Check for updates

G OPEN ACCESS

Citation: Buja A, Paganini M, Cocchio S, Scioni M, Rebba V, Baldo V (2020) Demographic and socioeconomic factors, and healthcare resource indicators associated with the rapid spread of COVID-19 in Northern Italy: An ecological study. PLoS ONE 15(12): e0244535. https://doi.org/ 10.1371/journal.pone.0244535

Editor: William Joe, Institute of Economic Growth, INDIA

Received: April 27, 2020

Accepted: December 11, 2020

Published: December 28, 2020

Copyright: © 2020 Buja et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: Data analysis was performed on ecological and not on individual data, derived from the publicly available Italian National Institute of Statistics databases (http://dati.istat.it/ Index.aspx, https://www.istat.it/it/archivio/14562) and from the Italian National Olympic Committee database (https://www.coni.it/it/registro-societasportive.html). Variables are listed in Tables 1 and 2. The authors of the present study have no special access privileges in accessing these datasets. RESEARCH ARTICLE

Demographic and socio-economic factors, and healthcare resource indicators associated with the rapid spread of COVID-19 in Northern Italy: An ecological study

Alessandra Buja¹, Matteo Paganini^{2*}, Silvia Cocchio¹, Manuela Scioni³, Vincenzo Rebba⁴, Vincenzo Baldo¹

1 Department of Cardiologic, Vascular and Thoracic Sciences, and Public Health, University of Padova, Padova, Italy, 2 Department of Biomedical Sciences, University of Padova, Padova, Italy, 3 Statistics Department, University of Padova, Padova, Italy, 4 'Marco Fanno' Department of Economics and Management, University of Padova, Padova, Italy

* matteo.paganini@unipd.it

Abstract

Background

COVID-19 rapidly escalated into a pandemic, threatening 213 countries, areas, and territories the world over. We aimed to identify potential province-level socioeconomic determinants of the virus's dissemination, and explain between-province differences in the speed of its spread, based on data from 36 provinces of Northern Italy.

Methods

This is an ecological study. We included all confirmed cases of SARS-CoV-2 reported between February 24th and March 30th, 2020. For each province, we calculated the trend of contagion as the relative increase in the number of individuals infected between two time endpoints, assuming an exponential growth. Pearson's test was used to correlate the trend of contagion with a set of healthcare-associated, economic, and demographic parameters by province. The virus's spread was input as a dependent variable in a stepwise OLS regression model to test the association between rate of spread and province-level indicators.

Results

Multivariate analysis showed that the spread of COVID-19 was correlated negatively with aging index (p-value = 0.003), and positively with public transportation per capita (p-value = 0.012), the % of private long-term care hospital beds and, to a lesser extent (p-value = 0.070), the % of private acute care hospital beds (p-value = 0.006).

Conclusion

Demographic and socioeconomic factors, and healthcare organization variables were found associated with a significant difference in the rate of COVID-19 spread in 36 provinces of

Funding: The author(s) received no specific funding for this work.

Competing interests: The authors have declared that no competing interests exist.

Northern Italy. An aging population seemed to naturally contain social contacts. The availability of healthcare resources and their coordination could play an important part in spreading infection.

Background

The disease caused by the COVID-19 virus first detected in Wuhan, China, in December 2019 [1] escalated rapidly into a pandemic [2], coming to threaten 213 countries, areas and territories across the globe [3].

Italy recorded its first imported cases in January 2020 [4], and local cases emerged towards the end of February in Northern Italy, in the Lombardia and Veneto regions [4, 5]. Restrictions on international travel, domestic mobility, mass gatherings, and sporting events were gradually enacted by the Italian Government in an effort to contain the contagion [4], until the country's complete lockdown on March 9th, 2020 [6]. Once implemented, these mitigation strategies (which sounded draconian to the population) proved effective in limiting the diffusion of COVID-19 to other parts of the country, but the infection continued to spread with different trends in Northern Italy.

Many demographic and socioeconomic factors, and healthcare organization variables can be associated with the variability of contagious disease propagation rates. It is important for public health systems to identify these factors and variables to produce solid evidence that can drive mitigation strategies. As well as having a direct influence on health outcomes in a given area, the findings of public health research also have important implications for ongoing global efforts to contain COVID-19. For example, a recent study found that even a small increase in long-term exposure to PM2.5 leads to a large increase in the virus-related death rate, with the magnitude of increase 20 times that observed for PM2.5 and all cause mortality [7].

Besides environmental conditions, factors such as employment rates, population density, and healthcare resources may help to account for the observed differences in rapidity of COVID-19 propagation.

With this ecological study we aimed to identify potential province-level demographic, socioeconomic and healthcare determinants of the COVID-19 pandemic's dissemination, and to explain between-province differences in the rate of the disease's spread, based on data from 36 provinces in four regions of Northern Italy.

