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Social and clinical vulnerability in stroke and STEMI management during the COVID-19 pandemic: A registry-based study

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ABSTRACT

Objective: To evaluate whether the first wave of the COVID-19 pandemic resulted in a deterioration in the quality of care for socially and/or clinically vulnerable stroke and ST-segment elevation myocardial infarction (STEMI) patients.

Design: Two cohorts of STEMI and stroke patients in the Aquitaine neuro-cardiovascular (CNV) registry.

Setting: Six emergency medical services, 30 emergency units, 14 hospitalisation units, and 11 catheterisation laboratories in the Aquitaine region in France.

Participants: This study involved 9218 patients (6436 stroke and 2782 STEMI patients) in the CNV registry from January 2019 to August 2020.

Method: Associations between social (deprivation index) and clinical (age > 65 years, neuro-cardiovascular history) vulnerabilities and care management times were analysed using multivariate linear mixed models, with an interaction on the time period (pre–, per–, and post–first COVID-19 wave).

Main outcome measures: STEMI cohort, first medical contact-to-procedure time; stroke cohort, emergency unit admission-to-imaging time.

Results: The first medical contact–procedure time was longer for elderly ($p < 0.001$) and "very socially disadvantaged" ($p = 0.003$) STEMI patients, with no interaction regarding the COVID-19 period (age, $p = 0.54$; neuro-cardiovascular history, $p = 0.70$; deprivation, $p = 0.64$). We found no significant association between vulnerabilities and the admission–imaging time for stroke patients, and no interaction with respect to the COVID-19 period (age, $p = 0.81$; neuro-cardiovascular history, $p = 0.34$; deprivation, $p = 0.95$).

Conclusions: This study revealed pre-existing inequalities in care management times for vulnerable STEMI and stroke patients; however, these inequalities were neither accentuated nor reduced during the first COVID-19 wave. Measures implemented during the crisis did not alter the well-structured emergency pathway for these patients.

Trial registration: NCT04979208

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The study analysed two large high-quality data cohorts comprising almost 10000 stroke and STEMI patients, managed in a large panel of care structures throughout the Aquitaine region, over a period of several months before and after the first wave.
- We studied vulnerabilities from two perspectives, a social perspective through an ecological social deprivation index and a clinical perspective through risk factors of severe COVID-19.
- The explanatory analyses yield robust results due to the large amount of data collected (clinical and socio-geographical characteristics, acute care management pathway data), enabling integration of a wide variety of confounders.
- The exclusion of patients who did not enter the healthcare system prevented quantification of healthcare system avoidance, that is supposed to have been more frequent among socially and/or clinically vulnerable patients during the COVID-19 pandemic.
- The study area was limited to the Aquitaine region, one of the regions least affected by the first wave of the COVID-19 pandemic in France; this situation could have led to the exertion of less pressure on health services.

INTRODUCTION

ST-segment elevation myocardial infarction (STEMI) and stroke are life-threatening and highly time-sensitive emergencies. The time elapsed from symptom onset to treatment is a predictor of patients' mortality and functional recovery.(1,2) The standardised and timed care pathways for these two diseases depend initially on a patient's use of the emergency medical service (EMS) system, followed by close collaboration between emergency structures and specialised technical platforms (e.g., catheterisation laboratories, stroke units).(1,2) The quality of care is often evaluated under the prism of the time from first medical contact (FMC) to treatment.(1,2)

Patients with STEMI and stroke face social and health inequality issues. Socially vulnerable (i.e., disadvantaged) patients with neuro-cardiovascular diseases have higher morbidity and mortality rates.(3,4) Four markers of social position and socioeconomic status have been associated with cardiovascular disease in high-income countries: income level, educational attainment, employment status, and environmental factors.(5) These inequalities are attributable to a higher prevalence of biological, behavioral and psychosocial cardiovascular risk factors in the more socially disadvantaged population but also to more difficulties in accessing healthcare and lower-quality acute care management.(4,6,7) The organisation of the healthcare system, as a social health determinant, leads to health inequalities, due mainly to challenges related to communication and health literacy, implicit bias, and/or a lack of culturally competent care.(8)

The 2019 coronavirus disease (COVID-19) dramatically modified healthcare systems worldwide and had major consequences for patients' access to care for stroke and STEMI.(9–11) From February to March 2020, many health authorities, including those in France, implemented strict nationwide lockdowns and series of policies to curb the surge of patients requiring critical care. This crisis, and particularly the lockdown periods, induced the major reorganisation of healthcare systems and modified the use of care to accommodate the onslaught of patients with COVID-19.(12) Studies of the association between the COVID-19 pandemic and the quality of stroke and STEMI management have yielded contrasting results, with most revealing longer management delays and reductions in the number of procedures performed.(9,10,13)

During pandemics (e.g., of influenza, plague), pre-existing inequalities affecting many aspects of patients' care pathways (e.g., loss of employment and income; social isolation, especially for elderly individuals; and mental health issues, particularly for young people) are usually amplified.(14–18) During the COVID-19 pandemic, COVID-19 exposure, severe disease, hospitalisation, and death were more frequent among socially disadvantaged people.(15,17–19) This population benefited less from the collective protective measures taken against COVID-19, had more difficulty accessing preventative healthcare, and had lower rates of COVID-19 testing and vaccination.(14) Some experts consider COVID-19 to be a syndemic, rather than a pandemic. These interactions between COVID-19 and pre-existing socioeconomic inequalities in non-communicable diseases are an illustration.(16) Indeed, "syndemics are characterised by biological and social interactions between conditions and states, interactions that increase a person's susceptibility to harm or worsen their health outcomes."(16)

In France, to protect more vulnerable patients and adapt care, health authorities identified several risk factors of severe COVID-19 based on demographic (advanced age) and medical (especially cardiovascular co-morbidities) characteristics.(20) Information about these risk factors was covered widely in the media which may have led exposed individuals with these underlying conditions to delay seeking treatment.(21) Additional protective measures may have been implemented for these exposed populations, resulting in increased management delays.

To our knowledge, only one study has evaluated whether COVID-19 modified the associations among the educational level, deprivation, hospital admission indicators, and quality of hospital care, especially for patients with neuro-cardiovascular diseases.(22) The researchers found larger declines in the hospital access of women, elderly, and less-educated individuals; in contrast, the timeliness of percutaneous coronary intervention (PCI) showed no education- or deprivation-related gradient.

Since 2012, the "CNV Registry" of neuro-cardiovascular diseases evaluate the care pathways for STEMI and stroke patients in the Aquitaine region of southwestern France (3 million inhabitants). This registry provides a unique opportunity to study differences in care management and their evolution over time in a country with universal health coverage.(23)

COVID-19 profoundly modified access to and the use and organisation of care, against a backdrop of pre-existing inequalities in neuro-cardiovascular disease.(12) The notion of a "syndemic" and our hypothesis that management times were longer for patients at risk of severe COVID-19 during its first wave prompted our investigation of whether first COVID-19 wave resulted in the deterioration of the quality of care for socially and clinically vulnerable stroke and STEMI patients, using data from the CNV Registry.

METHODS

Study design and population

We used two exhaustive retrospective cohorts of adult stroke and STEMI patients admitted to a care structure in the Aquitaine region whose data were entered into the CNV Registry between January 1, 2019, and August 31, 2020.(23)

The STEMI cohort comprised patients with recent (<24 h after symptom onset) STEMI managed in one of the six health territories in Aquitaine, each centered around an EMS, comprising 30 emergency units (EUs) and 11 catheterisation laboratories (nearly 1800 STEMIs are seen annually).

The stroke cohort comprised patients with recent ischemic or hemorrhagic stroke (excluding transient ischemic attacks), diagnosed by brain imaging and validated by neurovascular physicians, that was managed in five health territories in Aquitaine, comprising 14 (7 with stroke units) of the 20 hospitals caring for more than 30 strokes per year in Aquitaine (nearly 5000 strokes are seen annually).

The CNV Registry was approved by the French authority on data protection and met the regulatory requirements for the handling of patient information (file 2216283).

Data collection

The CNV Registry contains information on patients' sociodemographic (age, gender, place of residence) and clinical [medical history, cardiovascular risk factors, stroke clinical severity (modified Rankin scale and National Institute of Health Stroke Score), stroke type (ischemic/hemorrhagic)] characteristics, use of care (calls to emergency services, FMC, symptom onset–care time), acute care management quality (times between key management steps, pre-hospital and hospital pathway types, treatment), and structural characteristics of care (care during on-call activity, calls to emergency services during care, hospital administrative status, FMC–catheterisation laboratory distance). Data are collected prospectively by physicians; consolidated retrospectively by clinical research assistants and then extracted from the hospital information system. Data from the two cohorts were integrated into one data warehouse enabling the reconstruction of the STEMI or stroke management pathway.(12)

Outcomes

The primary endpoints were acute-care management times, which reflect the quality of care. For the STEMI cohort, we used the FMC–procedure time [delay (in minutes) between the FMC (mobile intensive care unit arrival or EU admission) and the start of a treatment procedure]. For the stroke cohort, we used the EU admission–imaging time [delay (in minutes) between EU admission and the start of the first imaging]. This selection of an interval that focused on the beginning of in-hospital stroke care was required due to the heterogeneity of the pre-hospital pathways and treatments applied.

Exposure

Clinically vulnerable persons at risk of severe COVID-19 were those aged > 65 years; with neuro-cardiovascular history including previous STEMI, stroke, or transient ischemic attack; and/or with coronary artery disease history. For the STEMI cohort, the history of a PCI, a coronary artery bypass graft was also included.

Due to the lack of individual socioeconomic data, an ecological social deprivation score was assigned to each commune (the smallest administrative unit in France) of patients' residence using the 2015 deprivation index (Fdep15) to assess social vulnerability.(24) This index is associated strongly with mortality at all geographic scales. It served as the first dimension of a principal component analysis (weighted by population size) of four socioeconomic ecological variables: the percentage of high-school graduates ≥ 15 years old, median household income, percentage of blue-collar workers, and unemployment rate. Quintiles of the Fdep15 scores were computed for metropolitan France, whereby the first quintile (Q1) represented the least and the fifth quintile (Q5) the most disadvantaged communes.

Statistical analyses

Analyses were performed separately for each cohort and exposure variable. Associations between clinical and social vulnerabilities' effects on care management times (introduced as continuous variables after logarithmic transformation) were analysed using multivariate linear mixed models (three each for stroke and STEMI), with random effects on hospital and health territories centered around single EMSs. Interactions on the time period were introduced. Three COVID-19 periods were defined according to the dates of first hospital reorganisation (mid-February) and the termination of national lockdown (May 10, 2020): pre-wave (January 1, 2019–February 9, 2020), per-wave (February 10–May 10, 2020), and post-wave (May 11–August 31, 2020). Inspired by the conceptual framework developed by the Health Care Quality Indicator Project of the Organization for Economic Cooperation and Development, we categorised determinants in four dimensions: patients, physicians, care organisations, and quality of care.(25) To develop the causal model, variables were classified into each of these dimensions and confounders were then identified by directed acyclic graphs (DAG; Supplementary Material 1). The relationships between vulnerabilities and care management times were quantified (β) using the contrast method, with statistical significance defined as $p < 0.05$. The exponentials of the beta values [exp(β)], associated 95% confidence intervals (CIs), and percentage changes [1−exp(β)] were then calculated. The statistical analyses were conducted using SAS 9.4.

Patient and public involvement statement

As members of the CNV registry scientific boards, patient representatives were involved in study conception, implementation, and dissemination; they validated data collection and analysis, and results diffusion. Dissemination of results was conducted on the CNV registry website, to the scientific boards, and to care-structure physicians.

This study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines and is registered with ClinicalTrials.gov (NCT04979208).

RESULTS

Sample characteristics

The sample comprised 9218 patients (6436 with stroke, 2782 with STEMI); 54.9% of the stroke patients and 73.1% of the STEMI patients were male. Patients aged > 65 years accounted for 81.3% and 50.1% of the stroke and STEMI patients, respectively. One-quarter of patients had neuro-cardiovascular history (stroke, 28.6%; STEMI, 20.5%). The distributions of the deprivation index quintiles in our sample, ordered from the most advantaged to the most disadvantaged, were 16.2%, 24.8%, 18.1%, 19.3%, and 21.6% for stroke patients and 12.8%, 23.5%, 22.8%, 22.8%, and 18.1% for STEMI patients (Supplementary Material 2).

Acute care management times

Stroke cohort

In the pre-wave period, the median admission–imaging time was longer for stroke patients aged > 65 years than for younger patients (84 vs. 79 min) and for patients without than for those with neuro-cardiovascular history (86 vs. 76 min). Acute-care management times were longest for the most advantaged and most disadvantaged patients (both 88 min vs. 77–86 min for the other social deprivation categories; Table 1).

The median admission–imaging time was longer during the per-wave period than during the pre-wave period, regardless of age or neuro-cardiovascular history, but was shorter for the most advantaged patients (80 vs. 88 min). This time was shorter during the post-wave period than during the per-wave period, regardless of age, but was longer for the most advantaged patients (90 vs. 80 min).

