Research in Economics 80 (2026) 101126

Contents lists available at ScienceDirect

Research in Economics

journal homepage: www.elsevier.com/locate/rie

The effect of COVID-19 pandemic on non-deferrable diseases ☆

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ARTICLE INFO

JEL classification:
I11
I18
L22
L33
D21
D22

Keywords:
COVID-19
AMI
Stroke
In-hospital mortality
Out-of-hospital mortality
Ambulance calls

ABSTRACT

The COVID-19 pandemic has profoundly disrupted healthcare systems globally, raising concerns about its impact on non-COVID-19 patients requiring immediate and intensive care. This paper investigates the effects of the pandemic on the quality of care for Acute Myocardial Infarction (AMI) and Stroke patients in Lombardy, Italy. Taking advantage of rich administrative data (hospital discharge data, emergency call and mortality registries) and leveraging the national lockdown as an exogenous shock in a quasi-experimental framework, we estimate the causal effects of COVID-19 on in- and out-of-hospital mortality rates, hospitalizations, and ambulance response times to discuss their implications for the regional healthcare system. We employed a Differences-in-Differences approach. In this way, this paper assesses the national healthcare service's ability to respond to an emergency situation promptly. Our results reveal a 60% increase in daily out-of-hospital deaths during the pandemic and significant delays in ambulance response times, with an average increase of 11 min for both AMI and Stroke patients. In-hospital mortality remained stable, suggesting that delays in ambulance transport did not directly affect patients who reached the hospital, who were fewer in number. These findings highlight the critical need for policies aimed at maintaining rapid emergency response capacity during health crises, ensuring that time-sensitive care for non-pandemic-related conditions is not compromised.

1. Introduction

The COVID-19 pandemic has been an unprecedented global shock, profoundly impacting the functioning and management of healthcare systems worldwide.

During the first wave of the COVID-19 epidemic, hospitals in many parts of the world were required to operate at crisis capacity, suffering dramatic reductions in their daily activities, including elective surgeries, non-critical patient services, as well as urgent surgeries and oncological programs (Torzilli et al., 2020), acute coronary syndrome admissions (De Filippo et al., 2020), pediatric emergency department activities (Clavenna et al., 2020), Emergency Department workload (Santi et al., 2021), sudden surges in demand (Seyedin et al., 2021) and mental health therapies (Holmes et al., 2020). While declining hospitalization rates may suggest that patients deferred care for life-threatening conditions or that COVID-19 modified hospitalization selection criteria (cutting hospitalizations for less severe patients), we expect that the organizational changes implemented at the hospital level to cope with the pandemic ensured appropriate levels of clinical care for critical patients with non-COVID conditions. In this context,

☆ This article is part of a Special issue entitled: 'Policy Interventions & Proposals for Social Improvement' published in Research in Economics.

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https://doi.org/10.1016/j.rie.2026.101126
Received 25 September 2025; Accepted 19 March 2026
Available online 4 April 2026

the literature has focused on a particular subset of hospital admissions, such as patients with Acute Myocardial Infarction, who require non-deferrable emergency care. Non-deferrable diseases are conditions for which timely medical intervention is critical to prevent death or serious long-term harm of the patient involved. Acute Myocardial Infarction (AMI) and Stroke are typical examples in the literature, as delays in treatment can lead to patients' severe complications or mortality, making them natural candidates for studying the effects of healthcare system disruptions during the pandemic. These patients can be considered natural candidates for studying volumes and mortality rates. During the first pandemic wave, declining volumes for acute AMI cases were recorded worldwide (De Rosa et al., 2020b; Arcaya et al., 2016; Mahmud et al., 2020; Solomon et al., 2020). In Italy, recent studies reported a threefold increase in myocardial infarction (AMI)-related mortality and complications during the COVID-19 period compared to the same period of the previous year (De Rosa et al., 2020b) in 15 hospitals in Northern Italy, as well as a significant increase in overall mortality for all causes (+7.5% (Santi et al., 2021) in a large area of Northern Italy). Another multicenter observational nationwide survey involving a network of intensive cardiac care units found that AMI-related hospitalizations were reduced by almost 50% during the COVID-19 period and accompanied by a threefold increase in mortality and complications (De Rosa et al., 2020a). While the literature presents several studies on in-hospital AMI patients (see a recent meta-analysis on this issue (Pourasghari et al., 2022)), the same cannot be said for out-of-hospital admissions and mortality. Studies regarding Italy are few, and apart from one ((Campo et al., 2021), which uses administrative data from all hospitals in Emilia-Romagna), the data are geographically heterogeneous (one metropolitan area in Emilia-Romagna, some provinces in Lombardy, and one province in Veneto), and the analyzed information, such as emergency medical service databases, ambulance databases, and mortality registers, is limited (see Discussion). The existing literature includes several studies examining the impact of the COVID-19 pandemic on the management of cardiovascular patients at the hospital level (Rossi et al., 2021; Kiss et al., 2021; Cannata et al., 2022a). However, this literature does not capture the full picture, missing information regarding what happened outside the hospital system.

This study addresses this gap by analyzing the overall impact of COVID-19, also in out-of-hospital environment. This paper seeks to compare the rate of AMI admissions and both in-hospital and out-of-hospital mortality during the first wave of the pandemic with pre-pandemic periods. Specifically, it compares the admissions and deaths that occurred during the first 26 weeks (6 months) of the COVID-19 outbreak (from January 1 to June 30, 2020) with those that occurred during the same period in 2019. To our knowledge, this is the first attempt to assess the impact of COVID-19 and related hospital stress burden on mortality for not-defferable diseases, particularly out-of-hospital excess AMI and Stroke mortality in the Lombardy region, using administrative data covering all hospitals and emergency registries.

Lombardy, a northern Italian region, was the epicenter of the first European COVID-19 cases and home to the so-called "patient zero". During the early months of 2020, Lombardy experienced an overwhelming surge in COVID-19 cases, leading to a healthcare system crisis, the reallocation of medical resources, and significant disruptions in routine care (Baccellieri et al., 2020). As one of the hardest-hit areas globally, its experience offers valuable insights into the resilience of healthcare systems and the indirect consequences of global health emergencies on non-COVID conditions. Both AMI and Stroke are considered non-deferrable conditions, as timely intervention is often critical for saving patients' lives (Cannata et al., 2022b; Nakahashi et al., 2021; Wu et al., 2019). Recent evidence analyzing the Lombardy context suggests that, during the early phase of the pandemic, intervention times increased (Gramegna et al., 2020) and hospitalizations decreased for both Stroke (Sacco et al., 2020) and AMI (De Rosa et al., 2020b) patients. However, comprehensive evidence on the outcomes of these patients – both within and beyond the hospital setting – remains scarce. Understanding these broader impacts is crucial for evaluating how healthcare systems coped with the dual challenge of managing COVID-19 while maintaining essential levels and quality of care for non-COVID-19 emergencies.

Additionally, these studies overlook critical information on the time between the onset of Stroke or AMI and the patient's arrival at the closest hospital (i.e., EMS-to-balloon time). For time-sensitive conditions, delays in pre-hospital care due to a reduction in EMS efficiency (i.e., limited ambulance availability) caused by the simultaneous pressure of COVID-19 patients may have significantly impacted non-COVID non-deferrable patient outcomes. Without precise information on such inefficiencies and delays, stable mortality rates in certain hospitals may simply reflect lower hospitalizations due to unobserved systemic pressures or actual inadequacies in the quality of care delivered or in care management, producing biased evaluations of hospital and NHS performance.

The aim of this study is threefold. First, using hospital discharge data, we examine variations in AMI mortality and hospitalizations across all hospitals in Lombardy comparing them with the previous year.

