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INDICE

DETERMINANTS OF THE CORONAVIRUS EPIDEMIC GENERATION IN ITALY

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1. Introduction

The coronavirus epidemic that has hit the world between the late 2019 and 2020 showed sharp differences across the various countries in terms of its onset time and spreading. As displayed in Figure 1, among the world's main countries in terms of population, after China – where the epidemic started but remained a regional phenomenon – Italy was the nation with the most rapid increase in the epidemic diffusion. Until late March 2020, Italy had the highest rate of infected people. The spread and rapid pace of the epidemic prompted the Italian government to adopt strict lockdown measures, including a national quarantine (8 March 2020). Italy's epidemic rates were then surpassed by Spain, later by Belgium, and much later by the US and the UK (EU 2020). The characteristics of the epidemic evolution in Italy are therefore relevant for understanding the epidemic reproduction mechanisms and the determinants behind a rapid diffusion of the epidemic.

Most statistical research work regarding epidemics has been strictly medicine-oriented and has focused on the analysis of epidemic reproduction, mortality and other medical aspects (Orea and Álvarez 2020). The usual statistical tools have been in tune with this approach.[1] In the present paper, we intend to study the coronavirus epidemic by means of standard socio-economic techniques and by focusing on a wider set of epidemic determinants. In this perspective, we shall concurrently analyse two epidemiological aspects relatively less studied. They are the spatial determinants of the epidemic – the effect produced on the epidemic diffusion at one location by the diffusion at nearby locations – and the ecological context: i.e. the territorial units' demographic and socio-economic features affecting the epidemic.

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[1] Within this approach, a common tool are the SIR models, which analyse the epidemic spreading by using the figures of, respectively, the Susceptible, Infected and Recovered people over time.

As for the spatial determinants, there is a long history of studies based on the spatial distribution of diseases, dating from John Snow's plotting of the locations of individuals affected by the cholera epidemic in London in 1854. More recently, the importance of the spatial component in epidemiology was highlighted by Cliff *et al.* (1981). Nevertheless, investigations of epidemiological outbreaks have tended to focus more on analyses of person and, especially, of time than of place (Moore and Carpenter 1999). In the recent literature on the coronavirus epidemic as well, the relevance of space has been treated marginally (Giuliani *et al.* 2020). In the present study, we intend to investigate more deeply the role of the spatial component in the secondary transmission by creating and testing a broad set of spatial matrices.

Figure 1 – *Coronavirus epidemic in some world's countries, February to May 2020: cumulative number of officially registered cases per 100K population.*
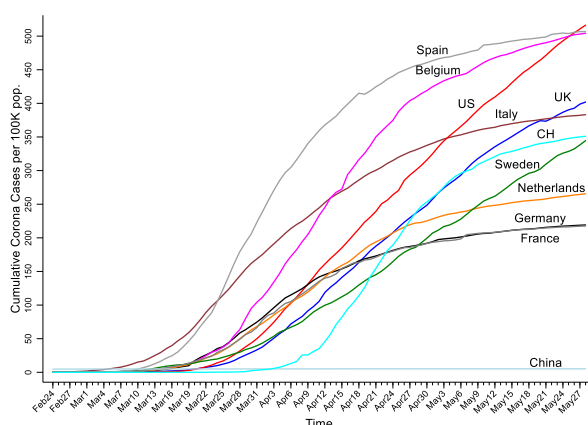
As for the ecological context, we intend to expand the set of socio-economic variables commonly used to explain epidemic spreading (Wang *et al.* 2020) and analyse their impact in a country presenting a high variance as to its internal features. Indeed, Italy is known for being a country with more marked regional differences than those found in other Western countries. These pronounced differences – primarily due to historical reasons – have attracted since many decades the social scientists' attention. Unsurprisingly, the coronavirus distribution too showed huge differences as to its spreading in Italy, so that, at the end of May 2020, the total number of coronavirus cases ranged, cross-province, from 28 to 1776 per 100K population. Although the epidemic touched all provinces, the most affected ones were in the Northern Macro-Region, in particular in Lombardy. An analysis of Italy's territorial differences, therefore, might be useful for identifying the epidemic determinants.