Table 1. Admission-to-imaging time according to vulnerabilities and COVID-19 periods - Stroke cohort (N=6436)

	Global (N=6436)			**Pre-wave (N=4140)**			**Per-wave (N=1080)**			**Post-wave (N=1216)**		
	n	Median	[IQR]	n	Median	[IQR]	n	Median	[IQR]	n	Median	[IQR]
All patients	4819	86	[47;194]	3014	83	[45;201]	889	91	[51;175]	916	88	[52;191]
Missing value	*1617*			*1126*			*191*			*300*		
Clinical vulnerability												
Age	4819			3014			889			916		
[18-65 years[	868	84	[45;193]	536	79	[43;208]	157	92	[48;177]	175	85	[45;174]
[65 years and older[	3951	86	[48;194]	2478	84	[45;199]	732	91	[51;175]	741	88	[52;197]
Missing value	*1617*			*1126*			*191*			*300*		
Neuro-cardiovascular history	4819			3014			889			916		
Absence	3430	88	[47;197]	2128	86	[45;204]	661	93	[51;177]	641	86	[50;197]
Presence	1389	83	[48;184]	886	76	[45;187]	228	87	[49;173]	275	90	[57;189]
Missing value	*1617*			*1126*			*191*			*300*		
Social vulnerability												
Deprivation (Fdep15)	4610			2821			884			905		
Most advantaged	743	87	[47;235]	469	88	[46;240]	145	80	[44;202]	129	90	[54;239]
Advantaged	1107	84	[45;206]	637	77	[42;216]	235	97	[51;181]	235	85	[48;202]
Intermediate	831	87	[48;179]	492	83	[46;189]	168	92	[53;153]	171	94	[54;188]
Disadvantaged	903	86	[47;183]	568	86	[46;186]	154	86	[47;170]	181	86	[51;179]
Most disadvantaged	1026	89	[52;192]	655	88	[51;198]	182	95	[55;175]	189	82	[52;148]
Missing value	*1826*			*1319*			*196*			*311*		

IQR=interquartile range

STEMI cohort

In the pre-wave period, the median FMC–procedure time was longer for STEMI patients aged > 65 years than for younger patients (103 vs. 96 min). Its length increased with the degree of disadvantage (from 82 min for the most advantaged to 129 min for the most disadvantaged patients; Table 2).

The median FMC–procedure time was slightly shorter during the per-wave period than during the pre-wave period, regardless of age or neuro-cardiovascular history, but was longer for the most advantaged patients (92 vs. 82 min). This time was longer during the post-wave period than during the per-wave period, especially for elderly patients (117 vs. 101 min), those with neuro-cardiovascular history (112 vs. 89 min), and those most advantaged (119 vs. 92 min).

Table 2. FMC-to-procedure time according to vulnerabilities and COVID-19 periods - STEMI cohort (N=2782)

	Global (N=2782)			Pre-wave (N=1868)			Per-wave (N=407)			Post-wave (N=507)		
	n	Median	[IQR]	n	Median	[IQR]	n	Median	[IQR]	n	Median	[IQR]
All patients	2364	99	[71;157]	1577	100	[71;158]	353	95	[69;152]	434	102	[71;153]
Missing value	*418*			*291*			*54*			*73*		
Clinical vulnerability												
Age	2364			1577			353			434		
[18-65 years[	1207	95	[69;147]	794	96	[69;152]	175	93	[68;134]	238	94	[69;134]
[65 years and older[	1157	105	[73;173]	783	103	[74;169]	178	101	[70;190]	196	117	[74;167]
Missing value	*418*			*291*			*54*			*73*		
Neuro-cardiovascular history	2364			1577			353			434		
Absence	1699	98	[71;156]	1115	99	[71;157]	267	97	[70;157]	317	96	[70;149]
Presence	468	101	[70;159]	318	102	[72;156]	67	89	[61;135]	83	112	[74;169]
Unknown	197	98	[74;161]	144	97	[73;180]	19	97	[81;134]	34	118	[78;154]
Missing value	*418*			*291*			*54*			*73*		
Social vulnerability												
Deprivation (Fdep15)	2343			1565			351			427		
Most advantaged	304	90	[64;152]	203	82	[63;149]	48	92	[62;127]	53	119	[79;177]
Advantaged	551	91	[66;145]	350	92	[68;139]	90	93	[62;162]	111	89	[65;150]
Intermediate	538	95	[70;150]	378	97	[69;156]	71	91	[68;157]	89	89	[72;129]
Disadvantaged	536	102	[73;150]	353	101	[75;154]	82	94	[70;140]	101	106	[73;151]
Most disadvantaged	414	124	[86;204]	281	129	[85;215]	60	120	[90;198]	73	122	[93;180]
Missing value	*439*			*303*			*56*			*80*		

IQR=interquartile range

Effects of the COVID-19 first wave

Stroke cohort models

The final stroke models showed no significant association among advanced age [n = 4819, exp(β) = 1.08, 95% CI 1.00–1.16, $p = 0.07$], neuro-cardiovascular history [n = 4610, exp(β) = 0.97, 95% CI 0.91–1.04, p = 0.44], deprivation (n = 4606, p = 0.30), and the EU admission–imaging time, and no interaction with the COVID-19 period (age, p = 0.81; neuro-cardiovascular history, p = 0.34; deprivation, p = 0.95; Figure 1).

STEMI cohort models

Advanced age was associated with a 15% increase in the FMC–procedure time [n = 2364, exp(β) = 1.15, 95% CI 1.07–1.24, $p < 0.001$]. No significant association was noted between patients' neuro-cardiovascular history and the FMC–procedure time [n = 2167, exp(β) = 1.08, 95% CI 0.98–1.19, p = 0.14]. Compared with those in the other four quintiles, FMC–procedure times were 15–22% longer for patients in the most disadvantaged quintile (n = 2343, p = 0.003). No significant COVID-19 period interaction affected the relationships between the vulnerabilities studied and the FMC–procedure time (age, p = 0.54; neuro-cardiovascular history, p = 0.70; deprivation, p = 0.64; Figure 2).

DISCUSSION

Main results

This analysis of the healthcare pathways for STEMI and stroke patients included in the CNV Registry showed that care management times for socially or clinically vulnerable patients did not worsen during the first wave of the COVID-19 pandemic, despite changes in the access to and use and organisation of care. Nonetheless, regardless of the COVID-19 period, acute-care management times were longer for elderly and the most disadvantaged STEMI patients.

Effects of the COVID-19 first wave

Our results are concordant with those of a study conducted in Italy, which revealed no educational or deprivation gradient for cardiovascular acute-care management times.(22) Several factors can explain the resilience of stroke and STEMI care pathways for vulnerable populations.

First, STEMI and stroke networks in France are structured as well-defined, organised, and dedicated pathways. Highly structured patient-centered clinical pathways improve the quality of care for chronic and acute conditions with predictable trajectories.(26,27) Guidelines and national stroke and STEMI improvement programs recommend the implementation of such structured pathways, which include close collaborations between healthcare professionals and patient orientation to the EMS system and specialised technical platforms. A study of the impacts of changes in the use of care and implementation of hospital reorganisation spurred by the COVID-19 pandemic on acute management times for stroke and STEMI revealed no deep alteration of the emergency pathway construct.(12) Socially and/or clinically vulnerable populations have also benefited from the resilience of the STEMI and stroke pathways.

Second, in the particular context of the first COVID-19 wave, the mass media widely relayed information from health institutions. The whole population was worried and very concerned about its health. Lockdown measures made people more available, and routinely exposed, to mainstream media that were highly focused on the pandemic and health messages. These factors are associated with a greater likelihood of the adoption of recommended prevention practices.(28) Thus, broad health-related media coverage may have had a positive influence on health literacy for the whole population, which may have positively influenced the use of the healthcare system.(29)

Third, the EMS was identified as the first contact to limit exposure and regulate urgent calls during the first COVID-19 wave in France. The media relayed this information. French hospitals increased regulation capacities to face the rise in EMS calls, in an attempt to preserve access to care and the capacity to handle vital emergencies for the entire population.(30)

Fourth, France adopted a specific strategy in March 2020 to support the economy, companies, and jobs through measures that include financial support for disadvantaged populations, salary preservation, the prohibition of layoffs, and housing assistance.(31) Associated with universal healthcare coverage, these actions may have contributed to mitigate the social consequences of the pandemic.

Global effects

Several studies, including the present work, have shown that acute-care management times are longer for elderly patients and socially vulnerable STEMI patients.(32–34) Regarding age, greater initial clinical severity, atypical symptoms, and a longer delay in admission may explain these findings.(33) However, findings with respect to socioeconomic status do not converge. Biswas et al. (32) found that the median time to reperfusion in Australia, a country with universal healthcare, between 2005 and 2015 was 4 min longer for lower socioeconomic quintiles than for the highest quintile. Vasaiwala et al. (34) found a direct correlation between income levels in the United States and the proportion of patients meeting the guideline-recommended door–balloon time. In contrast, Heo et al. (35) found no association between the educational level and door–balloon time in Korea. None of these studies involved control for the confounders. Additional dedicated analyses of the relationship between socioeconomic status and acute-care management time are needed, especially for elderly patients with accumulated comorbid factors due to their disadvantaged status.

We found no alteration in the acute-care management time for elderly and socially vulnerable stroke patients. This may be explained by our examination of the EU admission–imaging time focused on the beginning of in-hospital care. Unlike the STEMI pathway, this time involves such a small portion of stroke patients' pathways that it could have been difficult to detect an effect. Regarding age, half of the STEMI patients in our sample were aged > 65 years. The proportion of elderly stroke patients was 81%, which made it difficult to demonstrate an effect. To our knowledge, only one study, conducted in England, has revealed an association between older age and a longer admission–computerised tomography time.(36) Few studies have involved the exploration of acute stroke management times according to socioeconomic status, with contrasting results explained by the specificities of healthcare systems.(3,37) In a study conducted in England, socially vulnerable patients were less likely to undergo high-quality recommended processes and more likely to undergo early supported discharge.(3) A study conducted in Sweden showed that university-educated patients were more likely to be treated than were less-educated patients.(37)

Regardless of the COVID-19 period, we found no significant influence of patients' neuro-cardiovascular history on acute-care management times, consistent with reported findings for STEMI patients.(38) To our knowledge, no other study has evaluated this relationship for stroke care.

Strengths and weaknesses

Our study, one of the first to examine the effects of the COVID-19 crisis on the quality of care for STEMI and stroke patients in Europe with consideration of health and social inequalities, involved the parallel analysis of two high-quality databases containing data on large numbers of stroke and STEMI patients managed in a large panel of care structures in the Aquitaine region.

The sample is representative of stroke and STEMI patients managed in hospitals. However, our study has some limitations, particularly with regard to the population. The study area was limited to the Aquitaine region, one of the regions least affected by the first wave of the COVID-19 pandemic.(39)

This situation could have led to the exertion of less pressure on health services (especially the EMS, STEMI, and stroke network). It would be interesting to repeat the study in another region, or in another country more affected by the pandemic, to test the external validity of the results.

Moreover, patients who did not enter the healthcare system because they had died or did not benefit from hospital care, as well as STEMI patients with symptoms for >24 h, were not included. The exclusion of these patients may have generated selection bias, and prevented us from quantifying the phenomenon of healthcare system avoidance that is supposed to have been more frequent among socially and/or clinically vulnerable patients during the COVID-19 crisis; it also entails the risk that increases in the delay to use of care were underestimated for some patient subgroups.(40)

Our explanatory analyses yield robust results, with the inclusion of appropriate confounding variables identified by the DAG method. The large panel of data collected enabled the integration of a wide variety of confounders, including clinical characteristics and socio-geographical factors.

Given the lack of individual-level socioeconomic data in the CNV Registry, which prevented the assignment of social determinants for each patient, we used a residence area–based measure, which is a major limitation of our study. However, we determined deprivation indices using a validated tool that has been used in many studies conducted in France.(24) Moreover, the socio-ecological measure of deprivation tends to underestimate social inequalities observed using individual data; thus, caution is advised when attributing group-level estimates to individuals.(6) Additional limitations of this study include our inability to include all clinical risk factors of severe COVID-19 and information about patients' educational levels, individual resources, and social support to further explore their precariousness and health literacy. The COVID-19 pandemic may have had a greater impact on the access to and quality of care for the most precarious individuals.

A major methodological issue of this study is that we defined the per-wave period according to the implementation of healthcare reorganisation and transformation of societal functioning to fight the COVID-19 pandemic.(12) We began the per-wave period at the time of the first hospital reorganisation implementation and ended it at the time of lockdown lifting. Although data for the CNV Registry are collected continuously, we terminated the follow-up period at the end of August 2020 to enable the timely reporting of results.

Finally, we did not explore short- or long-term outcomes such as morbidity, mortality, disability, or rehospitalisation after initial hospitalisation for STEMI or stroke, for which a wide range of socioeconomic disparities exist, in the context of the COVID-19 pandemic.(3,40) This will be a key focus of our ongoing research.

Conclusions

The first wave of the COVID-19 pandemic induced no deep change in management times for the most socially and/or clinically vulnerable stroke and STEMI patients. Pre-existing inequalities in care management times were neither aggravated nor reduced by changes in the use of care or implementation of hospital reorganisation spurred by the pandemic. These encouraging results may be explained by the well-structured STEMI and stroke networks in France and the reorganisation of the healthcare structure to preserve access and the capacity to care for vital emergencies using the EMS.

- **Figure Legend/Caption**

Figure 1. Estimation of each clinical and social factor (95% confidence interval) on emergency unit admission-to-imaging time.