Second, we incorporate detailed data from EMS calls to the European emergency number (112) in Lombardy to extend the analysis beyond the hospital setting. The 112 number, known as the Single European Emergency Number (NUE), serves as a broader coordination center for all types of emergencies. It connects citizens to various emergency services, including law enforcement (Police, Carabinieri), fire departments, and medical emergencies (118). Analyzing data from EMS calls allows us to evaluate the time between the initiation of an emergency call and the ambulance's arrival at the nearest hospital. By examining this data, we can assess whether the pandemic disrupted EMS and ambulance availability due to the increased demand for transporting COVID-19 patients, and whether these disruptions impacted the outcomes for AMI and Stroke patients.

Third, leveraging the implementation of a national lockdown as an unexpected exogenous shock in a quasi-experimental framework, and exploiting regional administrative data, we identify the causal effects of the COVID-19 pandemic on the outcomes detailed above (in- and out-of-hospital mortality, number of hospitalizations, and time to hospital), providing a complete assessment of what happened to AMI and Stroke patients.

The results show significant changes in mortality rates for AMI and Stroke during the pandemic, particularly in out-of-hospital deaths, analyzed using mortality registry. We observe an approximately 60% increase in daily death counts attributable to the pandemic. Additionally, ambulance arrival times increased significantly, with an average delay of about 11 min across Lombardy for both AMI and Stroke patients. However, in-hospital mortality remained largely unchanged across all hospitals suggesting that an increase in arrival times – at least for patients who reached the hospital and were not among the out-of-hospital fatalities – did not directly translate into worse health outcomes within the hospital setting.

The paper is structured as follows: Section 2 provides details on the institutional background in the Lombardy region, Section 3 describes the administrative data used, while Section 4 provides some descriptive evidence. Section 5 discusses the identification strategy, and results are presented in Section 6. Finally, Section 7 concludes.

2. Institutional background

The Italian National Health Service (NHS) ensures universal access to medical services for all citizens. Established in 1978 by Law 833/1978, the NHS was structured as a Beveridge system, emphasizing equitable, state-funded healthcare provision.

Over the decades, the NHS has undergone significant reforms aimed at enhancing its efficiency and effectiveness. Structural reforms in 1992 and 1999 marked a shift toward a decentralized system, granting greater autonomy to regional authorities.

The NHS operates across three different levels: national, regional, and local. The Ministry of Health oversees national health policies, while regional authorities are responsible for organizing and managing healthcare services within their territories. Healthcare governance is supported by various institutions, such as the Technical-Scientific Committee, the Regional Health Agencies, and the Local Health Authorities (ASLs), which play essential roles in overseeing, controlling, and implementing health policies, ensuring compliance with national standards.

Emergency medical services (EMS), including ambulance dispatches, are an integral part of the NHS. These services provide critical pre-hospital care, ensuring a prompt response to medical emergencies and the safe and rapid transportation of patients to healthcare facilities.

This study focuses on Lombardy, the largest region in Italy (accounting for 16% of Italy's total population) and one of the wealthiest and best educated in Europe. Its population of 10 million inhabitants makes it comparable in both size and economic competitiveness to a mid-sized European country such as Portugal or The Netherlands.

Lombardy's healthcare system is one of the largest in Italy, encompassing approximately 150 hospitals that collectively handle 1.7 million discharges annually. The region's healthcare expenditure totals around €20 billion per year, representing approximately 75% of its regional budget.

An important healthcare reform[1] in 1997 transformed Lombardy's system into a quasi-market model,[2] allowing citizens to freely choose healthcare providers regardless of their ownership (whether public, private for-profit, or private not-for-profit). The system operates entirely on a prospective payment structure based on diagnosis-related groups (DRGs). Each hospital receives an annual budget allocation from the regional administration, which sets a maximum reimbursement cap. The reform also assigned the Lombardy administration the responsibility of monitoring the performance of the healthcare services delivered by hospitals within the framework of the regional accreditation system, thereby ensuring both system accountability and quality standards (Brenna, 2011).

The reason why Lombardy was chosen for this analysis is precisely because it was the first region, excluding China, to be severely affected by the pandemic worldwide and was hit with the greatest intensity. Furthermore, Lombardy's experience during the early stages of the COVID-19 crisis makes it a particularly relevant case study for examining how healthcare systems respond to large-scale health emergencies. Lombardy is particularly interesting for cardiovascular diseases due to its high incidence of conditions like AMI and Stroke, which have among the highest prevalences in Italy. Additionally, Lombardy has a well-developed healthcare network, with numerous hospitals and advanced healthcare facilities, providing unique opportunities to study the effectiveness of treatments and access to care for time-dependent patients with these conditions (Frigerio et al., 2017).

3. The data

3.1. Administrative sources

We analyze unique administrative data, covering the periods from January 1 to May 31 in both 2019 and 2020, from three different Lombardy regional sources: the Hospital Discharge Records (HDR) database, the Mortality Registry and the Emergency medical calls registry managed by 112.

The HDR data used to study in-hospital mortality and the number of hospitalizations for AMI patients offer detailed information on all hospitalizations in public and private facilities across Lombardy for the years 2019 and 2020. The dataset includes patient demographics (e.g., age, gender, residence, education), hospitalization characteristics (e.g., hospital and department, admission type, discharge method, admission date and admission priority), and clinical details (e.g., primary and secondary diagnoses, diagnostic or therapeutic procedures).

The mortality registry, combined with the HDR dataset, was used to analyze out-of-hospital mortality. This registry provides anonymized data on all deaths among residents of Lombardy, including in-hospital fatalities. By cross-referencing these records with the HDR dataset, it is possible to identify out-of-hospital deaths as those cases not included in the HDR records. The mortality

[1] Riforma Bindi, Legge Regionale 11 luglio 1997, N. 31.

[2] A quasi-market refers to a system where public and private providers compete to deliver services, but with public funding and regulation to ensure universal access and control.

registry contains comprehensive demographic information about the deceased including sex, citizenship, municipality of residence, date and cause of death, age, place of death, marital status, and education level.

Finally, emergency call data collected by 112 were used to examine ambulance response and hospital arrival times. This dataset was constructed by merging two sources: one detailing patient information and the other focusing on characteristics of the rescue operation. The patient-related variables include demographic details, residence, pathology, severity codes (for both the patient and the rescue), and information on the department and hospital of destination. Additionally, the dataset records several timestamps, such as the emergency initiation time, hospital arrival time. The rescue-related variables cover the reason for the call, the originating province, and details about the rescue classification, including the number of people involved, severity codes, and the number of critical patients. Key timestamps for the rescue process, including the rescue closing time, filter start and end times, and call completion time, are also recorded.

3.2. Outcomes

The outcome variables analyzed from the three data sources include the number of hospitalizations, in-hospital mortality, out-of-hospital mortality, and ambulance arrival times. These four measures, observed during the first six months of 2020 compared to the same period in 2019, are essential for assessing the impact of a shock on time-sensitive diseases.

In-hospital mortality serves as a key indicator of the quality and effectiveness of medical care within the hospital system, assuming external healthcare services are functioning properly. The number of hospitalizations helps capture changes in healthcare-seeking behavior and provides a more accurate context for interpreting in-hospital mortality trends. In contrast, out-of-hospital mortality reflects the performance of healthcare services outside hospital settings. A rise in out-of-hospital deaths may indicate delays or failures in emergency care delivery. Lastly, ambulance arrival times serve as a crucial proxy for the healthcare system's ability to provide timely emergency assistance. This measure reflects the responsiveness of emergency services, which is particularly vital for conditions like AMI and stroke, where rapid intervention can significantly impact patient outcomes (Van de Werf et al., 2003; Minnerup et al., 2014; Dudas et al., 2011).

