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Title

COVID-19 in Italy: is the virus running through an ancient Roman road?

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Conflicts of interest

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Availability of data and material (data transparency)

Data are publicly available

Code availability (software application or custom code)

Not applicable

Ethics approval

Not applicable

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Abstract

In late February 2020, Coronavirus disease-2019 (COVID-19) has aggressively spread around many bordering provinces of the three most productive regions of northern Italy (Lombardy, Veneto and Emilia Romagna). The first outbreak exploded in the municipality of Codogno (Lombardy). The province of Ferrara (Emilia Romagna) has been indicated as an anomaly due to the lower number of confirmed cases (1·065 cases per 1000 population). We argue that the spread of the virus throughout Emilia Romagna has a possible explanation in the geographical location of most of its provinces along the *Via Emilia*, an ancient Roman road that runs throughout the region, which we consider as a proxy for citizens' movement, number of contacts, and social interactions. In order to test this hypothesis, we used a non-linear multiple regression analysis on aggregate province data to investigate the association between the rates of confirmed cases and the distance from the *Via Emilia.* The results indicate that the infection rate decreases proportionally to the distance from *Via Emilia* (-14% every 10 km, $p<0·001$). Further studies are needed, but Ferrara's "peculiarity" might have a geographical/behavioral explanation, due to its isolation from the regional main connection routes, which are still revolving around a road built by the ancient Romans 2,000 years ago.

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Case Report

In late February 2020, Coronavirus disease-2019 (COVID-19) [1] has aggressively spread around many bordering provinces of the three most productive regions of northern Italy: Lombardy, Veneto and Emilia Romagna [2], the Italian "economic engine" that account for 40·1% of country's GDP [3]. The first outbreak exploded in the municipality of Codogno (Lombardy). Before the country's lockdown of March 10th, the virus has indeed freely circulated throughout northern Italy and beyond[1]. Sadly, some provinces' death toll now reflects a war bulletin [4], such as Bergamo (Lombardy, 1,114,590 inhabitants) and Piacenza (Emilia Romagna, 287,152 inhabitants) with 2,292 and 605 deaths, and 8·559 and 9·789 cases per 1,000 population[4], respectively.

Emilia Romagna and Veneto showed a similar, though less dramatic, trend, compared to Lombardy, with provinces presenting a high number of cases and others, just a few kilometers (km) away, with a lower incidence (Figure 1). The latter is the case of Ferrara (Emilia Romagna, 345,691 inhabitants), presenting a number of confirmed cases much lower than the other provinces (1·065 cases per 1000 population).

Ferrara has been indicated as an anomaly and several hypotheses have been put forward to explain it.

The Ferrara anomaly

The ancient city that hosted the Duchy of Este in the XV and XVI centuries represents a real outlier. In fact, the data provided by the Civil Protection and Italian Ministry of Health [5] clearly demonstrate that Ferrara is an area less affected by the infection with only 368 confirmed cases (total positive cases in Emilia Romagna: 15,932). What are the reasons for this anomaly? One of the hypotheses is the high prevalence of thalassemia/microcythemia among the *ferraresi* which may have protected the population as it did in the last century for malaria [6].

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However, till now this theory doesn't have a convincing biological basis. Accordingly, we sought to test a geographical/behavioral hypothesis.

Currently, the cities of Emilia Romagna are culturally, socially and economically connected through an ancient Roman road called *Via Emilia* (completed in 187 BC), that runs through the Po River valley (*Pianura Padana*) from Piacenza (16 km from Codogno) to Rimini (Adriatic coast) passing through Forlì, Bologna, Modena, Reggio Emilia, and Parma. The construction of the *Via Aemilia* launched the intensive Roman colonization of the *Pianura Padana* and soon rendered it the most economically important part of Italy. The area has remained economically preeminent in recent times, and the *Via Emilia* (also named in the maps Highway 9 - SS9) runs parallel to the main regional motorway (Motorway A1) and to the high speed railway line. Every day, a consistent number of people and goods moves along these important communication routes.

We argue that the spread of the virus throughout Emilia Romagna has a possible explanation in the geographical location of most of its provinces along the *Via Emilia*, which we consider as a proxy for citizens' movement, number of contacts, and social interactions.

In order to test this hypothesis, we used a non-linear multiple regression analysis on aggregate province data to investigate the association between the rates of confirmed cases and the distance from the *Via Emilia* (proportionally scored for every 10 km), adjusted for the distance from the cluster of Codogno, the mean annual income and the density of the population.