Before tackling the spatial and ecological aspects underlying the epidemic spreading, however, we must tackle the problem of identifying the correct nation-wide serial interval, i.e. the interval between the new, confirmed cases of coronavirus in Italy and the past cases originating them. Understanding these dynamics is crucial for evaluating the pattern and time of the virus *generation*, namely its *secondary* or human-to-human transmission. In turn, the understanding of secondary transmission is necessary for any further analysis.

The next section reports data information and presents the results, while the third section illustrates conclusions and a discussion of the present paper contribution.

2. Data and results

We used, as our primary dataset, the new daily cases of coronavirus registered from 25 February to 26 May 2020. We chose this period because, on the one hand, the first cases of coronavirus in Italy were registered on 25 February, and, on the other, the number of new cases at the end of May became fractional (see Figure 1). These figures, provided by the Italian Ministry of Health, are available for all provinces and the entire nation. We used the cross-province data and focused on their daily sum (equivalent to the nation's daily total). Other data, regarding the provinces socio-economic characteristics, came from the National Statistical Office (Istat). We noticed, first of all, some differences in the average number of total daily cases of coronavirus over the days of the week, probably owing to differences in their registration. We noticed as well the presence of a unit root in the time series: Figure 2 (left), indeed, suggests problems of non-stationarity concerning both mean and variance of the series. The Dickey-Fuller test confirmed the presence of a unit root (Table 1). In order to stabilise the time series, first, we ran a 3 DD mobile average on the original data, thus obtaining a neat reduction in the relative standard deviation of the number of cases over the days of the week (from 12.1% to 8.8%). We then logarithmised (natural logarithm) the series to reduce its variance and calculated the first differences in order to reduce variations as to the mean. The final result was a new time series (Figure 2, right) that can be regarded as stabilised enough, as confirmed by the Dickey-Fuller test (Table 1). Having done all this, we began to consider which lag would be the best predictor of the subsequent new cases of coronavirus. *A priori*, we took into account information about relevant facts, such as the incubation time, i.e. the period between exposure and onset of clinical symptoms. The median incubation period was estimated to be 5.1 days (Lauer *et al.* 2020) and the mean period 6.4 days (Backer *et al.* 2020). The WHO reported an incubation period between 2 and 10 days (WHO 2020). The estimated median

incubation period in Italy was 5.1 days; the average value of the means found by several studies being 5.9 days (Gatto *et al*. 2020).

Figure 2 – *Time series (left) and stabilised time series (right) of Italy's total number of new daily cases of coronavirus: February to May 2020.*
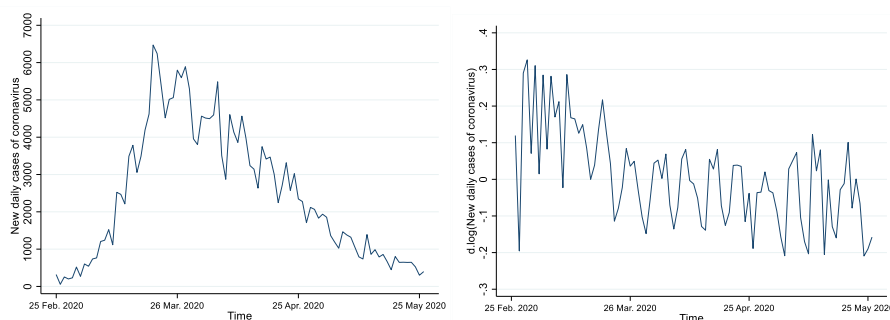
Table 1 – *Time series of Italy's total number of new daily cases of coronavirus, February to May 2020: unit root test.*