In-hospital mortality is available at the patient level and is classified using a dummy variable that is equal to one if the patient died during hospitalization and zero if the patient survived. The number of hospitalizations is measured at aggregate level as the daily count of admissions for AMI, while out-of-hospital mortality is measured at the aggregate level as the daily count of deaths for AMI and Stroke occurring outside the hospitals. Ambulance arrival time, measured in minutes, represents the difference between the time the emergency call was made and the time of the patient's arrival at the hospital.

For the first three outcomes, the analysis was limited to the following ICD-9-CM code 410 (Acute Myocardial Infarction) and 433, 434, and 436 (Stroke) detected as the principal diagnosis, while for ambulance arrival times the analysis was limited to patients whose disease description rows contained the terms ‘infarction’ and ‘stroke’ and for whom ambulance arrival time was not missing (patients with missing data were excluded from the analysis).

4. Descriptive evidence

Fig. 1 presents excess mortality from cardiovascular diseases during the first four months of the year (January to April), comparing 2020 with the corresponding monthly average of the preceding five years. The data are disaggregated by place of death: home, hospital, nursing homes, and other places.

Fig. 1 shows notable increases in excess mortality both at home and in nursing homes, particularly in months of March and April 2020, following the implementation of lockdown measures. At home, excess mortality rose dramatically, exceeding 150% of the 2015–2019 average (around 800 deaths) in March and above 60% in April (711 deaths). By contrast, February showed a modest increase, while in January mortality was close to the levels registered in the previous five years. Similarly, nursing homes experienced a sharp rise in excess mortality, peaking in March with an increase of approximately 100% from a pre-COVID average mortality of around 751 patients.

Interestingly, hospitals did not exhibit a comparable increase in mortality, with excess mortality remaining close to 0% (baseline level was 1214 deaths) across all months or even showing a slight decline in April. This pattern may indicate that patients with cardiovascular conditions faced barriers to accessing hospital care or that hospital resources were primarily allocated to managing the unexpected inflow of COVID-19 patients. In contrast, the “Other” category showed a rise in excess mortality during March 2020 (baseline 52 deaths), while January, February and April exhibited small reductions compared to the past. Overall, the most pronounced increase in cardiovascular-related excess mortality occurred outside hospitals, particularly at home and in nursing homes, making the analysis of what happened outside hospitals important for understanding the broad impact of COVID-19 pandemic on cardiovascular diseases.

In Italy, excess mortality during the first wave of the pandemic was concentrated in nursing homes (NH) and at home. The high number of deaths recorded in NH is attributable to conditions that characterized specialized facilities for the care of the elderly (Lai et al., 2020), namely: (i) the patients, of advanced age, were suffering from chronic diseases; (ii) residents shared spaces and medical care; (iii) visitors and workers entered and exited these facilities without restriction. Finally, in the Lombard context, the decision to transfer patients affected by COVID-19 to nursing homes to conclude the quarantine or convalescence cycle had significant consequences, reducing on the one hand pressure on hospital facilities.

Additionally, for cardiovascular diseases such as AMI and Stroke, a crucial role -especially before hospitalization - is played by the efficiency of the emergency ambulance service and the subsequent ability of the NHS to ensure quick and effective arrival times

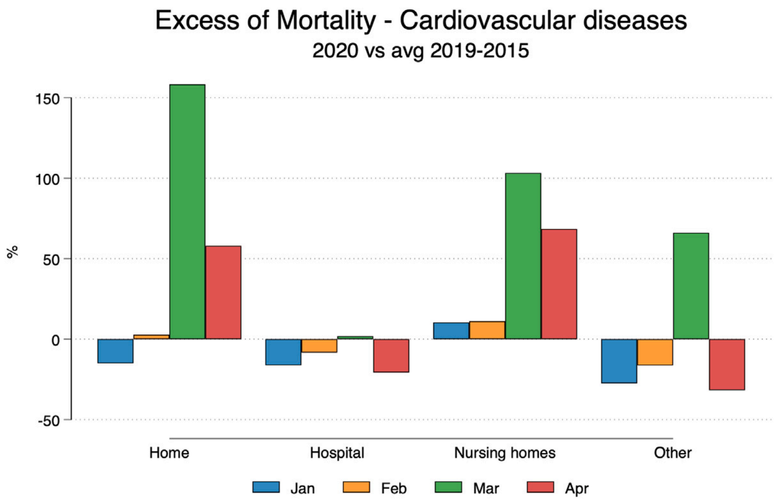

Fig. 1. Excess mortality by place of death in 2020 compared with the 2015–2019 average, by month. Deaths in 2015–2019 were as follows: Home (March: 800.6; April: 711.6), Hospital (March: 1214.6; April: 1094.0), Nursing Homes (March: 751.4; April: 652.8), Other (March: 52.4; April: 49.8).
Source: ISTAT.

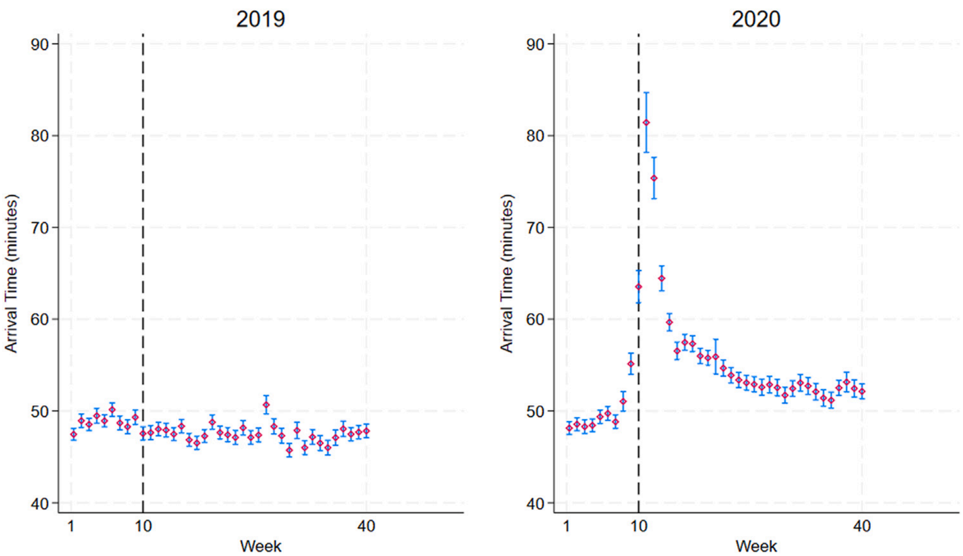

Fig. 2. Hospital arrival time by week in 2019 and in 2020.
Source: Emergency Calls File

at hospital facilities. Fig. 2 illustrates the boxplot of the weekly variation in the time between emergency dispatch and hospital arrival by ambulance for all cardiac conditions comparing the COVID-19 year (2020) and the year before (2019). In Fig. 2, we considered week 1 to 40, while in the models week 1 to 22. Week 10 is the week of lockdown date.

Fig. 2 highlights a clear increase in hospital arrival times during the weeks affected by the COVID-19 pandemic.

In 2019, arrival times were slightly below 50 min. The same occurred for the first 8 weeks of 2020, while from week 9 of 2020 onward, a substantial and unexpected increase occurred the ambulance arrival times. Average times increased sharply, peaking at an average of 82 min and showing greater variability (with significantly larger boxplots).

This increase in hospital arrival times at week 11 during the early pandemic period likely reflects the pressure experienced by the Lombardy EMS and the strain of COVID-19 patients on regional healthcare resources. Over the weeks from 12 to 40, the average time begins to decline, suggesting an improvement in resource allocation and a quick adaptation of the NHS to the unexpected demands of the pandemic . Nonetheless, even by June 2020, hospital arrival times remained slightly above the corresponding period in 2019.