Estimated overall effects expressed as exp(ß) with 95% CI; results of multivariate linear regression mixed models; variable to be explained: Y=log (emergency unit admission-to-imaging time); (A) results adjusted on period and gender; (B) cardiovascular history was a history of stroke, transient ischemic attack, coronary artery disease, or myocardial infarction; results adjusted on period, age, gender, diabetes and smoking as risk factors, deprivation index; (C) the reference modality for the deprivation index Fdep15 in five categories was "most disadvantaged"; results adjusted on period, age, gender, country of birth, urbanicity of residence.

Figure 2. Estimation of each clinical and social factor (95% confidence interval) on FMC-to-procedure time.

Estimated overall effects expressed as exp(ß) with 95% CI; results of multivariate linear regression mixed models; variable to be explained: Y=log (FMC-to-procedure time); (A) results adjusted on period and gender; (B) cardiovascular history was a history of stroke, transient ischemic attack, coronary artery disease, or myocardial infarction; results adjusted on period, age, gender, diabetes, hypertension, dyslipidemia, obesity and smoking as risk factors ; (C) the reference modality for the deprivation index Fdep15 in five categories was "most disadvantaged"; results adjusted on period, age, gender, country of birth, urbanicity of residence.

- **Data sharing statement**

Deidentified participant data will be available upon reasonable request. Proposals may be submitted to the corresponding author. Data requestors will need to sign a data access agreement

- **Patient consent for publication**

Not applicable.

- **Ethics statements**

According to French authority on data protection "Commission Nationale Informatique et Libertés", in the category of studies not involving humans based on secondary use of health data, the CNV registry met regulatory requirements for patient information and do not require a patient consent form.

Ethics approval

Not applicable

- **Authors' contributions**

EL, FF, SD, FSa and FSe were responsible for the study concept and design. EL and FF conducted the literature review. EL and FSe had full access to all of the data and takes responsibility for their integrity and accuracy. SD and SMH performed the statistical analysis. FSa, EL, SD, FF, FSe, SV, LC, PC, FR, IS, CP interpreted the data. EL, FF, SV, FSa and SD wrote the manuscript. FSe, LC, PC, FR, IS and CP critically reviewed the manuscript.

- **Competing interests statement**

The authors declare that they have no competing interests with this study.

- **Funding statement**

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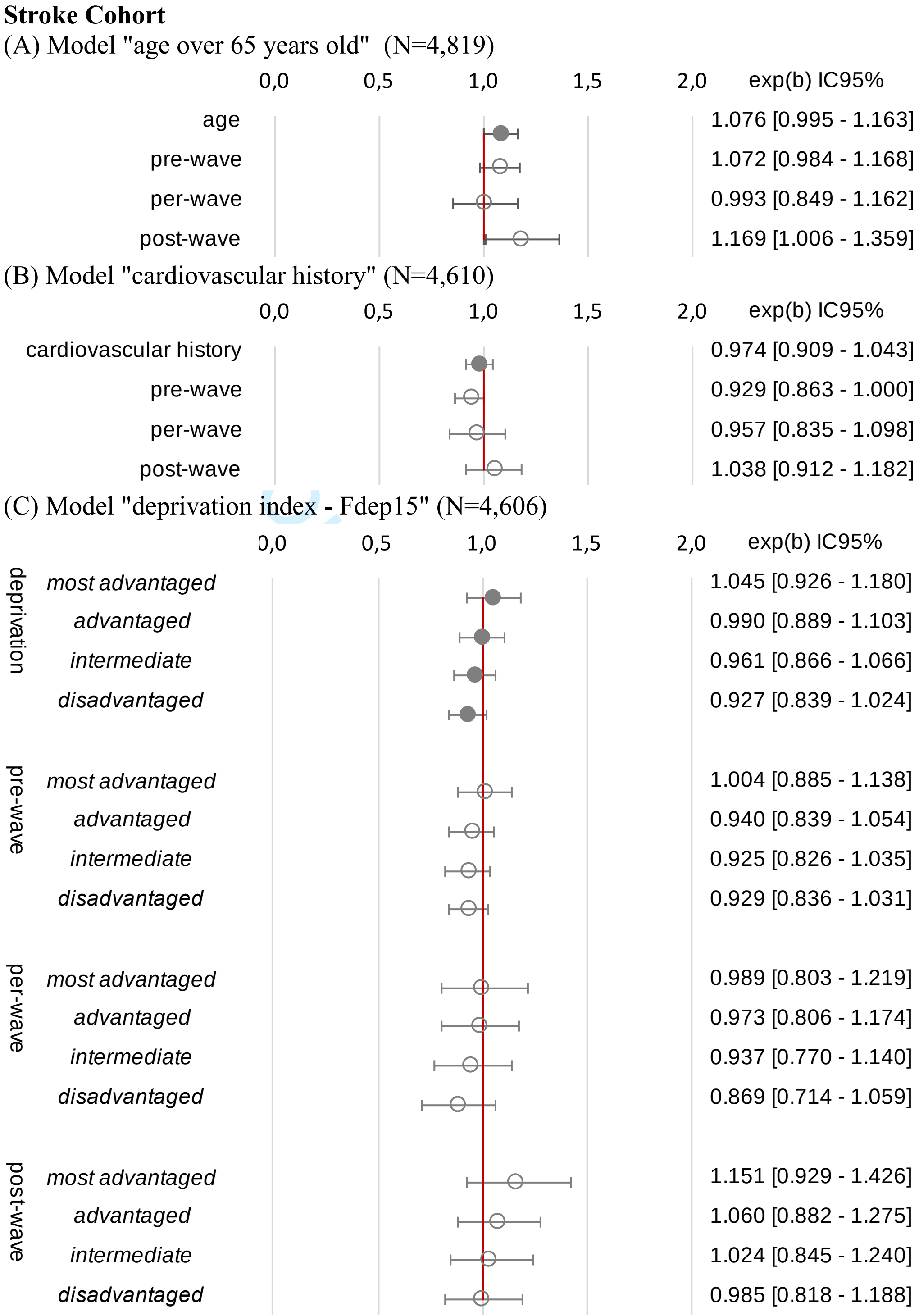


Figure 1. Estimation of each clinical and social factor (95% confidence interval) on emergency unit admission-to-imaging time.

Estimated overall effects expressed as exp(ß) with 95% CI; results of multivariate linear regression mixed models; variable to be explained: Y=log (emergency unit admission-to-imaging time); (A) results adjusted on period and gender; (B) cardiovascular history was a history of stroke, transient ischemic attack, coronary artery disease, or myocardial infarction; results adjusted on period, age, gender, diabetes and smoking as risk factors, deprivation index; (C) the reference modality for the deprivation index Fdep15 in five categories was “most disadvantaged”; results adjusted on period, age, gender, country of birth, urbanicity of residence.

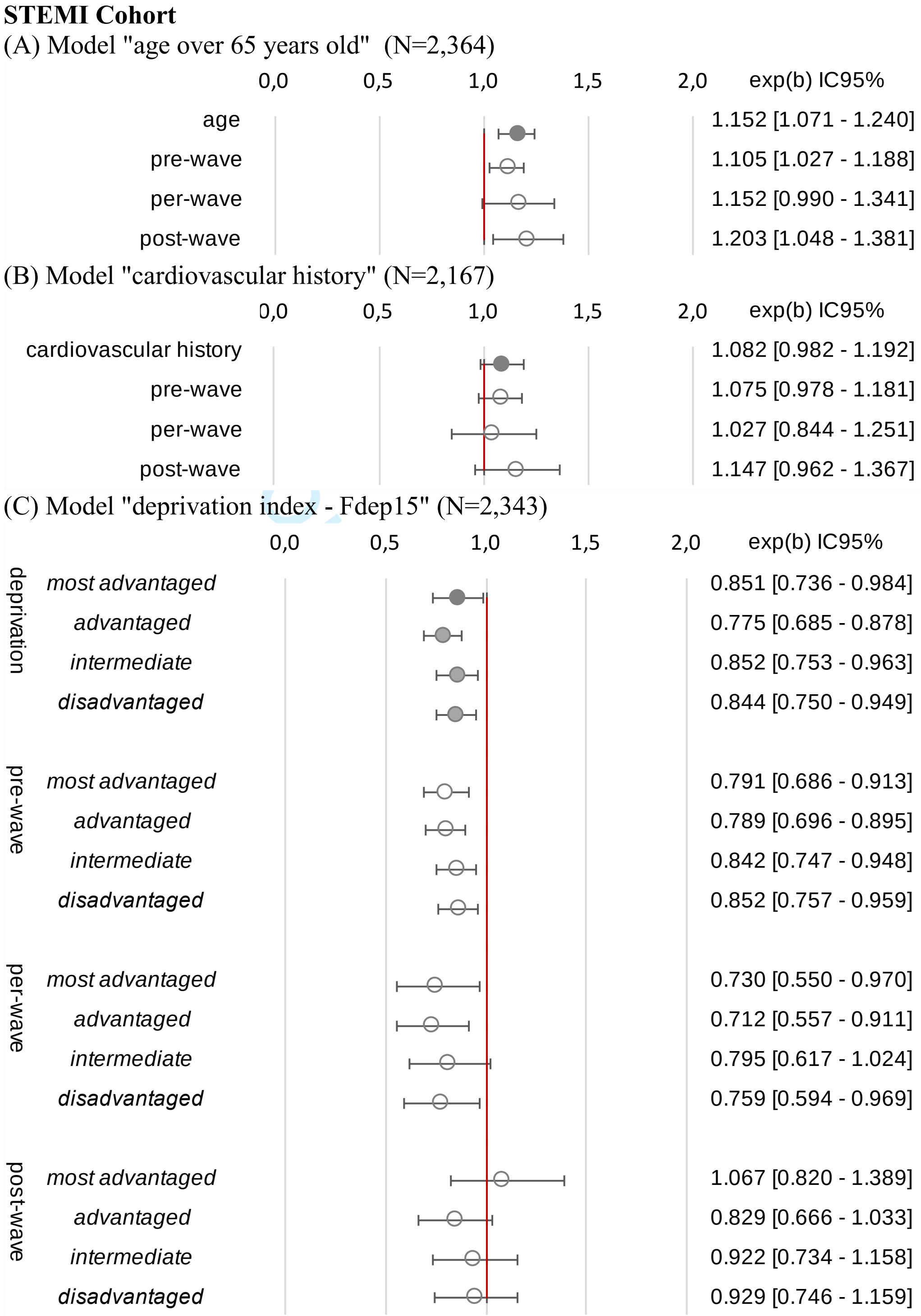
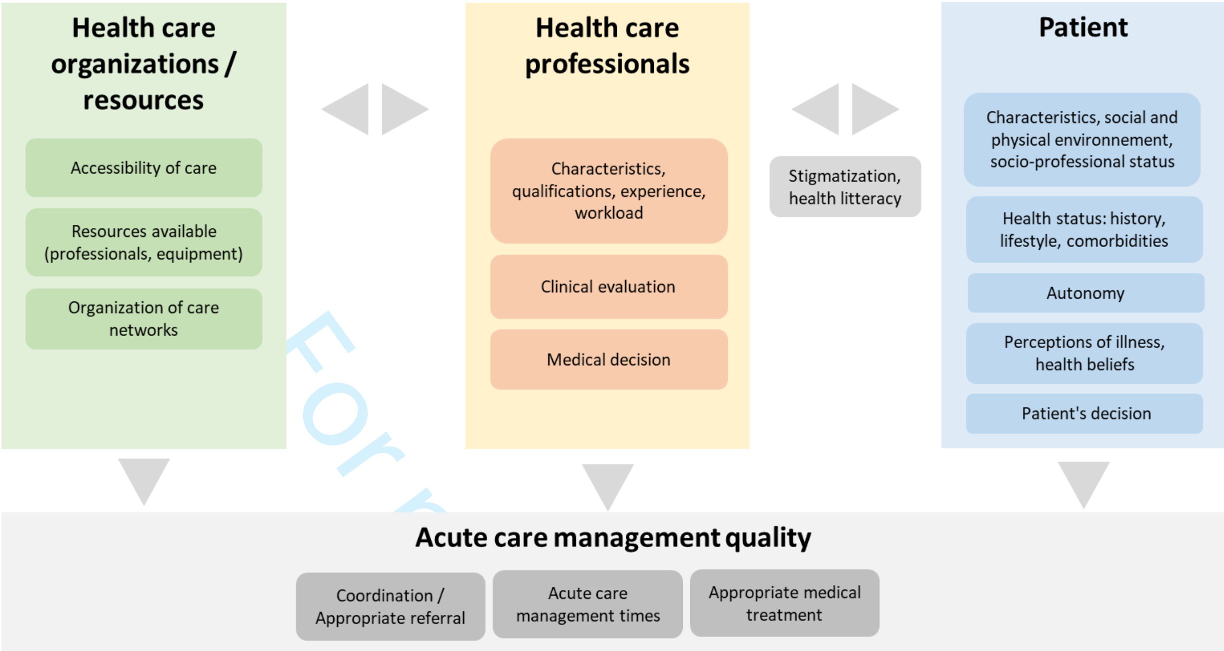


Figure 2. Estimation of each clinical and social factor (95% confidence interval) on FMC-to-procedure time.
Estimated overall effects expressed as exp(ß) with 95% CI; results of multivariate linear regression mixed models; variable to be explained: Y=log (FMC-to-procedure time); (A) results adjusted on period and gender; (B) cardiovascular history was a history of stroke, transient ischemic attack, coronary artery disease, or myocardial infarction; results adjusted on period, age, gender, diabetes, hypertension, dyslipidemia, obesity and smoking as risk factors ; (C) the reference modality for the deprivation index Fdep15 in five categories was "most disadvantaged"; results adjusted on period, age, gender, country of birth, urbanicity of residence.