Time series		Interpolated Dickey-Fuller			
		Test statistics	1% Critical value	5% Critical value	10% Critical value
Daily cases of coronavirus (original data)	Z(t)	−1.619	−3.523	−2.897	−2.584
		MacKinnon approximate p-value for Z(t) = 0.474			
Daily cases of coronavirus (after stabilisation)	Z(t)	−5.872	−3.524	−2.898	−2.584
		MacKinnon approximate p-value for Z(t) = 0.000			

However, the viral load was found to be highest one day before the symptom onset (Zou *et al.* 2020): this implies that the *latent period*, i.e. the time from infection to infectiousness, would be slightly shorter than the *incubation period*. In turn, also the serial interval calculated on the new cases would be slightly shorter than the effective incubation period. On the other hand, people affected by the virus could well transmit it during the days after its onset, although no infectious virus was isolated after D8 from the symptom onset (Woelfel *et al.* 2020). This suggests that the serial interval between a registered case and the next one, representing the effect of secondary transmission, would be longer than the incubation period. This fact, in turn, would make up for the abovementioned fact that the viral load slightly antedates the symptom onset. A preliminary graph of autocorrelations with confidence intervals (Figure 3) indicates lag6-7 DD as the most significant ones, the best lag being the 7th. The partial autocorrelations graph (Figure 3) confirms the particular relevance of lag7.

Figure 3 – *Stabilised time series of Italy's total number of new daily cases of coronavirus: graph of autocorrelations (left) and partial autocorrelations (right), with pointwise confidence intervals.*
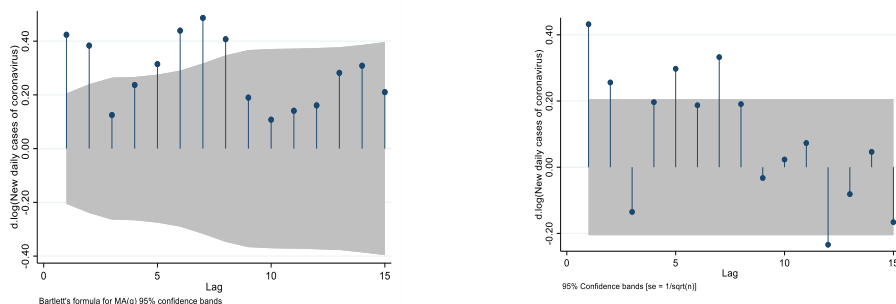
An Autoregressive model,[2] applied to the series of Italy's total number of new daily cases, produced the results shown in Table 2. We notice that the relationship between the new daily cases and lag4 DD is already significant. Lag6-7-8 show closer correlations, and lag7 exhibits the closest of all the correlations. The correlations become non-significant after lag9. The further results obtained by applying the same Autoregressive model to the cross-province means and medians of new daily cases over the same period support the reliability of the previous results. This procedure allows us to identify the most significant serial interval. This interval, which is calculated over the entire period of time taken into consideration, however, does not clear up the evolution over time of the expected number of cases directly generated, in the population susceptible to infection, by one case. Using the most significant serial interval (lag7) we calculated the *effective reproduction number*, as the ratio between the new cases of coronavirus and the lagged cases, considering as well as the fraction of the population susceptible to infection.[3] Figure 4 shows the result of this calculation. We notice that the reproduction number decreased after the national lockdown decree of 8 March 2020 (Sebastiani *et al.* 2020), but it crossed the crucial watershed of reproduction =1only around 27 March. These calculations are meant to identify both the timing of the secondary transmission and its reproduction ratio. The next fundamental issue is the spatial origin of secondary transmission. We hypothesise that people coming from other territorial units contributed to the epidemic transmission in each territorial unit. To test this hypothesis, we used data concerning new cases of coronavirus registered across the 107 Italian provinces.

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[2] A simple Autoregressive model notation is $y_t = y_{t-1...nth} + \varepsilon_t$ where y_t is the value of a time series at a given time, $y_{t-1...nth}$ are y various lagged values, and ε_t is a white-noise disturbance.