While these descriptive evidences aggregate all cardiac conditions, separated models will be conducted for AMI and Stroke to explore whether out-of-hospital deaths increased during the pandemic and whether the observed increase in ambulance times raised patient mortality during the COVID-19 period.

5. Methods

The paper is an observational retrospective, pre- and post-implementation study using registry data from the Lombardy region, where the COVID-19 epidemic had a relevant impact in March–May 2020.

The identification strategy leverages the national lockdown policy as an exogenous shock (Kapoor and Ravi, 2020; Carneiro et al., 2020; Rossi et al., 2021), providing a quasi-natural setting for the causal estimation of the pandemic effect on selected outcomes using a standard Difference-in-Differences (DiD) approach. The Difference-in-Differences (DiD) approach estimates the causal effect of the COVID-19 pandemic by comparing how the relevant outcomes changed before and after the lockdown in 2020 relative to the same comparison in 2019. Specifically, the DiD estimator captures the differential change in hospitalizations, in- and out-of-hospital mortality, and EMS arrival times, isolating the effect of the pandemic from other confounding factors that could have affected these outcomes over time. A crucial requirement for this approach to be valid is the parallel trends assumption, which posits that, in the absence of the pandemic, the trends in these outcomes would have been similar in 2019 and 2020. In other words, any difference in the outcomes observed after the lockdown can be attributed to the COVID-19 shock, rather than pre-existing divergences in the trajectories of hospitalizations or mortality among the two groups. To assess this assumption, we examine pre-lockdown data (January 1 to March 8) for both years, inspecting trends visually and confirming them statistically using event-study models to gain information on the plausibility of the identifying assumption. The pre-treatment and post-treatment periods are defined according to the following calendar periods: the pre-treatment period spans from January 1st to the day before the lockdown date (March 8th), while the post-treatment period extends from the lockdown date to May 31st. In the Appendix, we report alternative definitions of pre- and post-treatment periods that do not rely on the national lockdown date (March 9th). Specifically, we consider February 24th, when initial regional containment measures were introduced, and March 7th, when Lombardy and surrounding provinces were placed under local lockdown. Using March 7th produces results consistent with the main analysis, while February 24th reveals slightly larger effects, suggesting that the pandemic's impact on our outcomes began before the national lockdown, which is in line with literature. In this framework, the treatment group includes observations from the year 2020, while the control group consists of data from 2019, with the *Treat* variable defined as a binary indicator, that equals 0 for 2019 and 1 for 2020, respectively.

The pre–post variable (denoted as *Post*) indicates whether the observations fall before or after the lockdown date of March 9th. To assess the immediate response capacity of the National Health System to the emergency, the period under study extends through May 31st. Accordingly, the *Post* dummy variable equals 0 from January 1st to March 8th and equals to 1 from March 9th (the lockdown date) to May 31st.

The econometric strategy aims at estimating the causal impact of the COVID-19 pandemic on the following outcomes for AMI and Stroke patients separately: (i) the number of daily hospitalizations (ii) the probability of in-hospital mortality (iii) the number of daily out-of-hospital deaths (iv) the hospital rescue times. The first two outcomes are analyzed only for AMI patients because the limited number of Stroke cases prevents reliable model estimation for that condition.

5.1. In-hospital mortality

The first model in our analysis estimates the impact of COVID-19 on the probability of death during the hospitalization (in-hospital mortality) using a multilevel logistic regression model.

Denoting with p_{ij} the probability that patient i dies in hospital j and with $Y_{ij} = \frac{p_{ij}}{1-p_{ij}}$ the odds of death for a patient i in hospital j, we estimate the following multilevel logistic regression:

$$\begin{aligned} log(\frac{p_{ij}}{1-p_{ij}}) =& \beta_0 + \boldsymbol{\beta}_1 \boldsymbol{X}_{ij} + \beta_2 \text{Treat}_{ij} + \beta_3 \text{Post}_{ij} + \\ &+ \beta_{4j} \text{Treat}_{ij} \times \text{Post}_{ij} + \boldsymbol{u}_{0j} \end{aligned} \tag{1}$$

where $\boldsymbol{X}_i$ is a vector of individual covariates (i.e. sex, age and Elixhauser index[3]). In addition to the standard DiD terms ($Treat_{ij}$, $Post_{ij}$ and their interaction term $Treat_{ij} \times Post_{ij}$), the model incorporates $\boldsymbol{u}_{0j}$, a hospital-level random effect, to account for variation in underlying mortality probabilities across the different hospitals. The term $\boldsymbol{u}_{0j}$ accounts for all the observable and unobservable hospital-level factors that predict mortality and are uncorrelated with the individual and hospital-level predictors. The model assumes a normal distribution for $\boldsymbol{u}_{0j}$ with mean zero and variance τ^2. In addition, the model includes a random interaction term, $Treat_{ij} \times Post_{ij}$ (β_{4j}), that can be separated in β_4 (the average effect at regional level) and ($\boldsymbol{u}_{1j}$), random effects, to capture hospital-specific differences in causal impact of COVID-19 on in-hospital mortality rates for AMI patients. This term reflects the variability in how hospitals were impacted by the pandemic's pressures, potentially influencing mortality rates among hospitalized patients. $\boldsymbol{u}_{1j}$ is normally distributed with mean zero and variance τ_1^2. This specification reflects expected heterogeneity in hospital capacity, resources, and crisis management during the pandemic, providing a more flexible alternative to a fixed-effects model. Our data have a hierarchical structure, with patient-level observations nested within hospitals. This nesting implies that observations from the same

[3] Elixhauser index is included as a proxy of severity measured by the amount of comorbidities detected (Elixhauser et al., 1998)

hospital are not independent, as patients within the same hospital may share unobserved characteristics, protocols, or resource constraints that affect outcomes. To account for this intra-hospital correlation and the resulting non-independence of errors, we include a random intercept for each hospital. Additionally, we include a random slope for the DiD interaction, allowing the effect of COVID-19 on mortality to vary across hospitals, reflecting differences in hospital-specific responses and capacities. This approach captures both the baseline heterogeneity between hospitals and the differential impact of the pandemic across institutions.

5.2. Out-of-hospital mortality and number of hospitalizations

The second model estimates the impact of the Covid-19 pandemic on out-of-hospital mortality by analyzing the daily count of deaths attributed to AMI and Stroke using the mortality registry. To this end, given that the number of deaths can only assume non-negative values, we estimate a Poisson regression model, specified as follows:

$$\lambda_d = \exp[\beta_0 + \boldsymbol{\beta}_1 \boldsymbol{X}_d + \beta_2 \text{Post}_d + \beta_3 \text{Treat}_d + \beta_4 (\text{Post}_d \times \text{Treat}_d)] \tag{2}$$

Where λ_d represents the expected mean of the count of deaths for each day d and $\boldsymbol{X}_d$ is the vector of covariates including week of year and day of the week fixed effects to account for seasonality. The terms $Post_d$ and $Treat_d$ represent the post-lockdown period and the treatment year (2020 vs 2019) respectively, while their interaction term captures the causal impact of the Covid-19 pandemic during the post-lockdown period. The model assumes that the number of deaths follows a Poisson distribution, where the likelihood of observing y_d deaths on day d is given by:

$$P(y_d|\lambda_d) = \frac{\lambda_d^{y_d} e^{-\lambda_d}}{y_d!} \tag{3}$$

The analysis about the estimates of the COVID-19 pandemic impact on hospitalizations by analyzing the daily count of hospitalizations attributed to AMI is made with the same specification of Eq. (2) where λ_d represents the expected mean of the count of hospitalizations for each day d.