Supplementary material 1.

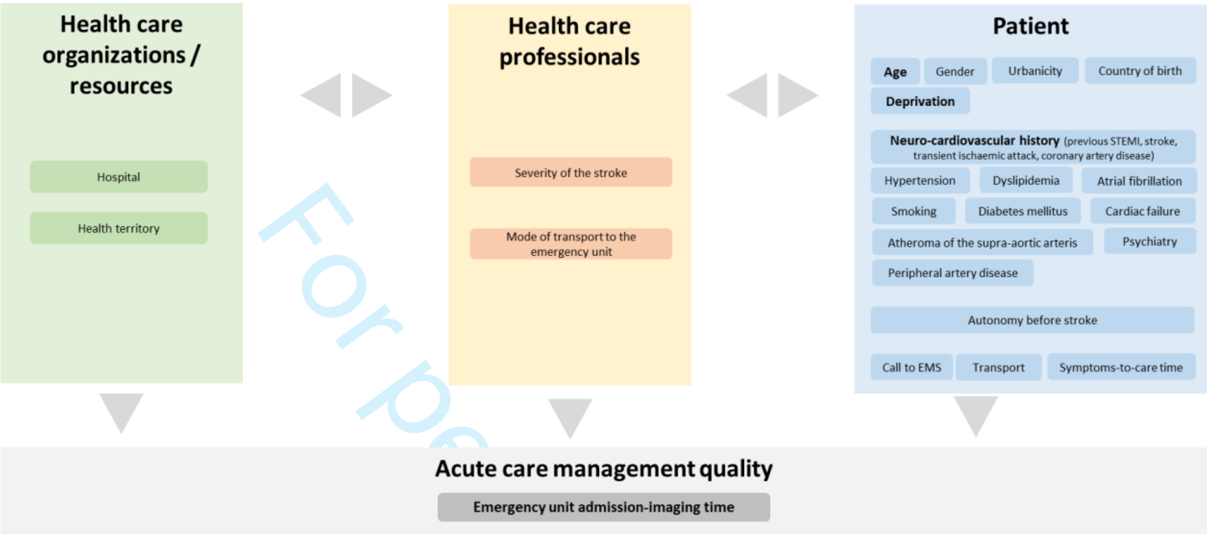
Conceptual framework



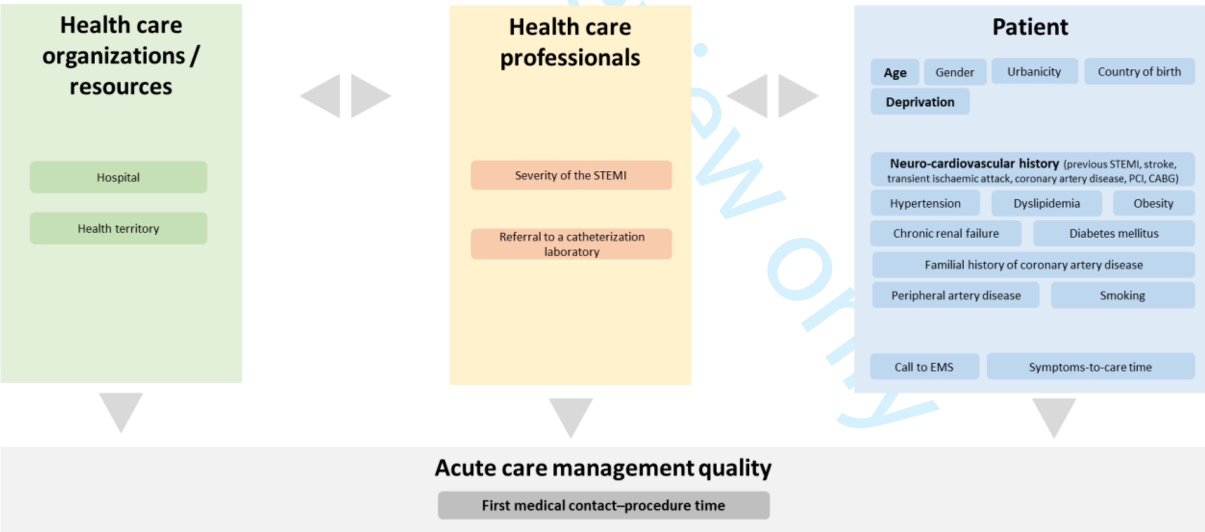
Classification of the variables according to the conceptual framework and used for the directed acyclic graphs (DAG)

Variables identified in the literature and available in the databases were classified into each dimension. Selected confounders were then identified by six DAG, one for each model. We forced adjustment for age and gender.

Stroke cohort



STEMI cohort



In bold: exposure variables,
CABG=coronary artery bypass graft, EMS=emergency medical service, PCI= percutaneous coronary intervention, STEMI=segment elevation myocardial infarction.

Confounders introduced in the stroke and STEMI final models estimating the association between clinical and social vulnerabilities effects on care management times

Category of exposure	STEMI cohort Models	Stroke Cohort Models
Age	Gender, hospital (random effect), health territory (random effect)	Gender, hospital (random effect), health territory (random effect)
Neuro-cardiovascular history	Age, gender, diabetes mellitus, hypertension, dyslipidemia, obesity, smoking, hospital (random effect), health territory (random effect)	Age, gender, diabetes mellitus, smoking, FDep15, hospital (random effect), health territory (random effect)
Fdep 15	Age, gender, country of birth, hospital (random effect), health territory (random effect)	Age, gender, urbanicity, country of birth, hospital (random effect), health territory (random effect)

FDep15=deprivation index; STEMI=segment elevation myocardial infarction; urbanicity of residence: urban of the patient's residence area defined as commune or group of communes with a continuous built-up area with at least 2,000 inhabitants.

Supplementary material 2.

Description of the stroke and STEMI cohorts study sample (N=9,218)

		Stroke cohort (N=6,436)		STEMI cohort (N=2,782)	
		n	(%)	n	Median
Patient socio-demographic characteristics					
Sexe		6,436		2,782	
	Male	3533	(54.9)	2033	(73.1)
	Female	2903	(45.1)	749	(26.9)
Age		6,436		2,776	
	[18-65 years[	1201	(18.7)	1381	(49.7)
	[65 years and older[	5235	(81.3)	1395	(50.3)
	Missing values			6	
Urbanicity		6,153		2,543	
	Urban	4,451	(72.3)	1,843	(72.5)
	Rural	1,702	(27.7)	700	(27.5)
	Missing values	283		239	
Accessibility to general practitioners (APL MG 2018)		6,171		2,537	
	[0 - 3,1[	989	(16.0)	399	(15.7)
	[3,1 - 3,8[	1139	(18.5)	460	(18.1)
	[3,8 - 4,7[	1939	(31.4)	773	(30.5)
	[4,7 et plus]	2104	(34.1)	905	(35.7)
	Missing values	265		245	
Deprivation (Fdep15)		6,145		2,537	
	Most advantaged	994	(16.2)	325	(12.8)
	Advantaged	1522	(24.8)	596	(23.5)
	Intermediate	1115	(18.1)	578	(22.8)
	Disadvantaged	1185	(19.3)	578	(22.8)
	Most disadvantaged	1329	(21.6)	460	(18.1)
	Missing values	*291*		*245*	
Patient clinical history and risk factors					
Neuro-cardiovascular history		6,436		2,782	
	Absence	4594	(71.4)	1822	(65.5)
	Presence	1842	(28.6)	569	(20.5)
	Unknown			391	(14.0)
Coronary artery disease or STEMI history		6,436		2,782	
	No	5660	(87.9)	2,031	(73.0)
	Yes	776	(12.1)	530	(19.1)
	Unknown			221	(7.9)
Coronary artery disease		6,436			
	Absence	5,877	(91.3)		
	Presence	559	(8.7)		
Previous STEMI		6,436			
	Absence	6,057	(94.1)		
	Presence	379	(5.9)		
Previous stroke or transient ischemic attack		6,436			
	Absence	5,166	(80.3)		
	Presence	1,270	(19.7)		
Peripheral arterial disease		6,436		2,782	
	No	6,144	(95.5)	2,245	(80.7)
	Yes	292	(4.5)	70	(2.5)
	Unknown			467	(16.8)
Chronic renal failure				2,782	
	No			2,264	(81.4)
	Yes			47	(1.7)
	Unknown			471	(16.9)
Atrial fibrillation		6,436			
	Absence	5,348	(83.1)		
	Presence	1,088	(16.9)		
Cardiac failure		6,436			
	Absence	6,114	(95.0)		
	Presence	322	(5.0)		

Obesity				2,782	
	Absence			1801	(64.7)
	Presence			513	(18.4)
	Unknown			468	(16.8)
Diabetes mellitus		6,436		2,782	
	No	5,198	(80.8)	2,119	(76.2)
	Yes	1,238	(19.2)	414	(12.9)
	Unknown			249	(9.0)
Arterial hypertension		6,436		2,782	
	No	2,419	(37.6)	1,278	(45.9)
	Yes	4,017	(62.4)	1,356	(48.7)
	Unknown			148	(5.3)
Dyslipidemia		6,436		2,782	
	No	4,618	(71.8)	1,708	(61.4)
	Yes	1,818	(28.2)	887	(31.9)
	Unknown			187	(6.7)
Active smoking		6,436		2,782	
	No	5,103	(79.3)	1,194	(42.9)
	Yes	1,333	(20.7)	1,163	(41.8)
	Unknown			425	(15.3)
Familial history of coronary artery disease				2,782	
	No			2070	(74.4)
	Yes			455	(16.4)
	Unknown			257	(9.2)

APL MG=potential accessibility to general practitioners, STEMI=segment elevation myocardial infarction.

STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	ok, page 1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	ok, page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	ok, page 4
Objectives	3	State specific objectives, including any prespecified hypotheses	ok, page 6
Methods			
Study design	4	Present key elements of study design early in the paper	ok, page 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	ok, pages 6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	ok, pages 6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	ok, pages 6,7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	ok, pages 6,7
Bias	9	Describe any efforts to address potential sources of bias	ok, page 6,7,8
Study size	10	Explain how the study size was arrived at	ok, page 6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	ok, page 8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	ok, page 8
		(*b*) Describe any methods used to examine subgroups and interactions	ok, page 8
		(*c*) Explain how missing data were addressed	ok, page 7
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	ok, page 8
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	ok, page 8,9, suppl mat.
		(b) Indicate number of participants with missing data for each variable of interest	ok, tables

		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	ok, tables
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	ok, page 9,10
		(*b*) Report category boundaries when continuous variables were categorized	ok, tables
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	ok, pages 10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	ok, pages 12,13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	ok, pages 10,11,12
Generalisability	21	Discuss the generalisability (external validity) of the study results	ok, pages 13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	ok, page 15

NA= not applicable

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Social and clinical vulnerability in stroke and STEMI management during the COVID-19 pandemic: A registry-based study

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Social and clinical vulnerability in stroke and STEMI management during the COVID-19 pandemic: A registry-based study

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ABSTRACT

Objective. To evaluate whether the first wave of the COVID-19 pandemic resulted in a deterioration in the quality of care for socially and/or clinically vulnerable stroke and ST-segment elevation myocardial infarction (STEMI) patients.

Design. Two cohorts of STEMI and stroke patients in the Aquitaine neuro-cardiovascular registry.

Setting. Six emergency medical services, 30 emergency units, 14 hospitalisation units, and 11 catheterisation laboratories in the Aquitaine region in France.

Participants. This study involved 9218 patients (6436 stroke and 2782 STEMI patients) in the neuro-cardiovascular registry from January 2019 to August 2020.

Primary outcome measures. Care management times in both cohorts: first medical contact-to-procedure time for the STEMI cohort; emergency unit admission-to-imaging time for the stroke cohort. Associations between social (deprivation index) and clinical (age > 65 years, neuro-cardiovascular history) vulnerabilities and care management times were analysed using multivariate linear mixed models, with an interaction on the time period (pre–, per–, and post–first COVID-19 wave).

Results. The first medical contact–procedure time was longer for elderly ($p < 0.001$) and "very socially disadvantaged" ($p = 0.003$) STEMI patients, with no interaction regarding the COVID-19 period (age, $p = 0.54$; neuro-cardiovascular history, $p = 0.70$; deprivation, $p = 0.64$). We found no significant association between vulnerabilities and the admission–imaging time for stroke patients, and no interaction with respect to the COVID-19 period (age, $p = 0.81$; neuro-cardiovascular history, $p = 0.34$; deprivation, $p = 0.95$).

Conclusions. This study revealed pre-existing inequalities in care management times for vulnerable STEMI and stroke patients; however, these inequalities were neither accentuated nor reduced during the first COVID-19 wave. Measures implemented during the crisis did not alter the structured emergency pathway for these patients.