Materials and methods

Context

The Italian National Health Service (NHS) was set up in 1978 with universal coverage, solidarity, human dignity, and human health as its guiding principles. It is regionally based, and organized at national, regional and local levels. Under the Italian Constitution, central government controls the distribution of tax revenue for publicly-financed healthcare and decides on a national statutory benefits package of "essential levels of care"—offered to all residents in every region. The country's 19 regions and two autonomous provinces are responsible for organizing and delivering healthcare services through local health units. Depending on the region, public funds are allocated by local health units to public hospitals and accredited private clinics. In 2017, there were approximately 213,700 hospital beds, including day hospital and day surgery beds: 170,000 in public hospitals (2.8 beds per 1,000 population, including 2.5/1,000 for acute care and 0.3/1,000 for long-stay patients), and 43,700 in accredited private clinics (0.7 beds per 1,000 population, including 0.4/1,000 for acute care and 0.3/1,000 for long-stay patients) [8]. Public hospitals are either managed directly by local health units and coordinated with other local health services such as preventive medicine departments and primary care districts, or they operate as semi-independent public enterprises. A prospective payment system based on diagnosis-related groups (DRG) operates across the country and accounts for most hospital revenue, but is generally not applied to hospitals run directly by local health units, where global budgets are common.

Study design and data sources

In the present ecological study we included all confirmed cases of SARS-CoV-2 reported between February 24th and March 30th, 2020, drawn from the Italian Civil Protection Department's official data [9]. This agency operates certified surveillance systems for the Italian government, with a two-stage testing procedure for SARS-CoV-2, one at local health unit level, and one at national laboratory level for confirmation purposes. All reported cases of COVID-19 infection met the laboratory criteria for confirmation established in the EU case definition procedure, which includes using RT-PCR.

We collected data on 36 provinces in four regions of Northern Italy–Piemonte, Lombardia, Veneto, and Emilia-Romagna–which have had the highest numbers of infections during the COVID-19 pandemic. In order to standardize as much as possible the period analyzed, we chose to evaluate the onset phase of the disease and we considered as starting point for each province $_i$ (T_{0 i}) the first day when that province reached 10 cases. For each province, we calculated the trend of contagion was computed as the relative increase in the number of individuals infected between two time endpoints: T_{0 i} and T_{20 i} (20 days after T₀). Demographics were extracted from the most recently updated databases on the website of the Italian Institute of Statistics (ISTAT) [10], and the ISTAT's Health for All database [11]. The number of sporting associations for each province was obtained from the registry of the Italian National Olympic Committee (CONI) [12].

In particular, the variables introduced in the last model are defined as subsequent:

- Aging Index: Number of elderly in a population for 100 youngster, source ISTAT
- Population Density: Number of people on the province territory divided by the territorial extension, source ISTAT
- Density Inside Housing: Number of family members per square meter, source ISTAT
- % Sport Associations / Resident Population: Number of sport associations divided by the resident population, source CONI–Registro Società Sportive
- Unemployment Rate: Ratio of people searching for a job and the work forces population, source ISTAT
- Employment Rate: Ratio of employed people and the work forces population, source ISTAT
- % of Active Companies / Resident Population: Number of active companies divided by the resident population, source ISTAT
- Local Public Transport Use Per Capita: Local public transport demand in provinces capital towns, source ISTAT
- % of Private Long-term Care Beds: Percentage of hospital beds for long-term care in private clinics on the total number of hospital beds for long-term care, source Health For All– ISTAT

- % of Private Acute Care Hospital Beds: Percentage of hospital beds for acute care in private clinics on the total number of hospital beds for long-term care, source Health For All– ISTAT
- % of Anesthesiologists / Resident Population: Number of anesthesiologist divided by the resident population, source Health For All–ISTAT
- General Practitioners Rate: Number of general practitioners for 10.000 inhabitants, source Health For All–ISTAT
- Dentists Rate: Number of dentists for 10.000 inhabitants, source Health For All-ISTAT
- Nursing Staff Rate: Number of nurse for 10.000 inhabitants, source Health For All-ISTAT
- Acute Care Hospital Beds Rate: Acute care hospital beds for 10.000 inhabitants, source Health For All–ISTAT
- Long-term Care Hospital Beds Rate: Long-term care hospital beds for 10.000 inhabitants, source Health For All–ISTAT
- Emergency Medical Service Rate: Number of emergency medical services for 10.000 inhabitants, source Health For All–ISTAT

Data analysis

We modeled the disease's spread assuming an exponential growth with the number of infections multiplying by a certain factor each day. Assuming no recoveries during the three-week period considered, the total number of people infected at the time t, y_t can be written as:

$$y_t = y_1 (\beta + 1)^{(t-1)}$$

where y_1 is the number of cases on day 1 and β is the transmission factor.

Since we know the number of cases on day 1 and day 20, we can compute β_i , the transmission factor, for the i-th province as:

$$\beta_i = (y_t/y_1)^{(1/(t-1))} - 1$$

A descriptive analysis was conducted, calculating minimum, maximum and mean values, to illustrate the spread of the disease. Pearson's test was applied to correlate β_i with a set of healthcare-associated, economic and demographic parameters at province level (see Table 1).