5.3. Out-of-hospital arrival times

The last model evaluates the impact of the COVID-19 pandemic on EMS Time to Door, a critical metric for assessing the efficiency of emergency medical response. It represents the delay between symptoms onset and hospital arrival, providing insight into the responsiveness of the emergency medical system. The model is specified using a standard Difference-in-Difference (DiD) linear regression as follows:

$$Y_r = \beta_0 + \boldsymbol{\beta}_1 \boldsymbol{X}_r + \boldsymbol{\beta}_2 \text{Post}_r + \boldsymbol{\beta}_3 \text{Treat}_r + \boldsymbol{\beta}_4 (\text{Post}_r \times \text{Treat}_r \times \text{Province}_r) + \epsilon_r \tag{4}$$

where Y_r is the time between call and arrive in hospital for single ambulance run r, $\boldsymbol{X}_r$ represents a vector of observable characteristics at ambulance dispatch level including patients' sex, age, ambulance call duration and a progressive of the number of call in that hour (proxy of the overload of NHS in that hour) and ϵ_r is normally distributed with a mean of 0 and variance σ^2.

In addition to the Difference-in-Differences (DiD) approach, we also employ an event study methodology to measure dynamically the weekly impact of COVID-19 lockdown on the EMS Time to Door. The event study approach allows us to assess the validity of the parallel trends assumption and capture variations in the policy effects at different points in time after the lockdown implementation date. The event study model is specified as follows:

$$Y_{rw} = \boldsymbol{\beta}_0 + \boldsymbol{\beta}_1 \boldsymbol{X}_r + \boldsymbol{\beta}_2 \text{D}_w + \boldsymbol{\beta}_3 \text{Treat}_r + \boldsymbol{\beta}_{4w} (\text{Treat}_r \times \text{D}_w) + \epsilon_{rw} \tag{5}$$

In this model, Y_{rw} represents the time in minutes for ambulance run r to arrive at the hospital during week w (w assumes values from 1 to 22). The variable D_w is a dummy variable indicating the week number, with week 9 (last week before lockdown implementation) set as baseline. The variable $\boldsymbol{X}_r$ includes a vector of covariates such as sex, age, call duration, a progressive call number within that hour and province. The vector of parameters $\boldsymbol{\beta}_{4w}$ is the set of estimated coefficients of interest, as it captures the causal effect of the COVID-19 pandemic on the outcome variable at each week w relative to the baseline. Standard errors are clustered at the province level, the lowest administrative level available, to account for within-province correlation in ambulance runs and ensure valid inference for treatment effects.

6. Results

6.1. Number of hospitalizations

The following map, 3, displays the difference in the average number of hospitalizations per 100,000 inhabitants for each province in the two years under analysis, focusing on the period corresponding to the pandemic months, from March 9 to May 31. In the Appendix, here, we also report the maps showing the average number of hospitalizations for the two years separately.

All provinces, except for Pavia, Mantua, and Lecco, show negative values for the difference in the number of hospitalizations between 2020 and 2019. This reduction can be interpreted as a positive aspect, suggesting fewer hospitalizations in 2020 compared to 2019. Even in the worst-performing provinces, the differences are relatively close to zero, indicating that the pandemic did not lead to a significant change in hospitalizations. However, this apparent decrease in hospitalizations does not necessarily reflect a

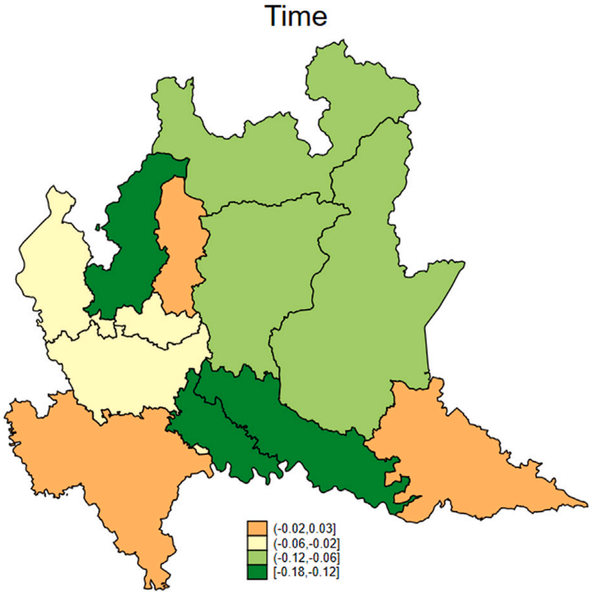

Fig. 3. Average number of hospitalizations for AMI per 100,000 residents at the municipality level, comparing 2020 and 2019.

Table 1
Effect of the COVID-19 pandemic on number of hospitalizations — AMI.

Variable	Coefficient	Std. Err.	P-value
Intercept	2.88	0.31	<0.001
Treat	−0.08	0.03	0.02
Post	0.58	0.21	0.007
Treat × *Post*	−0.22	0.05	<0.001
N. Obs.	303		
Log likelihood	16 558.12		

Note: Results of a DID Poisson model estimating the effect of the COVID-19 pandemic on hospitalizations for AMI patients. *Treat* refers to hospitalizations in 2020 (vs 2019), and *Post* refers to the post-lockdown period (March 9–May 31) compared to the Pre-lockdown period (Jan 1–March 8).

positive outcome in absolute terms. It is possible that individuals avoided seeking hospital care due to fears of infection or were unable to access medical treatment promptly due to the healthcare system being overwhelmed. In every case, it seems that COVID-19 pandemic did not affect hospitalizations.

Table 1 shows the estimated coefficients of the Poisson DiD regression model specified in Eq. (2), focusing exclusively on AMI for hospitalizations and only on *Treat* and *Post* coefficient (week and day-of-week are many coefficients not of our interest).

Table 1 reports a significant decrease in daily hospitalizations for AMI during the lockdown period in 2020 compared to 2019. The coefficient of the interaction term (*Treat* × *Post*) is −0.22, which implies a 20% decrease in daily hospitalizations for AMI with the introduction of the COVID-19 lockdown if compared to the same periods in 2019; in absolute terms this corresponds to approximately 6.9 fewer AMI hospitalizations per day (DID calculation based on model-predicted means: 23.57 vs 16.44 for 2020 post vs pre, and 31.82 vs 17.81 for 2019 post vs pre).

This result is consistent with the fact that fear definitely increased, leading to a tendency for people to visit hospitals less frequently. Additionally, hospitals were overwhelmed with COVID-19 patients, leaving less space for those with other conditions, including AMI. However, this represents a negative aspect, since timely treatment is crucial for AMI. Therefore, based on this result, we would expect an increase in out-of-hospital deaths.

6.2. In hospital mortality

Table 2 shows the estimated coefficients of the multilevel logistic DiD regression model specified in Eq. (1), focusing exclusively on AMI. In addition, we restricted the sample of analysis to the hospitals with at least 50 admissions of AMI patients in both 2019 and 2020 to ensure enough statistical power for our estimates.

Table 2
Effect of the COVID-19 pandemic on In-hospital mortality — AMI.

Variable	Coefficient	Std. Err.	P-value
Intercept	−5.32	0.34	<0.0001
Female	0.49	0.11	<0.0001
Age	0.03	0.005	<0.0001
Elixhauser	−0.062	0.04	0.08
Treat	0.014	0.15	0.92
Post	−0.18	0.24	0.22
Treat × *Post*	0.37	0.21	0.08
N. Obs.	7481		
−2 Res Log Pseudo-likelihood	43 879.44		

Note: Results of a DID multilevel logistic model estimating the effect of the COVID-19 pandemic on in-hospital mortality for AMI patients. *Treat* refers to hospitalizations in 2020 (vs 2019), and *Post* refers to the post-lockdown period (March 9–May 31) compared to the Pre-lockdown period (Jan 1–March 8).