[3] In this case, the effective reproduction number is $x_t / x_{t-7} * s_{t-7}$ where x is the number of new cases, t is time and s is the fraction of susceptible population, which in turn is (total pop. $- \sum x$) / total pop.

Table 2 – *Autoregressive model, applied to the time series of Italy's total number of new daily cases of coronavirus, February to May 2020.*

Time Series	Lags	Lagged cases		Constant		Sigma		Log likely-hood	AIC
		Coef.	Z	Coef.	Z	Coef.	z		
d.log	Lag3	0.144	1.09	0.0062	0.37	0.127	10.83	58.44	−110.88
(New	Lag4	0.293	2.97	0.0063	0.35	0.124	12.66	60.89	−115.78
daily	Lag5	0.385	2.84	0.0064	0.31	0.120	11.87	63.51	−121.02
cases	Lag6	0.573	6.80	0.0086	0.36	0.109	15.00	71.05	−136.10
of	Lag7	0.629	8.18	0.0104	0.40	0.104	13.96	74.71	−143.43
coron	Lag8	0.557	6.57	0.0125	0.54	0.111	13.85	69.59	−133.17
a-	Lag9	0.260	1.96	0.0088	0.51	0.125	11.42	59.92	−113.85
virus)	Lag10	0.160	1.39	0.0082	0.51	0.127	11.39	58.40	−110.81

Figure 4 – *Evolution over time of the effective reproduction number of Italy's coronavirus epidemic, March to May 2020: reproduction number calculated considering lag7 cases as the secondary transmission vehicle.*
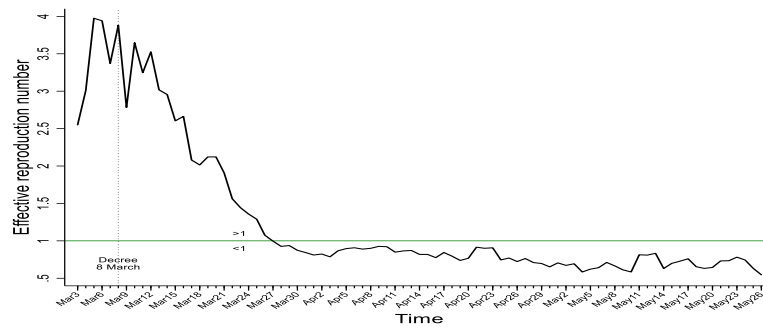
Preliminarily, we ran a 7 DD moving average, because the background noise in the cross-province data was higher than in the nation-level data. Then, we regressed these new cases on lagged cases, incorporating a set of 14 spatial matrices created ad hoc.[4] This set includes various contiguity matrices – nearest neighbour, first order, second order, combinations of the first and second order – an inverted distance matrix, combinations of contiguity and inverted distance matrices, and a commuting matrix.[5] All matrices are spectral-normalised. Some preliminary Moran

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[4] A spatial regression model assumes that the response variable value at one location is affected by the values at the nearby locations. Here, we assume that coronavirus cases in place *i* depend on a weighted average of lagged cases in the other places and (where useful) a linear function of covariates

$$coronavirus\ cases_i = \lambda \sum_{j=1}^{N} w_{i,j}\ lag.coronavirus\ cases_{j,j \neq i} + \beta x_i + \varepsilon_i$$

where $x_i =$ (covariates, constant).

[5] This matrix concerns province's commuters coming from other provinces, no matter the distance. The matrix values are the number of commuters divided by the host province's population. The matrix is based on census (2011) mobility fluxes at municipal level, that we converted to the provincial level.