The results (Supplementary material) indicate that the infection rate decreases proportionally to the distance from *Via Emilia* (-14% every 10 km, $p<0{\cdot}001$). The other covariates contribute independently to the model, showing that the infection rate declines with the increase of the distance from Codogno and mean income, and increases with density of the population.

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Reflections

The data on the spread of COVID-19 highlights that Ferrara has a lower vulnerability to the virus when compared to the other provinces. Ferrara is the most distant from the *Via Emilia*. Its "peculiarity" might have a geographical/behavioral explanation, due to its isolation from the regional main connection routes, which are still revolving around a road built by the ancient Romans 2,000 years ago. Further studies are needed, but in order to stop the spreading of the virus, the Ferrara case may reinforce the evidence supporting measures of social distancing, which is a matter of discussion and concern all over the world.

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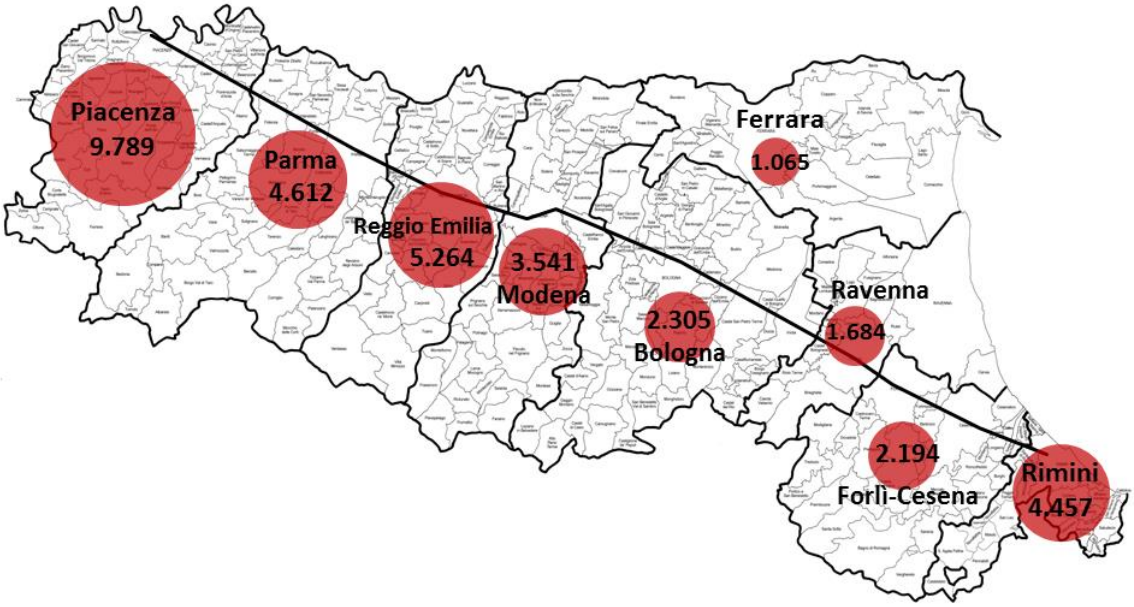

Figure 1. COVID-19 infection rate per 1000 inhabitants for the 9 provinces of the Emilia-Romagna region, Italy (April 3rd 2020). Red shadow is the infection rate. Black line is the *Via Emilia*.

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Supplementary material

Data sources and analysis

Data were retrieved from different institutional sources: Ministry of health for data on confirmed COVID-19 cases (http://www.salute.gov.it), the National Institute of Statistics (ISTAT, http://dati.istat.it/) for data on provinces (number of residents and density of population) available until 2019, and Ministry of Economy and Finance for data on annual income (https://www1.finanze.gov.it), available until 2017.

Distances in km were calculated using Google maps.

Data were analysed at aggregate province level using negative binomial regression analysis to investigate the association between the rates of confirmed cases and the covariates of interest. Incidence rate ratios (IRR) were reported with 95% confidence intervals (95%CI) and p-values. Results are shown in Table 1.

Table 1. Results of non-linear regression showing the relationship between the infection rate and covariates

Variable	**IRR**	**95% CI**	**p-value**
Distance from SS9 (+10 Km)	0·856	0·795 - 0·921	<0·001
Distance from Codogno (+10Km)	0·914	0·894 - 0·935	<0·001
Population density (+10 inhabitants/Km2)	1·027	1·010 - 1·045	0·002
Population income (+100 euro)	0·977	0·970 - 0·984	<0·001

IRR: incidence rate ratio; 95%CI: 95% Confidence Interval