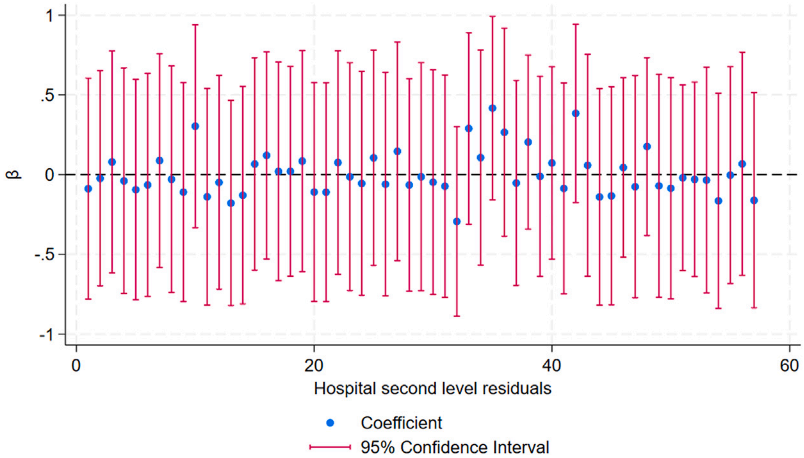

Fig. 4. Second-level hospital-specific DID residuals $\boldsymbol{u}_{1j}$ for in-hospital mortality — AMI.

Results reveal that demographic factors strongly influenced the individual probability of death, with female patients showing a significantly higher probability of in-hospital mortality compared to men ($\hat{\beta} = 0.49$, p-value < 0.0001) and a mortality likelihood increasing with age ($\hat{\beta} = 0.03$, p-value < 0.0001). The Elixhauser Index marginally influenced the individual probability of death , with a negative coefficient indicating that its effect, though limited, slightly reduces mortality rates ($\hat{\beta} = -0,062$, p-value $= 0.08$). This could be because a higher Elixhauser Index indicates a greater presence of comorbidities, which may be associated with more timely care, better healthcare resources, or the effect of comorbidities is balanced by protective factors.

However, the direct effect of the *Treat* variable identifying the pandemic year (2020) is not statistically significant ($\hat{\beta} = 0.014$, p-value $= 0.92$), and also the *Post* lockdown coefficient is not statistically significant at conventional levels ($\hat{\beta} = -0.18$, p-value $= 0.22$). The coefficient of the interaction term *Treat* × *Post*, β_4, representing the mean casual effect of the pandemic and lockdown policies over hospitals, indicates a marginal increase in mortality ($\hat{\beta}_4 = 0.37$, p-value $= 0.08$) and implies an approximate 45% increase in the odds of in-hospital mortality for AMI patients during the lockdown period. However, the effect is only marginally significant (p=0.08), suggesting that at the hospital level, the pandemic's impact on in-hospital AMI mortality rates was not different from 0 with the standard level of confidence, 95%.

By combining the results of this model with those from the previous one, where the outcome was the number of hospitalizations, it appears that the patients who are hospitalized – fewer during the pandemic – are as severe as those in the pre-pandemic period. Those who do not reach the hospital are likely either too severe (with a higher probability of death) or less severe (with a lower probability of death). The fact that the probability of death remains unchanged is even more striking, considering that the number of hospitalized patients is lower.

Fig. 4 shows the full set of 57 hospital-specific random coefficients of the interaction term *Treat* × *Post*, along with their 95% confidence intervals.

It reports the second-level residuals $\boldsymbol{u}_{1j}$ of the multilevel model which capture unmeasured hospital characteristics and unexplained factors. The confidence intervals for these residuals almost always include the null value, indicating no association with in-hospital mortality and suggesting a homogeneous response to the emergency, with no hospital performing notably better or particularly worse with respect to the others.

Table 3
Effect of the COVID-19 pandemic on out-of-hospital mortality — AMI, Poisson DID regression model.

Variable	Coefficient	Std. Err.	CI Low	CI Up	Pr > χ^2
Intercept	1.59	0.51	0.59	2.59	0.001
Treat	−0.17	0.06	−0.29	−0.05	0.004
Post	−0.44	0.22	−0.88	0.004	0.05
Treat × *Post*	0.49	0.08	0.33	0.65	<0.001
N. Obs	303				
Log Likelihood	2778.95				
AIC	1585.22				
DoF	271				
$Scaled\,Pearson_{\chi^2}$	358.83				

Note: Results of a Poisson DID regression model analyzing AMI out-of-hospital mortality. *Treat* indicates observations from 2020 versus 2019, while *Post* refers to the lockdown period (March 9–May 31). The interaction term *Treat* × *Post* captures the differential effect of the lockdown in 2020 compared to the same period in 2019.

Table 4
Effect of the COVID-19 pandemic on out-of-hospital mortality — Stroke, Poisson DID regression model.

Variable	Coefficient	Std. Err.	CI Low	CI Up	Pr > χ^2
Intercept	1.55	0.68	0.21	2.88	0.02
Treat	−0.19	0.08	−0.34	−0.03	0.02
Post	−0.65	0.31	−1.25	−0.04	0.04
Treat × *Post*	0.51	0.11	0.31	0.72	<0.001
N. Obs	302				
Log Likelihood	1223.81				
AIC	1436.91				
DoF	270				
$Scaled\,Pearson_{\chi^2}$	307.41				

Note: Results of a Poisson DID regression model analyzing stroke out-of-hospital mortality. *Treat* indicates observations from 2020 versus 2019, while *Post* refers to the lockdown period (March 9–May 31). The interaction term *Treat* × *Post* captures the differential effect of the lockdown in 2020 compared to the same period in 2019.

6.3. Out-of-hospital mortality

The Poisson DID model evaluates the impact of the COVID-19 pandemic on out-of-hospital mortality, leveraging daily death counts from registry data. Due to the absence of individual-level covariates for daily observations, the model does not control for patient-specific characteristics. Results are presented in Tables 3 and 4, showing the effects on AMI and Stroke-related out-of-hospital mortality, respectively.

Table 3 reports a significant increase in daily out-of-hospital deaths from AMI during the lockdown period in 2020 compared to 2019. The coefficient of the interaction term (*Treat* × *Post*) is 0.49, which implies a 63% increase in daily deaths for AMI with the introduction of the COVID-19 lockdown compared to the same periods in 2019. In absolute terms, this corresponds to an additional 1.96 deaths per day during the pandemic (baseline daily mortality in the pre-lockdown period of 2019 equals 4.90 deaths).

Similarly, Table 4 shows that Stroke-related out-of-hospital mortality also increased during the lockdown. The coefficient of the interaction term *Treat* × *Post* suggests an additional 67% increase in the daily number of deaths for stroke cases, a significant rise compared to the same periods in the previous year. In absolute terms, this corresponds to an additional 1.73 deaths per day during the pandemic (baseline daily mortality in the pre-lockdown period of 2019 equals 4.71 deaths).

6.4. Out-of-hospital arrival times

In Appendix, there are the maps that display the average number of ambulance calls per 100,000 inhabitants for each province during the two years under analysis for AMI and for stroke.

The results of the linear regression models on ambulance arrival times at the hospital are presented in Tables 5 and 6 with the reference level of province variable being Lodi. We observe evidence of an overall positive and significant impact of the COVID-19 pandemic on ambulance runs durations for both AMI and Stroke patients respectively. The coefficient of the interaction term *Treat*×*Post* indicates a statistically significant average increase of about 11.4, meaning that the ambulance transport duration for those AMI patients who needed hospitalization increased by around 11 mins with the introduction of the lockdown in 2020 compared to the control period in 2019, (considering that the baseline mean time in the pre-lockdown period of 2019 was 50 min). Patient-specific controls such as gender or age are statistically non-significant, suggesting that the patients' characteristics did not

Table 5
Effect of the COVID-19 pandemic on ambulance arrival times — AMI.