tests showed – with any matrix – a significant spatial correlation in the residuals of the simple regressions of cross-province new cases. The results of the spatial regressions (Table 3), in turn, show that the association between the coronavirus cases in each province and the cases in the other provinces was always significant, supporting the hypothesis of a spatially-related transmission. Despite being always significant, this association shows varying levels of closeness. These dissimilarities, however, can be traced back to the different construction of the matrices. For instance, when the contiguity regards only the nearest neighbour, the elasticity of the response variable is unsurprisingly lower than that produced by first-order contiguity matrices, which take into consideration all neighbours, not just the nearest one. Second-order contiguity matrices, which concern relatively less near territorial units, show elasticities lower than the first-order ones. However, at the end of the period investigated, these differences evaporated, owing most probably to the progressive territorial spreading of the epidemic. The closest associations are those obtained using the contiguity by inverted distance matrices, in particular those of first order, and of first order = 1 and second order = 0.5. Table 3 shows as well that the lagged cases impact had a decreasing trend over time, in tune with the decrease in the effective reproduction number (Figure 4). A drop involving all spatial matrices materialised as to the elasticity of the 22 March's cases to a change in the 15 March's ones, and a more massive drop came to the fore a week later. The results obtained with the spatial matrices have told us that the coronavirus epidemic had a spatial component. However, it is important to check how this spatial component interacts with the intra-territorial-unit characteristics, i.e. with the possible ecological determinants of the epidemic diffusion. Preliminarily, we inspected the cross-province correlations between the new cases of coronavirus around the peak of the epidemic and the territorial characteristics, including the previous cases. Table 4 shows the associations between coronavirus cases and, respectively, previous cases, latitude (more northerly, more cases), temperatures (higher temperatures, fewer cases), particulate matter (an indicator of vehicular traffic and industrial development), people 6 to 18-year old (an age group with frequent social interactions, and therefore an agent of transmission, even when asymptomatic), people 75-year or older (a group prone to develop more severe health problems when infected, and therefore probably over-recorded by the health services), intra-province commuters (an indirect indicator of social contacts), vehicles (an indicator of mobility, and, indirectly, of social contacts), employment to population ratio and firm workers (both being indicators of social contacts for work reasons), added value (an indicator of development and indirectly a measure of an *organic* labour division, implying a higher level of social interactions), lower-income population's share (an indicator of underdevelopment), and hospital beds (hospitals could be means of secondary transmission). Finally, we analysed these

variables within regression models (Table 5). The OLS model shows the impact, on coronavirus cases, of latitude, the 6 to 18-year age group, large firm workers, and vehicles. The contribution of past coronavirus cases becomes negative: the higher the rate of "recovered" people, the lower that of the susceptible ones. Intra-province commuters, correlated with large firm workers (r = 0.460), at parity of the latter is non-significant. Added value, closely correlated with large firms (r=0.780), becomes negative.

Table 3 – *Spatial regressions of Italy's cross-province new daily cases of coronavirus on lagged cases incorporating cross-province spatial effects.*

Spatial matrix type	Spatial lag order	Cases 8/03 on 01/03/20		Cases 15/03 on 08/03/20		Cases 22/03 on 15/03/20		Cases 29/03 on 22/03/20		Cases 05/04 on 29/03/20	
		E	R^2	E	R^2	E	R^2	E	R^2	E	R^2
None (base)	None	3.57	0.75	3.41	0.83	1.76	0.82	0.68	0.85	0.56	0.33
Cont.	Nearest neighb.	2.92	0.55	2.49	0.54	1.25	0.46	0.47	0.49	0.43	0.20
Cont.	1st	4.50	0.52	3.65	0.63	1.72	0.65	0.58	0.61	0.50	0.28
Cont.	2nd	1.71	0.08	2.20	0.23	1.37	0.43	0.50	0.50	0.55	0.37
Cont.	1st=1; 2nd=0.7	4.48	0.40	3.62	0.53	1.71	0.61	0.58	0.60	0.55	0.34
Cont.	1st=1; 2nd=0.5	4.70	0.45	3.72	0.57	1.74	0.63	0.58	0.61	0.54	0.32
Cont.	1st=1; 2nd=0.3	4.20	0.35	3.49	0.49	1.68	0.59	0.57	0.59	0.56	0.34
Inverted distance	0-1,406 Km	8.80	0.37	6.61	0.47	2.87	0.57	0.88	0.56	0.84	0.34
Cont. by i.v.	Nearest neighb.	9.33	0.59	7.46	0.55	3.50	0.45	0.97	0.39	0.76	0.14
Cont. by i.v.	1st	4.53	0.60	3.91	0.68	1.91	0.69	0.60	0.61	0.48	0.24
Cont. by i.v.	2nd	1.52	0.09	1.98	0.24	1.31	0.45	0.47	0.51	0.49	0.34
Cont. by i.v.	1st=1; 2nd=0.7	4.55	0.55	3.67	0.62	1.78	0.66	0.57	0.61	0.49	0.28
Cont. by i.v.	1st=1; 2nd=0.5	4.60	0.58	3.76	0.65	1.82	0.68	0.58	0.62	0.49	0.27
Cont. by i.v.	1st=1; 2nd=0.3	4.45	0.52	3.57	0.59	1.74	0.65	0.56	0.61	0.49	0.29
Comm. f. other prov.	None	7.56	0.62	4.74	0.56	2.15	0.54	0.59	0.42	0.42	0.14