 β_{-i} was input as a dependent variable in an OLS regression model to study the association between the rate of spread of COVID-19 infection and the variables that correlated with the dependent variable on a bivariate level with a p-value of less than 0.20. Density inside housing and the unemployment rate were not included in the multivariate model due to multicollinearity issues. A stepwise selection procedure was used. A residuals analysis was performed to check the assumptions of the model. This analysis included testing for the residuals' normal distribution (Shapiro-Wilk normality test) and independence (Durbin-Watson test).

A sensitivity analysis was conducted, considering different dependent variables as rates (t1/ t0) or incremental rates ([t1-t0]/t0), which produced the same results (data not shown). All data obtained were encoded in a master sheet using a Microsoft Office Excel spreadsheet (Version 2016, Microsoft Corporation, Redmond, WA). Data analysis was done with Stata 14 statistical software (Stata Corp LP, College Station, TX) and R Studio Integrated Development for R (RStudio, Inc., Boston, MA).

Table 1.	Environmental,	health, economic	, and population fact	ors by province.					
Provinces	Region	Resident population ^(a)	Aging index ^(b)	Population density	% of sports associations/ resident population	Unemployment rate	Employment rate	% of active companies/ resident population	Local public transport usage per capita
PD	Veneto	937908	169.6	429.7	0.186	5.84	52.36	9	133.1
BG	Lombardia	1114590	145.2	395.6	0.157	4.86	50.82	7.8	271.9
PV	Lombardia	545888	197.8	180.5	0.137	6.49	49.58	7.1	100.7
CR	Lombardia	358955	188.9	202	0.159	5.1	50.16	6.9	18.1
LO	Lombardia	230198	153.8	285.76	0.156	6.51	51.33	6.2	20.6
РС	Emilia Romagna	287152	195.9	110.07	0.157	5.59	51.54	8.2	70.1
TV	Veneto	887806	156.9	353.57	0.185	8.01	51.33	8.1	96.5
VE	Veneto	853338	198.2	342.5	0.166	6.4	47.83	7.7	655.7
МІ	Lombardia	3250315	166.9	1928.4	0.115	6.45	52.79	9.1	689.2
BR	Lombardia	1265954	151.2	258.7	0.165	5.16	51.72	8.2	167.7
PR	Emilia Romagna	451631	175.1	123.98	0.164	4.78	53.9	8.4	141.8
мо	Emilia Romagna	705393	164	255.13	0.142	6.04	52.68	7.5	43.9
то	Piemonte	2244488	198.16	329.25	0.147	9.22	48.31	33.3	230.4
RN	Emilia Romagna	339017	172.7	372.03	0.183	8.23	52.56	10.2	95.3
AT	Piemonte	223018	212.13	144.07	0.146	8.38	46.88	23.6	43.6
VR	Veneto	926497	157.6	290.83	0.164	7.04	51.8	8.1	148.7
MN	Lombardia	412292	177.9	174.39	0.155	6.68	50.2	7.2	78.5
RE	Emilia Romagna	531891	149.6	225.78	0.164	4.21	53.26	7.8	64.9
VI	Veneto	862418	158.6	315.59	0.175	5.26	51.73	8.2	50.8
VA	Lombardia	890768	174.6	727.71	0.161	5.93	50.7	7.4	71.9
МВ	Lombardia	873935	160.9	2072.09	0.124	6.04	51.61	7.7	38.9
во	Emilia Romagna	1014619	190.1	263.68	0.167	5.64	53.39	8.6	246.4
AL	Piemonte	434050	245.79	120.05	0.166	10.03	46.21	26.6	36.5
со	Lombardia	599204	169.3	458.72	0.145	7.31	50.99	7.6	109.9
LC	Lombardia	337380	174.8	412.86	0.145	5.63	51.48	7.6	61.7
BL	Veneto	202950	228.3	57.19	0.237	4.35	51.03	7.4	67
RA	Emilia Romagna	389456	201.4	206.92	0.205	5.85	50.84	8	39.9
vc	Piemonte	180272	236.2	85	0.173	7.18	47.7	23.5	12.9
VB	Piemonte	164647	233.79	70.88	0.183	5.68	46.57	21.2	46.9
FC	Emilia Romagna	394627	184	164.29	0.192	4.83	51.92	8.9	57.6
BI	Piemonte	184695	263.27	199.49	0.144	6.47	48.81	28.4	22.9
NO	Piemonte	367939	181.1	272.75	0.163	8.5	48.23	27.3	84
CN	Piemonte	594729	179.46	85.04	0.173	4.35	51.85	31.3	63.8
RO	Veneto	287152	234.3	133.21	0.161	6.85	47.4	6.9	11.4
so	Lombardia	181095	181.4	56.58	0.149	6.65	49.11	7.5	3.6
FE	Emilia Romagna	345691	255.5	134.14	0.166	9.06	47.57	7.6	54.1
Provinces	% of private long-term care hospital beds	% of private acute care hospital beds	% of anesthesiologists / resident population	GP rates (GPs / resident population))	Dentist rates	Nursing staff rates	Acute care hospital beds rates	Long-term care hospital beds rates	Emergency medical service rates
PD	16.63	5.6	0.023	8.81	18.28	49.87	32.61	4.62	0.18
BG	74.24	30.15	0.016	6.88	17.82	42.84	25.02	6.55	0.26
PV	23.25	10.64	0.023	7.87	26.92	57.41	36.32	15.37	0.31
CR	56.35	14.45	0.02	6.97	20.03	47.59	29.26	6.96	0.2
LO	0	0	0.013	_	13.6	42.48	19.36	3.4	_

Table 1. Environmental, health, economic, and population factors by province.