Variable	Coefficient	Std. Err.	*P*-value	CI Low	CI High
Intercept	55.77	3.43	<0.001	48.22	63.33
Treat	26.25	10.18	0.026	3.85	48.64
Post	2.07	2.70	0.460	−3.87	8.01
Treat × *Post*	11.38	1.14	<0.001	8.88	13.88
Patients Controls					
Male	−0.58	0.68	0.416	−2.08	0.92
Age	−0.047	0.050	0.367	−0.156	0.063
Ambulance Call Covariates					
Call Duration (min)	0.00001	0.000004	0.009	0.000003	0.000019
# of Hour Calls	−0.003	0.0019	0.140	−0.0071	0.0011
Year × Post × Province Dummies					
2020 × Post × Lodi *(ref.)*					
2020 × Post × Monza Brianza	0.61	1.14	0.600	−1.89	3.12
2020 × Post × Milano	−0.25	1.21	0.841	−2.91	2.41
2020 × Post × Mantova	−12.21	0.96	<0.001	−14.32	−10.10
2020 × Post × Pavia	5.49	1.41	0.002	2.39	8.58
2020 × Post × Sondrio	15.17	0.77	<0.001	13.47	16.86
2020 × Post × Varese	−10.96	0.37	<0.001	−11.76	−10.15
2020 × Post × Bergamo	10.20	0.96	<0.001	8.09	12.31
2020 × Post × Brescia	4.64	1.21	0.003	1.96	7.31
2020 × Post × Cremona	19.12	1.60	<0.001	15.60	22.64
N. Obs	3487				

Note: Results are from a DID regression model. The interaction term *Year* × *Post* captures the differential impact of the lockdown period in 2020 compared to 2019. The reference province is Lodi.

Table 6
Effect of the COVID-19 pandemic on ambulance arrival times — Stroke.

Variable	Coefficient	Std. Err.	*P*-value	CI Low	CI High
Intercept	47.72	2.17	<0.001	42.93	52.51
Treat	32.97	10.85	0.011	9.09	56.86
Post	29.75	0.82	<0.001	27.95	31.55
Treat × *Post*	9.59	0.70	<0.001	8.05	11.12
Patients Controls					
Male	1.03	0.49	0.059	−0.05	2.11
Age	−0.0022	0.017	0.897	−0.0395	0.0350
Ambulance Call Cov.					
Call duration (min)	0.000002	0.000008	0.815	−0.000015	0.000019
# of Hour Calls	−0.0044	0.0017	0.023	−0.0081	−0.0007
Year × Post × Province Dummies					
2020 × Post × Lodi (ref.)					
2020 × Post × Monza Brianza	0.71	0.76	0.372	−0.97	2.39
2020 × Post × Milano	0.32	0.65	0.636	−1.12	1.76
2020 × Post × Mantova	5.53	0.33	<0.001	4.81	6.26
2020 × Post × Pavia	11.18	0.80	<0.001	9.43	12.94
2020 × Post × Sondrio	3.05	0.38	<0.001	2.21	3.89
2020 × Post × Varese	1.61	0.54	0.012	0.42	2.79
2020 × Post × Bergamo	22.11	1.09	<0.001	19.72	24.51
2020 × Post × Cremona	1.16	0.63	0.094	−0.23	2.56
N. Obs	4471				

Note: Results are from a DID regression model. The interaction term *Year* × *Post* captures the differential impact of the lockdown period in 2020 compared to 2019. The reference province is Lodi.

significantly influence arrival times. The ambulance dispatch controls reveal that the call duration is significant and positive, but with a coefficient that is practically zero. On the other hand, the information regarding the number of calls per hour, which serves as a proxy for the NHS workload during that hour, does not appear to be statistically significant. From the coefficients of the interaction between treat, post, and province, it is clear that the provinces experienced different effects compared to Lodi, with some provinces showing a positive effect and others a negative one.

Table 6 reports similar results for Stroke patients. The coefficient of the interaction term *Treat* × *Post* is slightly lower with an average increase of 9.6 min in ambulance arrival times during the lockdown period in 2020 compared to the same period in 2019 (considering that the baseline mean time in the pre-lockdown period of 2019 was 48.27 min). Patient-specific controls evidence a longer time for males even if it is marginally significant at conventional (95%) significant levels, while age does not exhibit an impact. The ambulance dispatch controls reveal that the call duration is significant and positive, but with a coefficient that is practically zero. On the other hand, the information regarding the number of calls per hour, which serves as a proxy for the NHS workload during that hour, appears to be statistically significant and negative but with a coefficient null. From the coefficients of

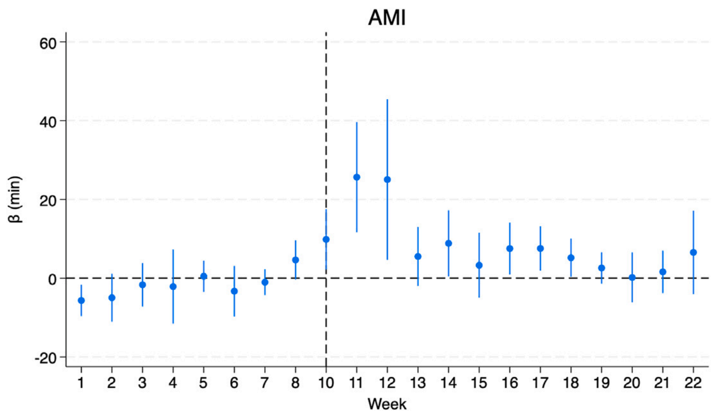

Fig. 5. Event study coefficients plot ambulance arrival times — AMI.

the interaction between treat, post, and province, it is clear that the provinces experienced different effects compared to Lodi, with some provinces showing a positive effect and others a negative one.

Comparing the main coefficient of interest in Tables 5 and 6, the impact of COVID-19 on the delay in EMS arrival times appears quite similar (11 min vs. 10 min). Since this average increase is nearly identical for both conditions, we can conclude that the time of ambulance arrival is not related to the patient's specific disease but rather to the overwhelming conditions of the emergency system during the pandemic.

Event study

Fig. 5 presents the event study plot for hospitalized patients with AMI, showing the set of estimated weekly coefficients of the interaction term. Each coefficient represents the average difference in ambulance arrival times in a week of 2020 compared to the same week of the previous year. From the graph, several observations can be made. First of all, in the period before week 10, the parallel trend assumption is almost always respected, with values close or equal to the null value, indicating the absence of differences in arrival times between the two years (2020 vs 2019) in the weeks preceding the lockdown date. Starting from week 8, the coefficients of the interaction term arise likely due to the rise in COVID-19 cases seeking hospitalization. The two weeks following the introduction of the lockdown show significantly higher values, with a difference of around 25 min in arrival times between the two years for the same weeks. After the initial rise, the values return to being non statistically significant from the pre-lockdown period.

Fig. 6 presents the event study plot also for hospitalized patients with Stroke. Prior to week 10, the coefficients are statistically indistinguishable from the baseline (week 9), confirming the validity of the parallel trend assumption. Again, following the implementation of the lockdown, the coefficients increased sharply, reaching around 25 min above the baseline week (9, before lockdown) for two consecutive weeks and 20 for the third following week. From week 14 onward the coefficients declined at a level of approximately 8 min above the baseline. However, this increase is not statistically significant.

7. Discussion

In a meta-analysis of 2022 (Pourasghari et al., 2022), patients hospitalized for AMI were 35% statistically significantly fewer in the COVID-19 era compared with pre-pandemic periods (OR = 0.65; 28 studies), both for STEMI and NSTEMI (29% and 34% respectively) and our hospitalization rates agree with this literature but the percentage that we found is lower.