Trial registration: NCT04979208

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The study analysed two large high-quality data cohorts comprising almost 10000 stroke and STEMI patients, managed in a large panel of care structures throughout the Aquitaine region, over a period of several months before and after the first wave.
- We studied vulnerabilities from two perspectives, a social perspective through an ecological social deprivation index and a clinical perspective through risk factors of severe COVID-19.
- The explanatory analyses yield robust results due to the large amount of data collected (clinical and socio-geographical characteristics, acute care management pathway data), enabling integration of a wide variety of confounders.
- The exclusion of patients who did not enter the healthcare system prevented quantification of healthcare system avoidance, that is supposed to have been more frequent among socially and/or clinically vulnerable patients during the COVID-19 pandemic.
- The study area was limited to the Aquitaine region, one of the regions least affected by the first wave of the COVID-19 pandemic in France; this situation could have led to the exertion of less pressure on health services.

INTRODUCTION

ST-segment elevation myocardial infarction (STEMI) and stroke are life-threatening and highly time-sensitive emergencies. The time elapsed from symptom onset to treatment is a predictor of patients' mortality and functional recovery.(1,2) The standardised and timed care pathways for these two diseases depend initially on a patient's use of the emergency medical service (EMS) system, followed by close collaboration between emergency structures and specialised technical platforms (e.g., catheterisation laboratories, stroke units).(1,2) The quality of care is often evaluated under the prism of the time from first medical contact (FMC) to treatment.(1,2)

In France, patients with acute chest pain or neurological deficit are advised to rapidly call the nationwide EMS using a unique medical dispatch number. In cases of suspected stroke or STEMI, the EMS dispatches rapid transport, including a doctor for STEMI and life-threatening situations, to transfer the patient to a specialised technical platform. If not suspected, the EMS physician may refer the patient to a general practitioner for initial evaluation, or advise them to go to the emergency unit (EU).

Patients with STEMI and stroke face social and health inequality issues. Socially vulnerable (i.e., disadvantaged) patients with neuro-cardiovascular diseases have higher morbidity and mortality rates.(3,4) Four markers of social position and socioeconomic status have been associated with cardiovascular disease in high-income countries: income level, educational attainment, employment status, and environmental factors.(5) These inequalities are attributable to a higher prevalence of biological, behavioral and psychosocial cardiovascular risk factors in the more socially disadvantaged population but also to more difficulties in accessing healthcare and lower-quality acute care management.(4,6,7) The organisation of the healthcare system, as a social health determinant, leads to health inequalities, due mainly to challenges related to communication and health literacy, implicit bias, and/or a lack of culturally competent care.(8)

The 2019 coronavirus disease (COVID-19) dramatically modified healthcare systems worldwide and had major consequences for patients' access to care for stroke and STEMI.(9–11) From February to March 2020, many health authorities, including those in France, implemented strict nationwide lockdowns and series of policies to curb the surge of patients requiring critical care. This crisis, and particularly the lockdown periods, induced the major reorganisation of healthcare systems and modified the use of care to accommodate the onslaught of patients with COVID-19.(12) Studies of the association between the COVID-19 pandemic and the quality of stroke and STEMI management have yielded contrasting results, with most revealing longer management delays and reductions in the number of procedures performed.(9,10,13)

During pandemics (e.g., of influenza, plague), pre-existing inequalities affecting many aspects of patients' care pathways (e.g., loss of employment and income; social isolation, especially for elderly individuals; and mental health issues, particularly for young people) are usually amplified.(14–18) During the COVID-19 pandemic, COVID-19 exposure, severe disease, hospitalisation, and death were more frequent among socially disadvantaged people.(15,17–19) This population benefited less from the collective protective measures taken against COVID-19, had more difficulty accessing preventative healthcare, and had lower rates of COVID-19 testing and vaccination.(14) Some experts consider COVID-19 to be a syndemic, rather than a pandemic. These interactions between COVID-19 and pre-existing socioeconomic inequalities in non-communicable diseases are an illustration.(16) Indeed, "syndemics are characterised by biological and social interactions between conditions and states, interactions that increase a person's susceptibility to harm or worsen their health outcomes."(16) We hypothesised that socially vulnerable patients, defined as those with low socioeconomic status, may experience longer acute management times during the COVID-19 pandemic.

In France, to protect more vulnerable patients and adapt care, health authorities identified several risk factors of severe COVID-19 based on demographic (advanced age) and medical (especially cardiovascular co-morbidities) characteristics.(20) For these populations defined as "clinically vulnerable patients", French authorities have stressed the importance of adhering to barrier measures, maintaining physical distancing, particularly during hospitalisation, and to limit travel to high-risk areas for SARS-CoV-2 transmission. Information about these risk factors was covered widely in the media which may have led exposed individuals with these underlying conditions to delay seeking treatment.(21) Based on these recommendations, we hypothesised that additional protective measures may have been implemented for these clinically more vulnerable populations, resulting in increased management delays.

To our knowledge, only one study has evaluated whether COVID-19 modified the associations among the educational level, deprivation, hospital admission indicators, and quality of hospital care, especially for patients with neuro-cardiovascular diseases.(22) The researchers found larger declines in the hospital access of women, elderly, and less-educated individuals; in contrast, the timeliness of percutaneous coronary intervention (PCI) showed no education- or deprivation-related gradient.

Since 2012, the "CNV Registry" of neuro-cardiovascular diseases evaluate the care pathways for STEMI and stroke patients in the Aquitaine region of southwestern France (3 million inhabitants). This registry provides a unique opportunity to study differences in care management and their evolution over time in a country with universal health coverage.(23)

COVID-19 profoundly modified access to and the use and organisation of care, against a backdrop of pre-existing inequalities in neuro-cardiovascular disease.(12) The notion of a "syndemic" and our hypothesis that management times were longer for patients at risk of severe COVID-19 during its first wave prompted our investigation of whether first COVID-19 wave resulted in the deterioration of the quality of care for socially and clinically vulnerable stroke and STEMI patients, using data from the CNV Registry.

METHODS

Study design and population

We used two exhaustive retrospective cohorts of adult stroke and STEMI patients admitted to a care structure in the Aquitaine region whose data were entered into the CNV Registry between January 1, 2019, and August 31, 2020.(23)

The STEMI cohort comprised patients with recent (<24 h after symptom onset) STEMI managed in one of the six health territories in Aquitaine, each centered around an EMS, comprising 30 EUs and 11 catheterisation laboratories (nearly 1800 STEMIs are seen annually).

The stroke cohort comprised patients with recent ischemic or hemorrhagic stroke (excluding transient ischemic attacks), diagnosed by brain imaging and validated by neurovascular physicians, that was managed in five health territories in Aquitaine, comprising 14 (7 with stroke units) of the 20 hospitals caring for more than 30 strokes per year in Aquitaine (nearly 5000 strokes are seen annually).

The CNV Registry was approved by the French authority on data protection and met the regulatory requirements for the handling of patient information (file 2216283). The study was approved by the Bordeaux University Hospital Ethics Board (CER–BDX 2023–131).

Data collection

The CNV Registry contains information on patients' sociodemographic (age, gender, place of residence) and clinical [medical history, cardiovascular risk factors, stroke clinical severity (modified Rankin scale and National Institute of Health Stroke Score), stroke type (ischemic/hemorrhagic)] characteristics, use of care (calls to emergency services, FMC, symptom onset–care time), acute care management quality (times between key management steps, pre-hospital and hospital pathway types, treatment), and structural characteristics of care (care during on-call activity, calls to emergency services during care, hospital administrative status, FMC–catheterisation laboratory distance). Data are collected prospectively by physicians; consolidated retrospectively by clinical research assistants and then extracted from the hospital information system. Data from the two cohorts were integrated into one data warehouse enabling the reconstruction of the STEMI or stroke management pathway.(12)

Outcomes

The primary endpoints were acute-care management times, which reflect the quality of care. For the STEMI cohort, we used the FMC–procedure time [delay (in minutes) between the FMC (mobile intensive care unit arrival or EU admission) and the start of a treatment procedure]. For the stroke cohort, we used the EU admission–imaging time [delay (in minutes) between EU admission and the start of the first imaging]. This selection of an interval that focused on the beginning of in-hospital stroke care was required due to the heterogeneity of the pre-hospital pathways and treatments applied.

Exposure

Clinically vulnerable persons at risk of severe COVID-19 were those aged > 65 years; with neuro-cardiovascular history including previous STEMI, stroke, or transient ischemic attack; and/or with coronary artery disease history. For the STEMI cohort, the history of a PCI, a coronary artery bypass graft was also included.

Due to the lack of individual socioeconomic data, an ecological social deprivation score was assigned to each commune (the smallest administrative unit in France) of patients' residence using the 2015 deprivation index (Fdep15) to assess social vulnerability.(24) This index is associated strongly with mortality at all geographic scales. It served as the first dimension of a principal component analysis (weighted by population size) of four socioeconomic ecological variables: the percentage of high-school graduates ≥ 15 years old, median household income, percentage of blue-collar workers, and unemployment rate. Quintiles of the Fdep15 scores were computed for metropolitan France, whereby the first quintile (Q1) represented the least and the fifth quintile (Q5) the most disadvantaged communes. We calculated the deprivation score for each patient of our sample with reference to the quintiles of the French population.

Statistical analyses

Analyses were performed separately for each cohort and exposure variable. Associations between clinical and social vulnerabilities' effects on care management times (introduced as continuous variables after logarithmic transformation) were analysed using multivariate linear mixed models (three each for stroke and STEMI), with random effects on hospital and health territories centered around single EMSs. Interactions on the time period were introduced. Three COVID-19 periods were defined according to the dates of first hospital reorganisation (mid-February) and the termination of national lockdown (May 10, 2020): pre-wave (January 1, 2019–February 9, 2020), per-wave (February 10–May 10, 2020), and post-wave (May 11–August 31, 2020). Inspired by the conceptual framework developed by the Health Care Quality Indicator Project of the Organization for Economic Cooperation and Development, we categorised determinants in four dimensions: patients, physicians, care organisations, and quality of care.(25) To develop the causal model, variables were classified into each of these dimensions and confounders were then identified by directed acyclic graphs (DAG; Supplementary Material 1). The relationships between vulnerabilities and care management times were quantified (β) using the contrast method, with statistical significance defined as $p < 0.05$. The exponentials of the beta values [exp(β)], associated 95% confidence intervals (CIs), and percentage changes [1−exp(β)] were then calculated. The statistical analyses were conducted using SAS 9.4.

Patient and public involvement statement

As members of the CNV registry scientific boards, patient representatives were involved in study conception, implementation, and dissemination; they validated data collection and analysis, and results diffusion. Dissemination of results was conducted on the CNV registry website, to the scientific boards, and to care-structure physicians.

This study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines and is registered with ClinicalTrials.gov (NCT04979208).

RESULTS

Sample characteristics

The sample comprised 9218 patients (6436 with stroke, 2782 with STEMI); 54.9% of the stroke patients and 73.1% of the STEMI patients were male. Patients aged > 65 years accounted for 81.3% and 50.1% of the stroke and STEMI patients, respectively. One-quarter of patients had neuro-cardiovascular history (stroke, 28.6%; STEMI, 20.5%). The distributions of the deprivation index quintiles in our sample, ordered from the most advantaged to the most disadvantaged patients of our sample, were 16.2%, 24.8%, 18.1%, 19.3%, and 21.6% for stroke patients and 12.8%, 23.5%, 22.8%, 22.8%, and 18.1% for STEMI patients (Supplementary Material 2).

Acute care management times

Stroke cohort

In the pre-wave period, the median admission–imaging time was longer for stroke patients aged > 65 years than for younger patients (84 vs. 79 min) and for patients without than for those with neuro-cardiovascular history (86 vs. 76 min). Acute-care management times were longest for the most advantaged and most disadvantaged patients (both 88 min vs. 77–86 min for the other social deprivation categories; Table 1).

The median admission–imaging time was longer during the per-wave period than during the pre-wave period, regardless of age or neuro-cardiovascular history, but was shorter for the most advantaged patients (80 vs. 88 min). This time was shorter during the post-wave period than during the per-wave period, regardless of age, but was longer for the most advantaged patients (90 vs. 80 min).