(Continued)

РС	70.36	14.34	0.02	8.12	16.07	39.27	25.15	11.59	0.33
TV	6.91	7.3	0.016	7.13	14.99	37.17	25.01	4.08	0.18
VE	5.14	2.79	0.017	8.41	13.51	31.34	25.44	6.57	0.22
MI	37.34	9.09	0.025	7.72	28.67	53.22	32.94	6.27	0.14
BR	68.52	29.81	0.017	6.65	21.67	48.9	28.59	8.25	0.3
PR	67.18	21.29	0.022	7.57	19.26	50.16	33.51	10.29	0.55
мо	40.23	13.13	0.021	8.04	16.54	44.76	26.5	6.2	0.35
то	58.05	7.33	0.023	8.22	21.02	45.12	25.46	9.44	0.22
RN	76.68	16.57	0.019	7.94	24.42	50.46	26.68	7.56	0.42
AT	41.96	0	0.014	12.96	14.24	32.73	17.76	6.51	0.8
VR	26.18	4.51	0.02	7.49	21.82	50.81	30.52	6.67	0.25
MN	42.01	28.67	0.012	7.37	21	45.33	20.5	7.69	0.36
RE	23.56	10.69	0.014	7.13	16.58	39.1	24.88	6.84	0.41
VI	30.54	6.85	0.017	7.38	14.9	39.55	24.02	2.75	0.24
VA	52.54	11.49	0.022	7.39	18.34	45.16	25.44	6.21	0.14
МВ	69.44	19.31	0.013	_	17.59	38.46	20.33	5	_
во	50.24	15.75	0.026	7.9	26.48	56.86	36.78	8.16	0.29
AL	53.79	15.02	0.025	3.74	26.05	50.89	30.3	6.4	0.14
со	53.87	11.76	0.014	7.11	18.39	36.75	20.57	9.48	0.28
LC	5.1	15.93	0.02	7.23	18.9	44.12	24.7	11.51	0.28
BL	0	_	0.023	7.4	20.69	64.67	33.83	6.23	0.75
RA	37.66	35.48	0.02	8.19	25.81	54.19	34.42	5.89	0.22
vc	80.88	23.08	0.021	22.01	21.02	38.52	22.08	7.7	1.02
VB	41.7	0	0.015	_	18.19	46.36	21.28	32.14	_
FC	38.77	28.83	0.019	8.2	25.63	49.34	29.32	5.73	0.35
BI	56.6	11.36	0.017	_	17.91	34.43	21.79	5.83	_
NO	30.1	13.03	0.024	11.2	24.75	51.54	22.72	13.86	0.62
CN	75.18	6.3	0.024	7.53	19.45	47.41	26.27	9.59	0.49
RO	28.45	7.61	0.023	2.45	19.17	43.31	31.85	9.54	0.12
so	0	0	0.022	7.86	17.59	63.39	27.92	7.46	0.61
FE	25.68	9.79	0.022	8.67	19.76	50.49	28.51	8.23	0.46

Table 1. (Continued)

PD: Padova; BG: Bergamo; PV: Pavia; CR: Cremona; LO: Lodi; PC: Piacenza; TV: Treviso; VE: Venezia; MI: Milano; BR: Brescia; PR: Parma; MO: Modena; TO: Torino; RN: Rimini; AT: Asti; VR: Verona; MN: Mantova; RE: Reggio Emilia; VI: Vicenza; VA: Varese; MB: Monza-Brianza; BO: Bologna; AL: Alessandria; CO: Como; LC: Lecco; BL: Belluno; RA: Ravenna; VC: Vercelli; VB: Verbano-Cusio-Ossola; FC: Forlì-Cesena; BI: Biella; NO: Novara; CN: Cuneo; RO: Rovigo; SO: Sondrio; FE: Ferrara.

https://doi.org/10.1371/journal.pone.0244535.t001

Results

Table 2 shows that the increase in the numbers of cases in 20 days varied considerably among the various provinces from a minimum of 115 cases in the province of Rovigo to a maximum of 3398 cases in Bergamo, with an average growth of 852 cases per province in 20 days. The rate of this increase was lowest in the province of Asti (4.5%) and highest in Brescia (330%), with an average over all provinces of 59.9%.

The scatter plot (Fig 1) shows significant correlations between the increase in transmission and several demographic, socioeconomic and healthcare variables.

