital excess deaths related to stroke. Prolonged surveillance of hospitalization for stroke will be needed to analyse the mid-term impact of the COVID-19 pandemic and the lockdown on stroke patients in France.

## ACKNOWLEDGMENTS

None.

#### CONFLICT OF INTEREST

There is no conflict of interest with the present work.

#### DISCLOSURES

Y.B. reports personal fees from AstraZeneca, BMS, Pfizer, Medtronic, MSD France, Amgen, Servier and Boehringer-Ingelheim.

#### AUTHOR CONTRIBUTIONS

Amélie Gabet: Conceptualization (lead); Data curation (lead); Formal analysis (lead); Funding acquisition (lead); Investigation (lead); Methodology (lead); Project administration (lead); Resources (lead); Software (lead); Supervision (lead);

Validation (lead); Visualization (lead); Writing - original draft (lead); Writing - review and editing (lead). Clémence Grave: Conceptualization (equal); Data curation (equal); Formal analysis (equal); Methodology (equal); Validation (equal); Visualization (equal); Writing - review and editing (equal). Edouard Chatignoux: Conceptualization (equal); Data curation (equal); Formal analysis (equal); Methodology (lead); Validation (equal); Visualization (supporting); Writing-review & editing (equal). Philippe Tuppin: Conceptualization (equal); Investigation (lead); Methodology (equal); Supervision (lead); Validation (equal); Visualization (lead); Writing-review & editing (equal). Yannick Bejot: Conceptualization (equal); Investigation (lead); Methodology (equal); Supervision (equal); Validation (lead); Visualization (equal); Writing - review and editing (lead). Valérie Olié: Conceptualization (lead); Funding acquisition (lead); Methodology (equal); Project administration (equal); Resources (lead); Supervision (lead); Validation (lead); Writing - review and editing (lead).

## DATA AVAILABILITY STATEMENT

Full access to the SNDS is granted to Santé Publique France by decree.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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