Note: "Cont"= Contiguity; "Comm"=Commuters; "Cases" = new coronavirus cases per 100K pop. Proximity pattern = queen. In the spatial regressions, R^2 is (pseudo)R^2. Spatial effects are significant (P > z) at <0.001 when (pseudo)R^2 is >0.100. Base regression is x_t on x_{t-7}. N = 107 provinces. Elasticity = $d\bar{y} / d\bar{x} * \bar{x}/ \bar{y}$. Spatial regression models use a max. likelihood estimator.

Table 4 – *Correlations between cross-province cases of coronavirus per population in Italy and various characteristics of the provinces.*

Explanatory variables	New cases 22/03/2020 per pop.	
	Coeff.	P. value
New cases 15/03/2020 per pop.	0.903	0.000
Cumulative past cases 08/03/2020 per pop.	0.704	0.000
Latitude	0.618	0.000
Average temperatures	–0.454	0.000
Particulate matter 10 microm.	0.404	0.000
Population 6 to18-year old percent	0.101	0.299
Population 75-year or older percent	0.125	0.199
Pop. density (population/Km^2)	0.067	0.495
ln(chief-town population)	0.019	0.849
Intra-province commuters per pop.	0.356	0.000
Local transport passengers per pop.	0.142	0.145
Vehicles per pop.	0.206	0.034
Commercial vehicles per pop.	0.181	0.062
Added value (per capita)	0.572	0.000
Lower-income population's share (<= €10K per capita %)	–0.633	0.000
Employment to population ratio (15 to 64-year old)	0.585	0.000
Firm 10 to 49 workers per pop.	0.492	0.000
Firm 50 to 249 workers per pop.	0.635	0.000
Firm 250 or more workers per pop.	0.367	0.000
Firm total workers per pop.	0.499	0.000
Hospital beds per pop.	0.304	0.001

Population density and chief town population are never significant. The same occurs with the elderly population's share. The first and second spatial models confirm the contribution made by the "spatial lag" at parity of previous and past cases, showing as well that the association with the coronavirus cases is slightly closer when we use the inverted distance between all provinces. The third spatial model (the full one) shows that previous and past cases, the ecological determinants and the spatial matrices are all good predictors of new coronavirus cases. Latitude, correlated with both added value and large firms, becomes non-significant if we use an inverted distance matrix. Hospital beds, correlated with added value ($r = 0.436$), are positive but non-significant.

3. Conclusions

This study on the coronavirus epidemic in Italy focused, first, on the identification of the secondary transmission serial interval, the premise for further

analyses of the spatial and ecological determinants of that transmission. By using nation-level new cases, we identified a 7 DD interval. On the basis of this interval, the present study analysed the spatial component of the epidemic. The results obtained when employing a broad set of spatial matrices confirmed the significant impact of this spatial component. A secondary transmission *spillover* between contiguous territorial units emerged, but so did the significance of *distance*, a fact implying that transmission went beyond *contiguity*.