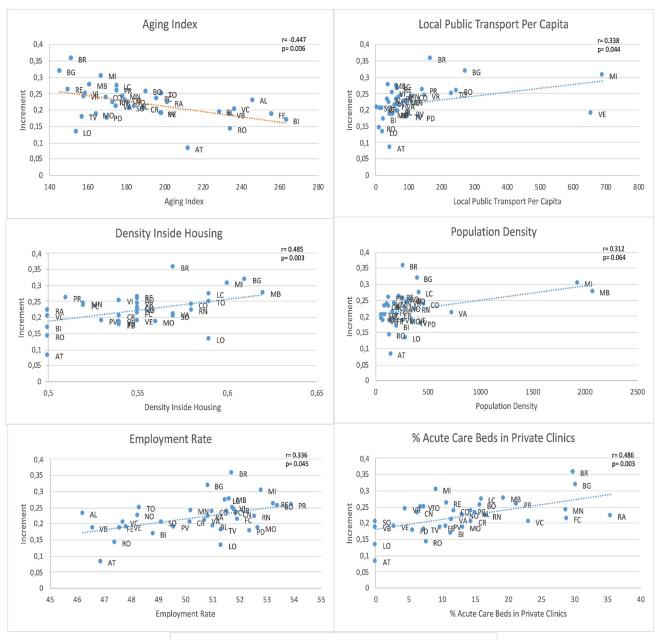
The spread of COVID-19 was correlated negatively with aging index and positively with the other indicators showed.

Provinces	T0 (date of first details. or 25.2. or report of 10th case)	Number of cases first data	T1—after 20 days	Number of cases at T1	Difference in cases	Rate of increase in cases (T1/T0)	Incremental rate (T1-T0)/T0	β (see Methods for calculation)
PD	25/02	30	15/03	658	628	21.9	20.9	0.176
BG	25/02	18	15/03	3416	3398	189.8	188.8	0.318
PV	25/02	27	15/03	722	695	26.7	25.7	0.189
CR	25/02	53	15/03	1792	1739	33.8	32.8	0.204
LO	25/02	125	15/03	1320	1195	10.6	9.6	0.132
РС	25/02	18	15/03	1012	994	56.2	55.2	0.236
TV	27/02	22	17/03	502	480	22.8	21.8	0.179
VE	27/02	14	17/03	378	364	27.0	26.0	0.189
MI	27/02	15	17/03	2326	2311	155.1	154.1	0.304
BR	27/02	10	17/03	3300	3290	330.0	329.0	0.357
PR	27/02	10	17/03	800	790	80.0	79.0	0.259
мо	27/02	18	17/03	460	442	25.6	24.6	0.186
то	28/02	11	17/03	749	738	68.1	67.1	0.249
RN	29/02	15	19/03	691	676	46.1	45.1	0.223
AT	02/03	37	21/03	166	129	4.5	3.5	0.082
VR	03/03	17	22/03	1046	1029	61.5	60.5	0.242
MN	03/03	15	22/03	905	890	60.3	59.3	0.241
RE	03/03	14	22/03	1167	1153	83.4	82.4	0.262
VI	04/03	10	23/03	691	681	69.1	68.1	0.25
VA	04/03	11	23/03	421	410	38.3	37.3	0.211
MB	04/03	11	23/03	1130	1119	102.7	101.7	0.276
BO	04/03	11	23/03	833	822	75.7	74.7	0.256
AL	04/03	16	23/03	817	801	51.1	50.1	0.23
СО	05/03	11	24/03	635	624	57.7	56.7	0.238
LC	06/03	11	25/03	1076	1065	97.8	96.8	0.273
BL	07/03	11	26/03	313	302	28.5	27.5	0.193
RA	07/03	10	26/03	451	441	45.1	44.1	0.222
VC	07/03	10	26/03	336	326	33.6	32.6	0.203
VB	07/03	10	26/03	255	245	25.5	24.5	0.186
FC	08/03	15	27/03	580	565	38.7	37.7	0.212
BI	08/03	19	27/03	367	348	19.3	18.3	0.169
NO	08/03	13	27/03	609	596	46.8	45.8	0.224
CN	09/03	11	28/03	558	547	50.7	49.7	0.23
RO	10/03	10	29/03	125	115	12.5	11.5	0.142
so	11/03	13	30/03	446	433	34.3	33.3	0.205
FE	11/03	12	30/03	306	294	25.5	24.5	0.186
MIN		10		125	115	4.5	11.5	0.082
Max		125		3416	3398	330	27.184	0.357
Mean		19		871.1	852.1	59.9	58.9	0.221

Table 2. Spread of COVID-19 (difference in cases, rate increase, incremental rate increase, and transmission rate β by province).