Moreover, the overall rate of in-hospital mortality in AMI patients increased by 26% in the COVID-19 era, although the effect was not statistically significant (OR = 1.26, six studies). These numbers are confirmed by a recent Italian study (Campo et al., 2021) reporting that, in Emilia-Romagna, Hospital Admissions for AMI significantly declined on February and March 2022 compared to 2017–2019 admissions (IRR = −19.5%, and −21.6%, respectively) and return to pre-COVID-19 AMI-related admission levels since middle May, whereas the 30-day mortality in 2020 remained in line with that expected based on previous years, as we found in our study.

Regarding out-of-hospital deaths, our results agree with those from Lombardy (the incidence of out-of-hospital death was 14.9 percentage points higher in 2020 than in 2019 in the period February 21 through March 31 in four Provinces of the Lombardy region, (Baldi et al., 2020) and Paris (Marijon et al., 2020) (the weekly OHCA incidence between March 16 to April 26, 2020 increased from 13.4 to 26.6 compared with the same period in 2012–2019, and the proportion of patients who had an OHCA and were admitted alive decreased from 22.8% to 12.8% during pandemic). These studies are based on regional Cardiac Arrest Registry (with enrollment on voluntary basis and available only for a subset of Provinces) or emergency service databases (ambulance or Fire Brigade teams).

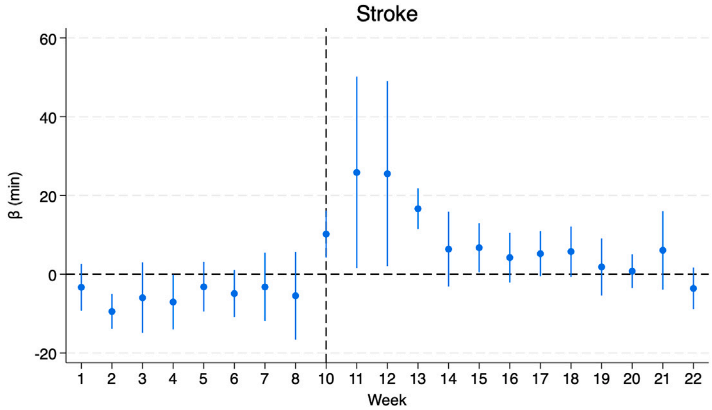

Fig. 6. Event study coefficients plot ambulance arrival times — Stroke.

Other studies (Campo et al., 2021) use mortality registry (Emergency Department Database) to identify subjects who died out-of-hospital for cardiac cause. In Emilia-Romagna, the number of out-of-hospital deaths for cardiac cause in 2020 was significantly higher than those expected in 2017–2019 (SMR = 1.17). The excess of out-of-hospital cardiac deaths was concentrated from February to April 2020, with the peak in April 2020 (SMR = 1.62). Another Italian study (Santi et al., 2021) in a large area in Northern Italy), reported a significant increase of out-of-hospital mortality (+43.2%) especially related to cardiovascular (+32.7%) during the COVID-19 period if compared with the same period of the year before. Our findings disagree with Veneto Paoli et al. (2020) where out-of-hospital mortality for cardiac arrest between March 1 and April 30 was 97%, the same rate in 2020 and 2019, and USA (Sayre et al., 2020) (the number of out-of-hospital total deaths was similar for 2020 (January 1 through April 15) compared with the same period of 2019–2018, IRR = 0.997). The differences between our findings and the U.S. evidence may partly reflect structural and organizational differences in healthcare systems, as well as a different level of COVID-19 spread. For instance, Italy's universal coverage and regionally coordinated emergency services contrast with the more fragmented and insurance-dependent U.S. system, which could influence patterns of hospital access, EMS response, and out-of-hospital mortality during the pandemic.

8. Conclusions

This study offers a comprehensive analysis of the impact of the COVID-19 pandemic on patients with Acute Myocardial Infarction (AMI) and Stroke in Lombardy, Italy. Leveraging a unique combination of administrative datasets and a quasi-experimental design, we explored changes in in-hospital and out-of-hospital mortality rates as well as hospitalizations and ambulance response times during the early phases of the pandemic.

Our findings highlight the significant strain imposed on healthcare systems, evidenced by a dramatic 60% increase in out-of-hospital deaths and substantial delays in ambulance response times, with an average increase of 11 min for both AMI and Stroke patients and a peak of 30 min delay in the two weeks following the lockdown date. These results show the critical role of pre-hospital care and the potentially harmful effects on patient outcomes.

Despite these challenges, in-hospital mortality rates remained stable, suggesting that the quality of care provided to patients who reached Lombardy hospitals was largely maintained. This result highlights the adaptability of hospitals under extreme pressure, but it also points to potential disparities in access to care for patients who could not reach the hospitals in time, especially considering that hospital admissions were lower due to the pandemic.

In the Lombardy context, the strong impact caused by the COVID epidemic has moved experts and health managers to re-thinking the health system, supporting new organizational models, capable of timely and safely reacting to the unexpected health emergency. Particularly, the regional system has shown a set of shortcomings during the epidemic period since the existing imbalances emerged both in the centralization of services in hospital structures, their privatization, and finally in the reduction of funding for general practitioners, who were reduced in number, considerably increasing the number of patients per capita and reducing the services traditionally provided at home (Petracca and Ricci, 2017). This produced one of the most serious territorial fragilities in Lombardy during the acute phase of the epidemic of the first wave of Covid-19 (Marzulli and Arlotti, 2021; Casti et al., 2022; Agenas, 2020). This structural lack of the basic public health service has also highlighted the poor integration between the local healthcare network and hospitals in relation to the location of the latter, which is concentrated in the Milan metropolitan area and in the main urban areas, such as the provincial capitals, preventing functional and capillary management of the infection.

These findings emphasize the crucial need for extremely robust and flexible emergency medical services (EMS), which are able to quickly adapt to high-pressure times, ensuring equitable access to emergency care during future pandemics or crises. Policymakers must prioritize investments in pre-hospital care infrastructure and develop strategies to mitigate systemic vulnerabilities during periods of high demand.

Lombardy represents a unique case study for examining the impact of the COVID-19 pandemic on regional healthcare systems, given the exceptionally high burden experienced during the first wave (Berta et al., 2025). While the quantitative effects observed here, such as increased out-of-hospital mortality and EMS delays, may be amplified compared to other regions, the key insights lie in the patterns revealed. Specifically, the results illustrate how sudden shocks, whether pandemics or other events that significantly increase healthcare demand, can strain emergency medical services and pre-hospital care. These findings are therefore generalizable in terms of the underlying dynamics to other regions and healthcare systems where EMS organization and hospital response are comparable, providing valuable lessons for strengthening resilience and preparedness in the face of future crises (e.g. ability to flexibly increase hospital beds, medical equipment and doctors and nursers shifts at demand).

Future research could expand on this work by exploring long-term effects on patient outcomes and evaluating policy interventions aimed at enhancing healthcare system resilience in the face of public health emergencies.

CRediT authorship contribution statement

Sara Muzzì: Writing – original draft, Software, Methodology, Formal analysis, Data curation, Conceptualization. **Paolo Berta:** Writing – original draft, Validation, Methodology, Formal analysis, Data curation, Conceptualization. **Pietro Giorgio Lovaglio:** Writing – original draft, Validation, Methodology, Conceptualization. **Stefano Verzillo:** Writing – original draft, Validation, Methodology, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The authors are willing to share all codes used to reproduce the paper results. Agreement with Lombardy region, the data provider, will be required for any data sharing. Stefano Verzillo has participated as external econometrician from European Commission, Joint Research Centre without access to the data and without receiving any funding. The information and views set out in this paper are those of the authors and do not reflect the official opinion of the European Union. Neither the European Union institutions and bodies nor any person acting on their behalf may be held responsible for the use which may be made of the information contained therein.

Appendix A. Supplementary data

Supplementary material related to this article can be found online at https://doi.org/10.1016/j.rie.2026.101126.

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