Table 5 – *OLS and spatial regressions of cross-province new coronavirus cases in Italy on time lagged cases, spatially lagged previous cases, and other territorial explanatory variables.*

Explanatory variables	Response variable: new coronavirus cases 22/03/2020 per pop.							
	OLS model		Spatial mod. 1		Spatial mod. 2		Spatial mod. 3	
	E	z	E	z	E	z	E	z
Direct impact								
New cases 15/03/2020 pp.	0.661	11.79	0.605	12.02	0.594	11.08	0.590	11.96
Cumulative past cases 08/03/2020 pp.	–0.062	–2.16	–0.057	–2.29	–0.097	–3.65	–0.068	–2.82
Population 6 to18-year old percent	1.213	2.66					1.426	3.67
Firm 250 or more workers pp	0.207	3.48					0.207	4.12
Hospital beds pp	0.133	0.89					0.211	1.64
Added value (per capita)	–0.474	–1.57					–0.684	–2.64
Latitude	3.324	3.32					0.220	0.21
Commercial vehicles pp.	0.276	2.74					0.394	4.46
Pop. density (pop/Km^2)	–0.004	–0.15					–0.020	–0.81
Indirect impact								
W inv. distance (New cases 15/03/2020 pp.			0.461	6.30			0.561	5.30
W cont. by i.v.(New cases 15/03/2020 pp.)					0.193	5.64		
N	107		107		107		107	
R^2 or (pseudo) R^2	0.890		0.871		0.864		0.913	

Note: "pp"= per population; Elasticity = $d\bar{y} / d\bar{x} * \bar{x}/\bar{y}$. Spatial regression models use a ML estimator.

The different construction of the various spatial matrices satisfactorily explained the dissimilarities as to the estimations obtained by means of these matrices. Moreover, when the temporal scenario associated with the epidemic varied, also all the estimations obtained by using the various spatial matrices changed in the same direction. It appeared as well that the impact had a decreasing trend over time. This trend could be traced back to decreasing and/or more cautious inter-provinces social contacts, due, in turn, either to fear of contagion or to the government lockdown measures. What is sure is that a first, distinct decrease in the spatial impact on the inter-provinces secondary transmission surfaced in the relationship between the 15 March 2020's infecting cases and the 22 March's infected cases, therefore a few days after the national quarantine was proclaimed (8 March). A further, massive drop in the spatial impact materialised as to the infected cases of 29 March: this seems to resonate well with the *effective reproduction number* trend, which, according to our calculations, passed the turning point of 1 on 27 March 2020.

Lastly, the present study analysed the contribution made to the epidemic secondary transmission by, concurrently, the lagged cases of coronavirus, the spatial component and several territorial features. The vast differences in development and social organisation traditionally existing between the Italian territorial units prompted us to hypothesise that these differences could explain the large disparities in the cross-province epidemic diffusion. The results show, indeed, that a significant statistical contribution to the epidemic reproduction came from the lagged cases of coronavirus, the spatial component but also from the territorial characteristics. Among the latter, indirect indicators of social interactions and mobility emerged as particularly relevant for the secondary transmission.

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SUMMARY

Determinants of the Coronavirus Epidemic Generation in Italy

This study intended to analyse the secondary transmission mechanisms of the 2020 coronavirus epidemic in Italy. To do so, this paper has identified, firstly, the serial interval of the transmission, the premise for further analyses of its spatial and ecological determinants. As for spatial determinants, a broad set of spatial matrices were created and tested. With all these matrices, the existence emerged of a secondary transmission spatial *spillover*. Both *contiguity* and *distance* proved to be significant for this transmission. The spatial component, however, was not the sole significant determinant of the secondary transmission. Various features of the territorial units (provinces) proved to be significant. The results of both OLS and spatial regression models suggested the particular relevance of indirect indicators of social interaction and mobility.

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