PD: Padova; BG: Bergamo; PV: Pavia; CR: Cremona; LO: Lodi; PC: Piacenza; TV: Treviso; VE: Venezia; MI: Milano; BR: Brescia; PR: Parma; MO: Modena; TO: Torino; RN: Rimini; AT: Asti; VR: Verona; MN: Mantova; RE: Reggio Emilia; VI: Vicenza; VA: Varese; MB: Monza-Brianza; BO: Bologna; AL: Alessandria; CO: Como; LC: Lecco; BL: Belluno; RA: Ravenna; VC: Vercelli; VB: Verbano-Cusio-Ossola; FC: Forlì-Cesena; BI: Biella; NO: Novara; CN: Cuneo; RO: Rovigo; SO: Sondrio; FE: Ferrara

https://doi.org/10.1371/journal.pone.0244535.t002



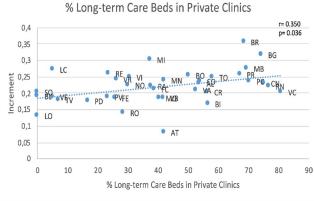


Fig 1. Significant correlations between β increment and socioeconomic and healthcare variables.

https://doi.org/10.1371/journal.pone.0244535.g001

Variable	Pearson's rho (p-value)	Full model coefficients (p-value)	Final model coefficients (p-value)
Intercept (0,934)	_	0.207 (<0.001)	0.220 (<0.001)
Aging index	-0.447 (0.006)	-0.013 (0.327)	-0.021 (0.003)
Population density	0.312 (0.064)	0.001 (0.892)	_
Density inside housing	0.485 (0.003)	_	_
% sports associations / resident population	-0.206 (0.227)	_	_
Unemployment rate	-0.274 (0.106)	_	_
Employment rate	0.336 (0.045)	0.010 (0.462)	_
% of active companies / resident population	-0.154 (0.368)	_	_
Local public transport use per capita	0.338 (0.044)	0.016 (0.037)	0.016 (0.012)
% of private long-term care beds	0.350 (0.036)	0.010 (0.311)	0.014 (0.070)
% of private acute care hospital beds	0.486 (0.003)	0.022 (0.019)	0.021 (0.006)
% of anesthesiologists / resident population	-0.083 (0.689)	_	_
General practitioners rate	-0.164 (0.369)	_	_
Dentists rate	0.201 (0.239)	_	_
Nursing staff rate	0.071 (0.681)	_	_
Acute care hospital beds rate	0.092 (0.593)	_	_
Long-term care hospital beds rate	-0.052 (0.761)	_	_
Emergency medical service rate	-0.187 (0.306)	_	_
Region: Veneto vs Lombardia	_	0.017 (0.458)	_
Region: Emilia Romagna vs Lombardia	-	-0.022 (0.385)	_
Region: Piemonte vs Lombardia	_	0.000 (1.000)	
Model parameters		Multiple $R^2 = 0.629$ Adjusted $R^2 = 0.475$ AIC = -118.35	Multiple $R^2 = 0.604$ Adjusted $R^2 = 0.551$ AIC = -128.01
		BIC = -99.69	BIC = -118.67

Table 3. As	sociation of c	ovariates with	COVID-19	transmission f	actor.
-------------	----------------	----------------	----------	----------------	--------

https://doi.org/10.1371/journal.pone.0244535.t003

A significant negative correlation emerged between increment β and population aging rates, while a significant positive correlation was found with employment rates, public transportation rates, in-house density, population density, and the proportions of private acute and long-term care beds in clinics and nursing homes.

Table 3 shows the bivariate and multivariate analyses, demonstrating that the spread of COVID-19 in the regional setting considered was negatively associated (p-value = 0.003) with the population aging index, i.e. the ratio of the number of people aged 65 or more to the number of people aged 0–14 years multiplied by 100. It was positively associated with: public transportation per capita, i.e. the ratio of the yearly number of public transport passengers to the total population(p-value = 0.012). It was also positively associated, albeit to a lesser extent (p-value = 0.070), with the % of private long-term care hospital beds, and more strongly with the % of private acute care hospital beds (p-value = 0.006).

The Shapiro-Wilk test showed that the residuals had a normal distribution (p-value = 0.870) and the Rubin-Watson test showed that the residuals were independent (p-value = 0.48). The high value of the adjusted R squared indicates that the model had a good fit.

Discussion

With this ecological study, we found correlations between higher SARS-CoV-2 contagion rates and certain demographic, socioeconomic and healthcare factors in the Italian provinces considered. Unlike the first cases imported from outbreak regions, the local spread of

communicable respiratory diseases seems to favor certain patterns and conditions, especially relating to social contact patterns [13].

We found a negative association between COVID-19 contagion rates and aging. This seems somewhat at odds with the currently-known epidemiology of the virus, that in Italy is more likely to infect and kill older people. The median age of people infected with COVID-19 nationwide is 62 years old, and the median age of the related deaths is 80 years old [14]. On the other hand, provinces with a higher aging index had a more gentle contagion curve. A possible explanation is that older people tend to move less outside their home and travel less far from where they live [15]. They are also less likely to take part in mass gatherings or social events, whereas younger people tend to spend more time with others outside their family [16]. Taken together, these behavioral factors could predispose the elderly to social distancing and self-isolation, naturally containing the propagation of communicable diseases in the provinces with the oldest populations.

In our analysis, higher levels of employment, public transportation usage, in-house density, and population density correlated positively with the spread of infection. What these socioeconomic factors have in common is the mobility of individuals and their exposure to close social contacts, both of which facilitate the propagation of SARS-CoV-2. This is consistent with recent analyses that associated a higher risk of COVID-19 transmission in mainland China with the use of trains [17], buses and flights from Wuhan, and the risk was higher the longer a journey lasted [18]. In-house density has also already been identified as a factor predisposing to higher transmission rates of pandemic influenza in Great Britain [19].