Table 1. Admission-to-imaging time according to vulnerabilities and COVID-19 periods - Stroke cohort (N=6436)

	Global (N=6436)	Pre-wave (N=4140)	Per-wave (N=1080)	Post-wave (N=1216)
	Median [IQR] (n)	Median [IQR] (n)	Median [IQR] (n)	Median [IQR] (n)
All patients	86 [47;194] (4819)	83 [45;201] (3014)	91 [51;175] (889)	88 [52;191] (916)
Missing value	*(1617)*	*(1126)*	*(191)*	*(300)*
Clinical vulnerability				
Age	*(4819)*	*(3014)*	*(889)*	*(916)*
[18-65 years[	84 [45;193] (868)	79 [43;208] (536)	92 [48;177] (157)	85 [45;174] (175)
[65 years and older[	86 [48;194] (3951)	84 [45;199] (2478)	91 [51;175] (732)	88 [52;197] (741)
Missing value	*(1617)*	*(1126)*	*(191)*	*(300)*
Neuro-cardiovascular history	*(4819)*	*(3014)*	*(889)*	*(916)*
Absence	88 [47;197] (3430)	86 [45;204] (2128)	93 [51;177] (661)	86 [50;197] (641)
Presence	83 [48;184] (1389)	76 [45;187] (886)	87 [49;173] (228)	90 [57;189] (275)
Missing value	*(1617)*	*(1126)*	*(191)*	*(300)*
Social vulnerability				
Deprivation (Fdep15)	*(4610)*	*(2821)*	*(884)*	*(905)*
Most advantaged	87 [47;235] (743)	88 [46;240] (469)	80 [44;202] (145)	90 [54;239] (129)
Advantaged	84 [45;206] (1107)	77 [42;216] (637)	97 [51;181] (235)	85 [48;202] (235)
Intermediate	87 [48;179] (831)	83 [46;189] (492)	92 [53;153] (168)	94 [54;188] (171)
Disadvantaged	86 [47;183] (903)	86 [46;186] (568)	86 [47;170] (154)	86 [51;179] (181)
Most disadvantaged	89 [52;192] (1026)	88 [51;198] (655)	95 [55;175] (182)	82 [52;148] (189)
Missing value	*(1826)*	*(1319)*	*(196)*	*(311)*

IQR=interquartile range

STEMI cohort

In the pre-wave period, the median FMC–procedure time was longer for STEMI patients aged > 65 years than for younger patients (103 vs. 96 min). Its length increased with the degree of disadvantage (from 82 min for the most advantaged to 129 min for the most disadvantaged patients; Table 2).

The median FMC–procedure time was slightly shorter during the per-wave period than during the pre-wave period, regardless of age or neuro-cardiovascular history, but was longer for the most advantaged patients (92 vs. 82 min). This time was longer during the post-wave period than during the per-wave period, especially for elderly patients (117 vs. 101 min), those with neuro-cardiovascular history (112 vs. 89 min), and those most advantaged (119 vs. 92 min).

Table 2. FMC-to-procedure time according to vulnerabilities and COVID-19 periods - STEMI cohort (N=2782)

	Global (N=2782)	Pre-wave (N=1868)	Per-wave (N=407)	Post-wave (N=507)
	Median [IQR] (n)	Median [IQR] (n)	Median [IQR] (n)	Median [IQR] (n)
All patients	99 [71;157] (2364)	100 [71;158] (1577)	95 [69;152] (353)	102 [71;153] (434)
Missing value	*(418)*	*(291)*	*(54)*	*(73)*
Clinical vulnerability				
Age	(2364)	(1577)	(353)	(434)
[18-65 years[	95 [69;147] (1207)	96 [69;152] (794)	93 [68;134] (175)	94 [69;134] (238)
[65 years and older[	105 [73;173] (1157)	103 [74;169] (783)	101 [70;190] (178)	117 [74;167] (196)
Missing value	*(418)*	*(291)*	*(54)*	*(73)*
Neuro-cardiovascular history	(2364)	(1577)	(353)	(434)
Absence	98 [71;156] (1699)	99 [71;157] (1115)	97 [70;157] (267)	96 [70;149] (317)
Presence	101 [70;159] (468)	102 [72;156] (318)	89 [61;135] (67)	112 [74;169] (83)
Unknown	98 [74;161] (197)	97 [73;180] (144)	97 [81;134] (19)	118 [78;154] (34)
Missing value	*(418)*	*(291)*	*(54)*	*(73)*
Social vulnerability				
Deprivation (Fdep15)	(2343)	(1565)	(351)	(427)
Most advantaged	90 [64;152] (304)	82 [63;149] (203)	92 [62;127] (48)	119 [79;177] (53)
Advantaged	91 [66;145] (551)	92 [68;139] (350)	93 [62;162] (90)	89 [65;150] (111)
Intermediate	95 [70;150] (538)	97 [69;156] (378)	91 [68;157] (71)	89 [72;129] (89)
Disadvantaged	102 [73;150] (536)	101 [75;154] (353)	94 [70;140] (82)	106 [73;151] (101)
Most disadvantaged	124 [86;204] (414)	129 [85;215] (281)	120 [90;198] (60)	122 [93;180] (73)
Missing value	*(439)*	*(303)*	*(56)*	*(80)*

IQR=interquartile range

Effects of the COVID-19 first wave

Stroke cohort models

The final stroke models showed no significant association among advanced age [n = 4819, exp(β) = 1.08, 95% CI 1.00–1.16, p = 0.07], neuro-cardiovascular history [n = 4610, exp(β) = 0.97, 95% CI 0.91–1.04, p = 0.44], deprivation (n = 4606, p = 0.30), and the EU admission–imaging time, and no interaction with the COVID-19 period (age, p = 0.81; neuro-cardiovascular history, p = 0.34; deprivation, p = 0.95; Figure 1).

STEMI cohort models

Advanced age was associated with a 15% increase in the FMC–procedure time [n = 2364, exp(β) = 1.15, 95% CI 1.07–1.24, p < 0.001]. No significant association was noted between patients' neuro-cardiovascular history and the FMC–procedure time [n = 2167, exp(β) = 1.08, 95% CI 0.98–1.19, p = 0.14]. Compared with those in the other four quintiles, FMC–procedure times were 15–22% longer for patients in the most disadvantaged quintile (n = 2343, p = 0.003). No significant COVID-19 period interaction affected the relationships between the vulnerabilities studied and the FMC–procedure time (age, p = 0.54; neuro-cardiovascular history, p = 0.70; deprivation, p = 0.64; Figure 2).

DISCUSSION

Main results

This analysis of the healthcare pathways for STEMI and stroke patients included in the CNV Registry showed that care management times for socially or clinically vulnerable patients did not worsen during the first wave of the COVID-19 pandemic, despite changes in the access to and use and organisation of care. Nonetheless, regardless of the COVID-19 period, acute-care management times were longer for elderly and the most disadvantaged STEMI patients.

Social and clinical vulnerability in stroke and STEMI management during the COVID-19 pandemic

Our results are concordant with those of a study conducted in Italy, which revealed no educational or deprivation gradient for cardiovascular acute-care management times.(22) Several factors can explain the resilience of stroke and STEMI care pathways for vulnerable populations.

First, STEMI and stroke networks in France are structured as well-defined, organised, and dedicated pathways. Highly structured patient-centered clinical pathways improve the quality of care for chronic and acute conditions with predictable trajectories.(26,27) Guidelines and national stroke and STEMI improvement programs recommend the implementation of such structured pathways, which include close collaborations between healthcare professionals and patient orientation to the EMS system and specialised technical platforms. A study of the impacts of changes in the use of care and implementation of hospital reorganisation spurred by the COVID-19 pandemic on acute management times for stroke and STEMI revealed no deep alteration of the emergency pathway construct.(12) Socially and/or clinically vulnerable populations have also benefited from the resilience of the STEMI and stroke pathways.

Second, in the particular context of the first COVID-19 wave, the mass media widely relayed information from health institutions. The whole population was worried and very concerned about its health. Lockdown measures made people more available, and routinely exposed, to mainstream media that were highly focused on the pandemic and health messages. These factors are associated with a greater likelihood of the adoption of recommended prevention practices.(28) Thus, broad health-related media coverage may have had a positive influence on health literacy for the whole population, which may have positively influenced the use of the healthcare system.(29)

Third, the EMS was identified as the first contact to limit exposure and regulate urgent calls during the first COVID-19 wave in France. The media relayed this information. French hospitals increased regulation capacities to face the rise in EMS calls, in an attempt to preserve access to care and the capacity to handle vital emergencies for the entire population.(30)

Fourth, France adopted a specific strategy in March 2020 to support the economy, companies, and jobs through measures that include financial support for disadvantaged populations, salary preservation, the prohibition of layoffs, and housing assistance.(31) Associated with universal healthcare coverage, these actions may have contributed to mitigate the social consequences of the pandemic.

Social and clinical vulnerability in stroke and STEMI management regardless of the COVID-19 pandemic

Several studies, including the present work, have shown that acute-care management times are longer for elderly and socially vulnerable STEMI patients.(32–34) Concerning stroke, we found no alteration in the acute-care management time for elderly and socially vulnerable stroke patients. The results pertaining to stroke patients may be explained by our examination of the EU admission–imaging time focused on the beginning of in-hospital care. Unlike the STEMI pathway, this time involves such a small portion of stroke patients' pathways that it could have been difficult to detect an effect.

Age

Regarding specifically age for STEMI patients, greater initial clinical severity, atypical symptoms, and a longer delay in admission may explain these findings.(33) Half of the STEMI patients in our sample were aged > 65 years. The proportion of stroke patients > 65 years was 81%, which made it difficult to demonstrate an effect. To our knowledge, only one study, conducted in England, has revealed an association between older age and a longer admission–computerised tomography time for stroke patients.(35)

Socioeconomic status

Findings with respect to socioeconomic status do not converge for STEMI. Biswas et al. (32) found that the median time to reperfusion in Australia, a country with universal healthcare, between 2005 and 2015 was 4 min longer for lower socioeconomic quintiles than for the highest quintile. Vasaiwala et al. (34) found a direct correlation between income levels in the United States and the proportion of patients meeting the guideline-recommended door–balloon time. In contrast, Heo et al. (36) found no association between the educational level and door–balloon time in Korea. None of these studies involved control for the confounders. Additional dedicated analyses of the relationship between socioeconomic status and acute-care management time are needed, especially for elderly patients with accumulated comorbid factors due to their disadvantaged status.

Few studies have involved the exploration of acute stroke management times according to socioeconomic status, with contrasting results explained by the specificities of healthcare systems.(3,37) In a study conducted in England, socially vulnerable patients were less likely to undergo high-quality recommended processes and more likely to undergo early supported discharge.(3) A study conducted in Sweden showed that university-educated patients were more likely to be treated than were less-educated patients.(37)

Neuro-cardiovascular history

Regardless of the COVID-19 period, we found no significant influence of patients' neuro-cardiovascular history on acute-care management times, consistent with reported findings for STEMI patients.(38) To our knowledge, no other study has evaluated this relationship for stroke care.

Implications for clinical practice and health system performance

While the COVID-19 pandemic crisis is nearly resolved, our findings remain valuable for health institutions and professionals to prepare for future health crises. The structured emergency pathway for strokes and STEMI patients and hospital reorganisations ensured sustained care quality.(12) In our study, the COVID-19 crisis did not have any differential impact on social health inequalities, suggesting a good resilience of the French healthcare network. Organisational strategies employed, such as a dedicated life-threatening emergency pathway, transversal reorganisations aiming at concentrating resources on emergency care (12), targeted communication, and increased regulation capacities, could be replicated in new crises and extended to other conditions. Pre-existing STEMI management inequalities partly result from the healthcare system organisation. In a study about disparities in cardiovascular disease, these inequalities are linked to language challenges, health literacy, implicit bias, and the absence of culturally competent care.(8) This may lead to less accurate medical interviews and suboptimal medical decisions. Further research is essential to investigate these hypotheses and evaluate potential corrective measures.

Strengths and weaknesses

Our study, one of the first to examine the effects of the COVID-19 crisis on the quality of care for STEMI and stroke patients in Europe with consideration of health and social inequalities, involved the parallel analysis of two high-quality databases containing data on large numbers of stroke and STEMI patients managed in a large panel of care structures in the Aquitaine region.

Our study has some limitations, particularly with regard to the population. The study area was limited to the Aquitaine region, one of the regions least affected by the first wave of the COVID-19 pandemic.(39) This situation could have led to the exertion of less pressure on health services (especially the EMS, STEMI, and stroke network). Arguments support the sample's representativeness for stroke and STEMI patients in hospitals during this period, making our results likely applicable to all of France. First, a stroke study showed that the use of care was similar regardless of pandemic intensity.(40) Second, a previous study with the same database highlighted results consistent with other French studies on the evolution of stroke and STEMI patient admissions.(12) Third, characteristics and acute management times for stroke and STEMI patients in the 'CNV registry' align with those in other French regions. It would be interesting to repeat the study in another region, or in another country more affected by the pandemic, to test the external validity of the results.

Moreover, patients who did not enter the healthcare system because they had died or did not benefit from hospital care, as well as STEMI patients with symptoms for >24 h, were not included. The exclusion of these patients may have generated selection bias, and prevented us from quantifying the phenomenon of healthcare system avoidance that could be supposed to be more frequent among socially and/or clinically vulnerable patients during the COVID-19 crisis, as stated in a Danish study;(41) it also entails the risk that increases in the delay to use of care were underestimated for some patient subgroups. A French study revealed a 24% decrease in emergency consultations for STEMI and an 18% decrease for stroke.(42) However, a national survey analysed the characteristics associated with not seeking care, in 2017 and 2020 , revealing factors such as younger age, foreign nationality, living alone, and lack of general practitioner care.(43) The proportion of patients not seeking care increased during COVID-19 pandemic, but the population was not significantly different from the one before, suggesting a limited selection bias.

Our explanatory analyses yield robust results, with the inclusion of appropriate confounding variables identified by the DAG method. The large panel of data collected enabled the integration of a wide variety of confounders, including clinical characteristics and socio-geographical factors.