A greater spread of the virus was seen in provinces with larger proportions of private acute care beds in clinics, and long-term care beds in nursing homes. These data should not be interpreted as a lack of involvement of the private sector in providing hospital care for COVID patients. These facilities are an important part of the services provided by the Italian health system and they responded promptly to the emergency situation. They have ordinary and intensive care beds for COVID patients just like public hospitals. The explanation should be sought by looking at the issue more in depth and speculating on the outcome variable analyzed in the present study, i.e. the rate of spread of the infection. Hospitals, clinics and care homes are only responsible for containing it within their walls, while the preventive medicine departments of local health units are in charge of wider containment efforts, based on epidemiological intelligence. It may be that provinces with higher proportions of private healthcare facilities experienced more communication difficulties with the reporting of cases to preventive medicine departments to gather epidemic intelligence because private facilities are usually less integrated with preventive medicine and community healthcare services than public hospitals. This could hamper the early identification of patients through the sort of epidemic intelligence activities strongly recommended by the WHO in the case of COVID-19 [20]. Another explanation could relate to how private clinics are funded, i.e. based on DRG-based tariffs for each patient admitted. Owing to incentives linked to this particular funding mechanism, provinces with a relatively high concentration of private hospital beds might have paid less attention to avoiding the hospitalization of patients with COVID-19 symptoms who could have been successfully treated at home with the involvement of community and primary care services. In fact, primary healthcare services have a crucial role in ensuring that people caring for a family member suffering from COVID 19 manage their contact with the patient appropriately, and follow national or local policies regarding home quarantine. Caregivers should wear medical masks or the best available protection against respiratory droplets when in close contact with the patient, and observe hand hygiene recommendations. The WHO emphasized the importance of notifying healthcare providers of the diagnosis in order to receive instructions on where to seek care, when and where to enter healthcare facilities, and what precautions to take to

prevent and control the infection [20]. Our findings would suggest the importance of improving communications between private clinics and the Italian NHS responsible for their accreditation (i.e. the issue of the public license to provide hospital care on the NHS's behalf) to ensure a real consistency of their activities with regional health plans (including their integration with the preventive medicine and primary care services of local health units), and an effective assessment of their activities and results.

This study has at least two important limitations. First, we collected data from available health indicators, which do not measure all the phenomena relevant to understanding and explaining the findings, even though our models performed well in explaining their variability ($MR^2 = ~60\%$). Second, the real number of SARS-CoV-2 contagions is known to be underestimated because not all individuals in the population considered were screened, and swabs were handled differently by the various regional healthcare systems. Even with such well-known limitations [21], ecological studies can still help healthcare workers and stakeholders to contain infections and fight pandemics, especially in the early stages of emerging diseases when clinical data are still limited [22].

Conclusions

Several demographic, socioeconomic and healthcare factors were found associated with significant differences in the rate of COVID-19 spread in 36 provinces of Northern Italy. An older population seemed to naturally slow the contagion due to fewer social contacts. Socioeconomic factors (especially the rates of employment and public transportation usage) and organizational features of local healthcare systems (particularly the proportion of private healthcare facilities) also seemed to play an important part in the infection's spread. These correlations could be helpful for the purpose of designing measures to reduce the propagation of COVID-19 in other countries now dealing with the first phase of this pandemic.

Author Contributions

Conceptualization: Alessandra Buja, Matteo Paganini, Vincenzo Rebba, Vincenzo Baldo.

Data curation: Alessandra Buja, Matteo Paganini, Silvia Cocchio.

Formal analysis: Manuela Scioni.

Investigation: Alessandra Buja, Matteo Paganini, Silvia Cocchio, Manuela Scioni.

Methodology: Alessandra Buja, Matteo Paganini, Silvia Cocchio, Vincenzo Rebba, Vincenzo Baldo.

Project administration: Alessandra Buja.

Resources: Alessandra Buja, Vincenzo Rebba, Vincenzo Baldo.

Software: Manuela Scioni.

Supervision: Alessandra Buja, Vincenzo Rebba, Vincenzo Baldo.

Validation: Alessandra Buja, Silvia Cocchio, Manuela Scioni.

Visualization: Alessandra Buja, Silvia Cocchio, Vincenzo Rebba.

Writing - original draft: Alessandra Buja, Matteo Paganini, Silvia Cocchio, Vincenzo Rebba.

Writing – review & editing: Alessandra Buja, Matteo Paganini, Vincenzo Rebba, Vincenzo Baldo.

References

- World Health Organization. Disease Outbreak News Update–January 12, 2020: Novel Coronavirus– China. [cited 2020 April 13]. Available from: <u>https://www.who.int/csr/don/12-january-2020-novelcoronavirus-china/en/</u>
- World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19–11 March 2020. [cited 2020 April 13]. Available from: https://www.who.int/dg/speeches/detail/whodirector-general-s-opening-remarks-at-the-media-briefing-on-covid-19–11-march-2020
- 3. World Health Organization. Coronavirus disease (COVID-19) Pandemic–April 12 Update. [cited 2020 April 13]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019
- 4. Italian Ministry of Health. COVID-19 –Italian Situation. [cited 2020 April 13]. Available from: http://www.salute.gov.it/portale/nuovocoronavirus/dettaglioContenutiNuovoCoronavirus.jsp?area= nuovoCoronavirus&id=5351&lingua=italiano&menu=vuoto
- Italian Civil Protection. Coronavirus disease 2019 (COVID-19) Italian Situation Map. [cited 2020 April 13]. Available from: http://opendatadpc.maps.arcgis.com/apps/opsdashboard/index.html#/ b0c68bce2cce478eaac82fe38d4138b1
- The Prime Minister of the Italian Republic–Decree March 9th, 2020. Urgent Measures of Containment and Management of Epidemiological Emergency COVID-19, further dispositions. [cited 2020 April 13]. Available from: https://www.gazzettaufficiale.it/eli/id/2020/03/09/20A01558/sg
- Wu X, Nethery RC, Sabath MB, Braun D, Dominici F. Exposure to air pollution and COVID-19 mortality in the United States. MedRxiv 2020.04.05.20054502 [Preprint]. doi: https://doi.org/10.1101/2020.04.05. 20054502
- Italian Ministry of Health. Annuario statistico del Servizio Sanitario Nazionale, Assetto organizzativo, attività e fattori produttivi del SSN—Anno 2017. Published on June 11th, 2018. [cited 2020 April 13]. Available from: http://www.salute.gov.it/portale/documentazione/p6_2_2_1.jsp?lingua=italiano&id= 2370
- Italian Civil Protection–Contagion Rates. [cited 2020 April 13]. Available from: https://github.com/pcm-dpc/COVID-19/tree/master/dati-province
- National Institute of Statistics (ISTAT). Main database. [cited 2020 April 13]. Available from: <u>http://dati.istat.it/Index.aspx</u>
- National Institute of Statistics (ISTAT). Health for All database. [cited 2020 April 13]. Available from: https://www.istat.it/it/archivio/14562.
- 12. Italian National Olympic Committee (CONI). Registry of Sports Associations. [cited 2020 April 13]. Available from: https://www.coni.it/it/registro-societa-sportive.html
- Leung K, Jit M, Lau EHY, Wu JT. Social contact patterns relevant to the spread of respiratory infectious diseases in Hong Kong. Sci Rep. 2017; 7(1):7974. Published 2017 Aug 11. <u>https://doi.org/10.1038/s41598-017-08241-1</u> PMID: 28801623
- Istituto Superiore di Sanità. Characteristics of SARS-CoV-2 patients dying in Italy. Report based on available data on April 13th, 2020. [cited 2020 April 13]. Available from: https://www.epicentro.iss.it/en/ coronavirus/bollettino/Report-COVID-2019_13_april_2020.pdf
- Mollenkopf H, Hieber A, Wahl H-W. Continuity and change in older adults' out-of-home mobility over ten years: a qualitative-quantitative approach. In: Meusburger P, Werlen B, Suarsana L, editors. Knowledge and Action. Knowledge and Space. Cham: Springer International Publishing; 2017:267–289. <u>https:// doi.org/10.1007/978-3-319-44588-5_15</u>
- Marcum CS. Age differences in daily social activities. Res Aging. 2013; 35(5):612–640. https://doi.org/ 10.1177/0164027512453468 PMID: 25190898
- Zhao S, Zhuang Z, Ran J, Lin J, Yang G, Yang L. The association between domestic train transportation and novel coronavirus (2019-nCoV) outbreak in China from 2019 to 2020: a data-driven correlational report. Trav Med Infect Dis. 2020; 30:101568 https://doi.org/10.1016/j.tmaid.2020.101568 PMID: 32006656
- Zheng R, Xu Y, Wang W, Ning G, Bi Y. Spatial transmission of COVID-19 via public and private transportation in China [published online ahead of print, 2020 Mar 14]. Travel Med Infect Dis. 2020;101626. https://doi.org/10.1016/j.tmaid.2020.101626 PMID: 32184132
- House T, Keeling MJ. Household structure and infectious disease transmission. Epidemiol Infect. 2009; 137(5):654–661. https://doi.org/10.1017/S0950268808001416 PMID: 18840319
- 20. World Health Organization. (2007). Infection prevention and control of epidemic- and pandemic-prone acute respiratory diseases in health care: WHO interim guidelines. Geneva: World Health Organization. [cited 2020 April 13]. Available from: https://apps.who.int/iris/handle/10665/69707

- Cohen HW. Limitations of an ecological study: a review. Am J Hypertens. 2005; 18(6):750. <u>https://doi.org/10.1016/j.amjhyper.2005.04.002</u> PMID: 15925730
- 22. Fauci AS. Pandemic influenza threat and preparedness. Emerg Infect Dis. 2006; 12:73–7 https://doi. org/10.3201/eid1201.050983 PMID: 16494721