Given the lack of individual-level socioeconomic data in the CNV Registry, which prevented the assignment of social determinants for each patient, we used a residence area–based measure, which is a major limitation of our study. However, we determined deprivation indices using a validated tool that has been used in many studies conducted in France.(24) Moreover, the socio-ecological measure of deprivation tends to underestimate social inequalities observed using individual data; thus, caution is advised when attributing group-level estimates to individuals.(6) Additional limitations of this study include our inability to include all clinical risk factors of severe COVID-19 and information about patients' educational levels, individual resources, and social support to further explore their precariousness and health literacy. The COVID-19 pandemic may have had a greater impact on the access to and quality of care for the most precarious individuals.

A major methodological issue of this study is that we defined the per-wave period according to the implementation of healthcare reorganisation and transformation of societal functioning to fight the COVID-19 pandemic.(12) We began the per-wave period at the time of the first hospital reorganisation implementation and ended it at the time of lockdown lifting. Although data for the CNV Registry are collected continuously, we terminated the follow-up period at the end of August 2020 to enable the timely reporting of results.

Finally, we did not explore gender as a distinct vulnerable group(9) and short- or long-term outcomes such as morbidity, mortality, disability, or rehospitalisation after initial hospitalisation for STEMI or stroke, for which a wide range of socioeconomic disparities exist.(3,41) Separate studies on gender inequalities and inequalities following acute care are currently underway, with a focus on the COVID period.

Conclusions

The first wave of the COVID-19 pandemic induced no deep change in management times for the most socially and/or clinically vulnerable stroke and STEMI patients. Pre-existing inequalities in care management times observed for elderly and most disadvantaged STEMI patients, were neither aggravated nor reduced by changes in the use of care or implementation of hospital reorganisation spurred by the pandemic. These encouraging results may be explained by the well-structured STEMI and stroke networks in France and the reorganisation of the healthcare structure to preserve access and the capacity to care for vital emergencies using the EMS. Additional studies are required to explore findings related to social health inequalities in STEMI management.

- **Figure Legend/Caption**

Figure 1. Estimation of each clinical and social factor (95% confidence interval) on emergency unit admission-to-imaging time.

Estimated overall effects expressed as exp(ß) with 95% CI; results of multivariate linear regression mixed models; variable to be explained: Y=log (emergency unit admission-to-imaging time); (A) results adjusted on period and gender; (B) cardiovascular history was a history of stroke, transient ischemic attack, coronary artery disease, or myocardial infarction; results adjusted on period, age, gender, diabetes and smoking as risk factors, deprivation index; (C) the reference modality for the deprivation index Fdep15 in five categories was "most disadvantaged"; results adjusted on period, age, gender, country of birth, urbanicity of residence.

Figure 2. Estimation of each clinical and social factor (95% confidence interval) on FMC-to-procedure time.

Estimated overall effects expressed as exp(ß) with 95% CI; results of multivariate linear regression mixed models; variable to be explained: Y=log (FMC-to-procedure time); (A) results adjusted on period and gender; (B) cardiovascular history was a history of stroke, transient ischemic attack, coronary artery disease, or myocardial infarction; results adjusted on period, age, gender, diabetes, hypertension, dyslipidemia, obesity and smoking as risk factors ; (C) the reference modality for the deprivation index Fdep15 in five categories was "most disadvantaged"; results adjusted on period, age, gender, country of birth, urbanicity of residence.

- **Data sharing statement**

Deidentified participant data will be available upon reasonable request. Proposals may be submitted to the corresponding author. Data requestors will need to sign a data access agreement

- **Patient consent for publication**

Not applicable.

- **Ethics statements**

The CNV registry was approved by the French authority on data protection "Commission Nationale Informatique et Libertés" (file 2216283) and the study by the Bordeaux University Hospital Ethics Board (CER–BDX 2023–131). All patients received individual information before inclusion in the Registry. The study is based on the secondary use of health data and does not involve human participants. A signed patient consent is not required.

- **Authors' contributions**

EL, FF, SD, FSa and FSe were responsible for the study concept and design. EL and FF conducted the literature review. EL and FSe had full access to all of the data and takes responsibility for their integrity and accuracy. SD and SMH performed the statistical analysis. FSa, EL, SD, FF, FSe, SV, LC, PC, FR, IS, CP interpreted the data. EL, FF, SV, FSa and SD wrote the manuscript. FSe, LC, PC, FR, IS and CP critically reviewed the manuscript.

- **Competing interests statement**

The authors declare that they have no competing interests with this study.

- **Funding statement**

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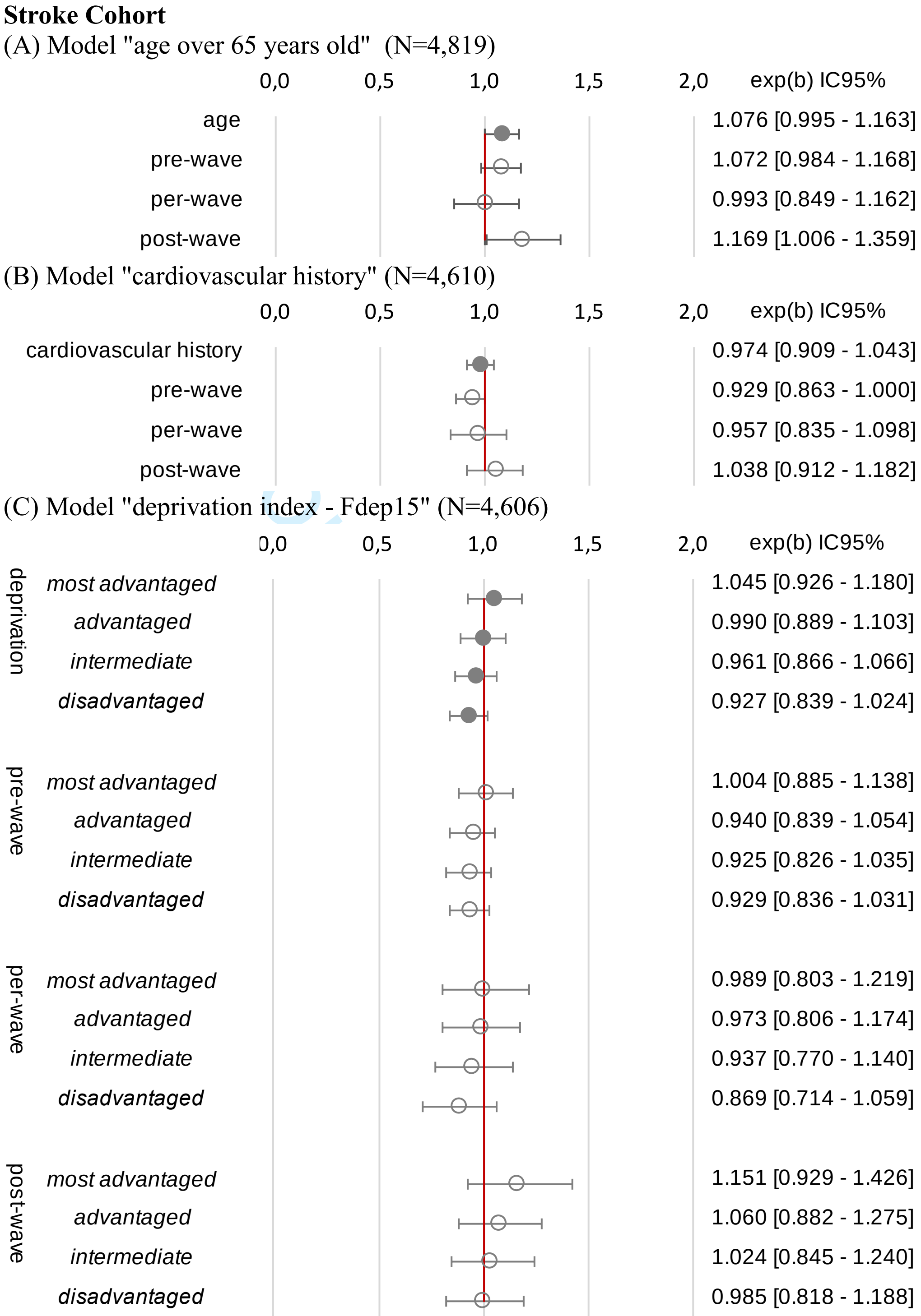


Figure 1. Estimation of each clinical and social factor (95% confidence interval) on emergency unit admission-to-imaging time.

Estimated overall effects expressed as exp(ß) with 95% CI; results of multivariate linear regression mixed models; variable to be explained: Y=log (emergency unit admission-to-imaging time); (A) results adjusted on period and gender; (B) cardiovascular history was a history of stroke, transient ischemic attack, coronary artery disease, or myocardial infarction; results adjusted on period, age, gender, diabetes and smoking as risk factors, deprivation index; (C) the reference modality for the deprivation index Fdep15 in five categories was “most disadvantaged”; results adjusted on period, age, gender, country of birth, urbanicity of residence.

STEMI Cohort

(A) Model "age over 65 years old" (N=2,364)

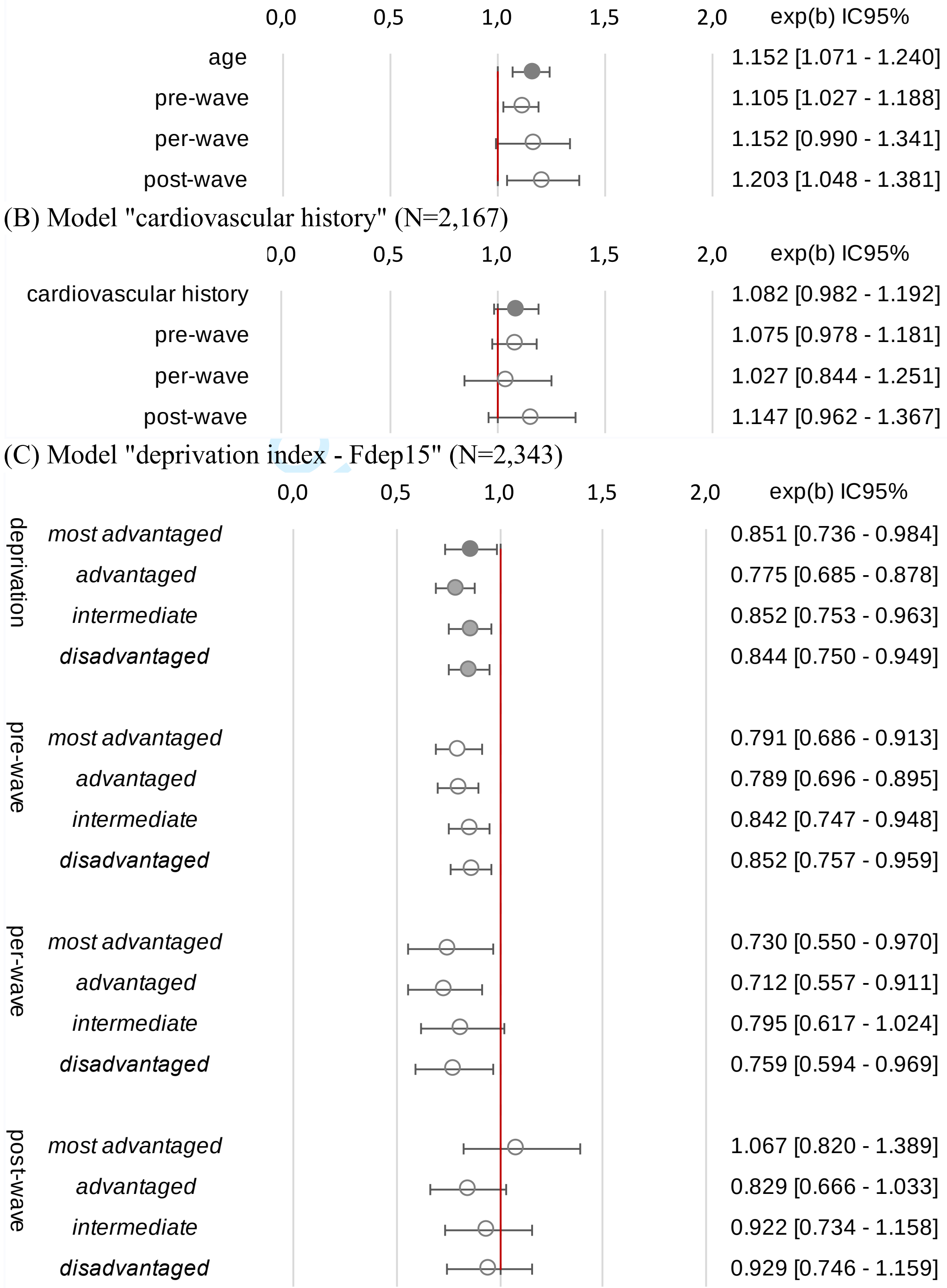
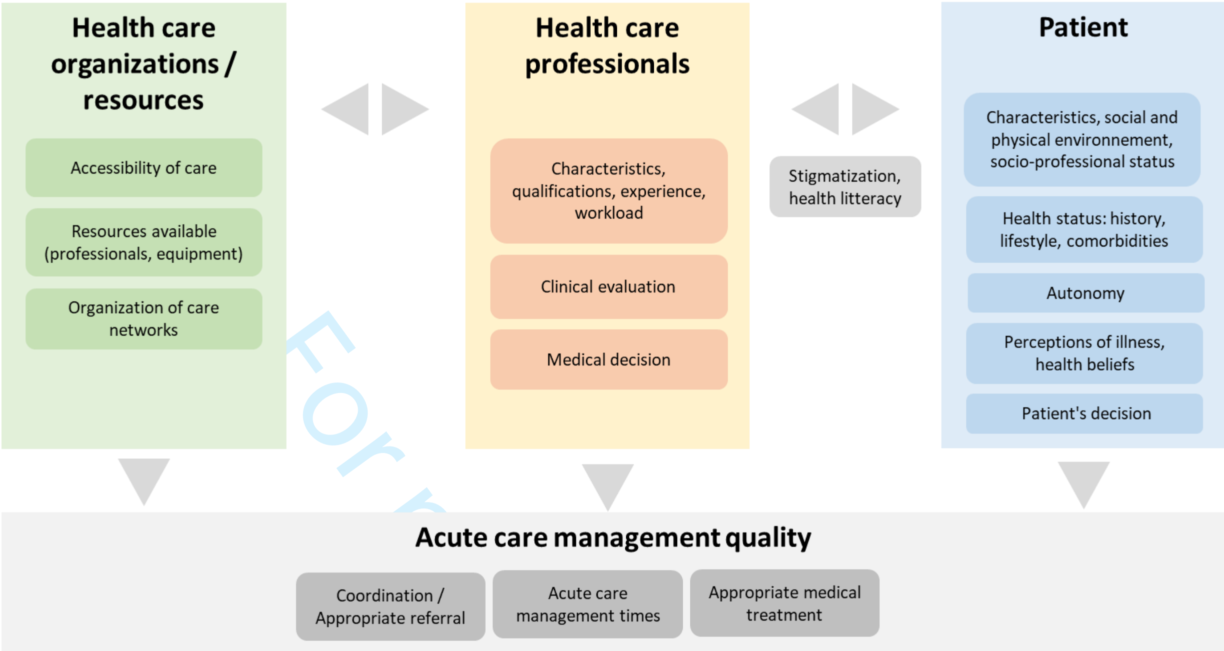


Figure 2. Estimation of each clinical and social factor (95% confidence interval) on FMC-to-procedure time.

Estimated overall effects expressed as exp(ß) with 95% CI; results of multivariate linear regression mixed models; variable to be explained: Y=log (FMC-to-procedure time); (A) results adjusted on period and gender; (B) cardiovascular history was a history of stroke, transient ischemic attack, coronary artery disease, or myocardial infarction; results adjusted on period, age, gender, diabetes, hypertension, dyslipidemia, obesity and smoking as risk factors ; (C) the reference modality for the deprivation index Fdep15 in five categories was "most disadvantaged"; results adjusted on period, age, gender, country of birth, urbanicity of residence.

Supplementary material 1.

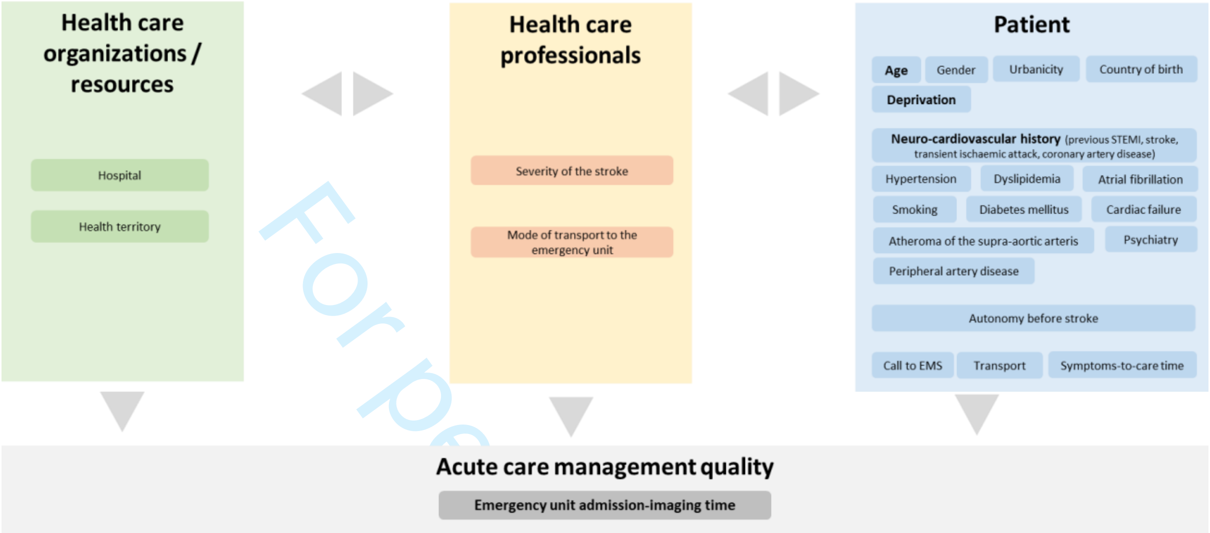
Conceptual framework



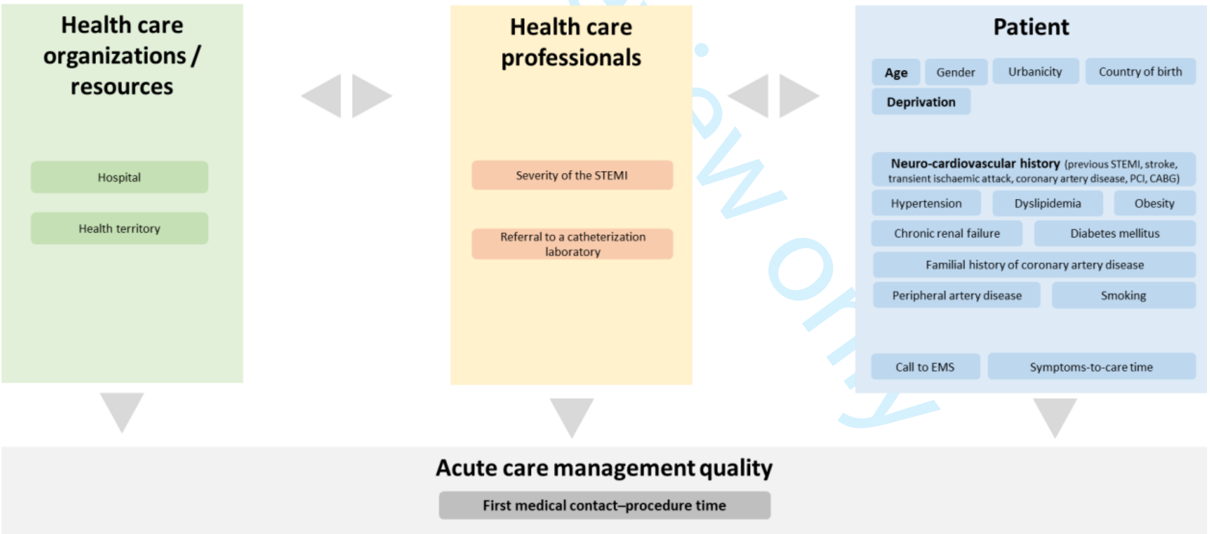
Classification of the variables according to the conceptual framework and used for the directed acyclic graphs (DAG)

Variables identified in the literature and available in the databases were classified into each dimension. Selected confounders were then identified by six DAG, one for each model. We forced adjustment for age and gender.

Stroke cohort



STEMI cohort



In bold: exposure variables,
CABG=coronary artery bypass graft, EMS=emergency medical service, PCI= percutaneous coronary intervention, STEMI=segment elevation myocardial infarction.

Confounders introduced in the stroke and STEMI final models estimating the association between clinical and social vulnerabilities effects on care management times

Category of exposure	STEMI cohort Models	Stroke Cohort Models
Age	Gender, hospital (random effect), health territory (random effect)	Gender, hospital (random effect), health territory (random effect)
Neuro-cardiovascular history	Age, gender, diabetes mellitus, hypertension, dyslipidemia, obesity, smoking, hospital (random effect), health territory (random effect)	Age, gender, diabetes mellitus, smoking, FDep15, hospital (random effect), health territory (random effect)
Fdep 15	Age, gender, country of birth, hospital (random effect), health territory (random effect)	Age, gender, urbanicity, country of birth, hospital (random effect), health territory (random effect)

FDep15=deprivation index; STEMI=segment elevation myocardial infarction; urbanicity of residence: urban of the patient's residence area defined as commune or group of communes with a continuous built-up area with at least 2,000 inhabitants.

Supplementary material 2.

Description of the stroke and STEMI cohorts study sample (N=9,218)

		Stroke cohort (N=6,436)		**STEMI cohort (N=2,782)**	
		n	(%)	n	Median
Patient socio-demographic characteristics					
Sexe		6,436		2,782	
	Male	3533	(54.9)	2033	(73.1)
	Female	2903	(45.1)	749	(26.9)
Age		6,436		2,776	
	[18-65 years[	1201	(18.7)	1381	(49.7)
	[65 years and older[	5235	(81.3)	1395	(50.3)
	Missing values			6	
Urbanicity		6,153		2,543	
	Urban	4,451	(72.3)	1,843	(72.5)
	Rural	1,702	(27.7)	700	(27.5)
	Missing values	283		239	
Accessibility to general practitioners (APL MG 2018)		6,171		2,537	
	[0 - 3,1[	989	(16.0)	399	(15.7)
	[3,1 - 3,8[	1139	(18.5)	460	(18.1)
	[3,8 - 4,7[	1939	(31.4)	773	(30.5)
	[4,7 et plus]	2104	(34.1)	905	(35.7)
	Missing values	265		245	
Deprivation (Fdep15)		6,145		2,537	
	Most advantaged	994	(16.2)	325	(12.8)
	Advantaged	1522	(24.8)	596	(23.5)
	Intermediate	1115	(18.1)	578	(22.8)
	Disadvantaged	1185	(19.3)	578	(22.8)
	Most disadvantaged	1329	(21.6)	460	(18.1)
	Missing values	*291*		*245*	
Patient clinical history and risk factors					
Neuro-cardiovascular history		6,436		2,782	
	Absence	4594	(71.4)	1822	(65.5)
	Presence	1842	(28.6)	569	(20.5)
	Unknown			391	(14.0)
Coronary artery disease or STEMI history		6,436		2,782	
	No	5660	(87.9)	2,031	(73.0)
	Yes	776	(12.1)	530	(19.1)
	Unknown			221	(7.9)
Coronary artery disease		6,436			
	Absence	5,877	(91.3)		
	Presence	559	(8.7)		
Previous STEMI		6,436			
	Absence	6,057	(94.1)		
	Presence	379	(5.9)		
Previous stroke or transient ischemic attack		6,436			
	Absence	5,166	(80.3)		
	Presence	1,270	(19.7)		
Peripheral arterial disease		6,436		2,782	
	No	6,144	(95.5)	2,245	(80.7)
	Yes	292	(4.5)	70	(2.5)
	Unknown			467	(16.8)
Chronic renal failure				2,782	
	No			2,264	(81.4)
	Yes			47	(1.7)
	Unknown			471	(16.9)
Atrial fibrillation		6,436			
	Absence	5,348	(83.1)		
	Presence	1,088	(16.9)		
Cardiac failure		6,436			
	Absence	6,114	(95.0)		
	Presence	322	(5.0)		

Obesity				2,782	
	Absence			1801	(64.7)
	Presence			513	(18.4)
	Unknown			468	(16.8)
Diabetes mellitus		6,436		2,782	
	No	5,198	(80.8)	2,119	(76.2)
	Yes	1,238	(19.2)	414	(12.9)
	Unknown			249	(9.0)
Arterial hypertension		6,436		2,782	
	No	2,419	(37.6)	1,278	(45.9)
	Yes	4,017	(62.4)	1,356	(48.7)
	Unknown			148	(5.3)
Dyslipidemia		6,436		2,782	
	No	4,618	(71.8)	1,708	(61.4)
	Yes	1,818	(28.2)	887	(31.9)
	Unknown			187	(6.7)
Active smoking		6,436		2,782	
	No	5,103	(79.3)	1,194	(42.9)
	Yes	1,333	(20.7)	1,163	(41.8)
	Unknown			425	(15.3)
Familial history of coronary artery disease				2,782	
	No			2070	(74.4)
	Yes			455	(16.4)
	Unknown			257	(9.2)

APL MG=potential accessibility to general practitioners, STEMI=segment elevation myocardial infarction.

STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	ok, page 1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	ok, page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	ok, page 4
Objectives	3	State specific objectives, including any prespecified hypotheses	ok, page 6
Methods			
Study design	4	Present key elements of study design early in the paper	ok, page 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	ok, pages 6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	ok, pages 6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	ok, pages 6,7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	ok, pages 6,7
Bias	9	Describe any efforts to address potential sources of bias	ok, page 6,7,8
Study size	10	Explain how the study size was arrived at	ok, page 6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	ok, page 8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	ok, page 8
		(*b*) Describe any methods used to examine subgroups and interactions	ok, page 8
		(*c*) Explain how missing data were addressed	ok, page 7
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	ok, page 8
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	ok, page 8,9, suppl mat.
		(b) Indicate number of participants with missing data for each variable of interest	ok, tables

		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	ok, tables
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	ok, page 9,10
		(*b*) Report category boundaries when continuous variables were categorized	ok, tables
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	ok, pages 10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	ok, pages 12,13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	ok, pages 10,11,12
Generalisability	21	Discuss the generalisability (external validity) of the study results	ok, pages 13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	ok, page 15

NA= not applicable