

Assessing the Impact of Individual Characteristics and Neighborhood Socioeconomic Status During the COVID-19 Pandemic in the Provinces of Milan and Lodi

International Journal of Health
Services
1–14

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DOI: 10.1177/0020731421994842
journals.sagepub.com/home/joh



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Abstract

Social inequalities in health are known to be influenced by the socioeconomic status of the territory in which people live. In the context of the ongoing coronavirus disease 2019 (COVID-19) pandemic, this study is aimed at assessing the role of 5 area-level indicators in shaping the risk of contagion in the provinces of Milan and Lodi (Lombardy, Italy), namely: educational disadvantage, unemployment, housing crowding, mobility, and population density. The study area includes the municipalities at the origin of the first Italian epidemic outbreak. Data on COVID-19 patients from the *Integrated Datawarehouse for COVID Analysis* in Milan were used and matched with aggregate-level data from the National Institute of Statistics Italy (Istat). Multilevel logistic regression models were used to estimate the association between the census block-level predictors and COVID-19 infection, independently of age, sex, country of birth, and preexisting health conditions. All the variables were significantly associated with the outcome, with different effects before and after the lockdown and according to the province of residence. This suggests a pattern of socioeconomic inequalities in the outbreak, which should be taken into account in the eventuality of future epidemics to contain their spread and its related disparities.

Keywords

COVID-19, SARS-CoV-2, social inequalities, health inequalities, social epidemiology

Introduction

Since the first person-to-person transmission, the Lombardy Region in Italy emerged as one of the largest clusters of coronavirus disease 2019 (COVID-19) in the world, with 77 528 people infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and 14 231 deaths as of May 3, 2020. Although a considerable amount of research has rapidly begun to investigate potential risk factors for COVID-19 contagion, hospitalization, and mortality, to our knowledge, there has been limited attention on the extent to which socioeconomic status (SES) might have contributed to heterogeneity in the distribution of the disease within specific contexts. Using multilevel modeling techniques, we aimed at assessing the association between census blocks' SES and the spread of COVID-19, over and above individual characteristics that are associated with the risk of being infected. We performed a population-based study based on individual administrative data from the Agency for Health Protection (ATS) of the Metropolitan City of Milan, covering a population of 3.48 million people in 193 municipalities

belonging to the provinces of Milan and Lodi, in the northern Italian region of Lombardy, where the outbreak initially took place. Data from the latest Italian Census were used to define measures of SES at the contextual level.

Background

On January 12, 2020, the World Health Organization (WHO) confirmed that a new coronavirus, named COVID-19, was the cause of a cluster of atypical pneumonia cases detected in December 2019 in the city of Wuhan (Hubei, China), which eventually spread to the rest of the country. The magnitude of contagions and deaths led the WHO to declare the

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outbreak an emergency of international concern on January 30 and a pandemic on March 11.

In Italy, on February 20, soon after a 38-year-old Italian tested positive for COVID-19 in Codogno—a small municipality in the province of Lodi, about 50 km south of Milan—the contagion started to spread exponentially, firstly in the adjacent areas and subsequently all over the country. This induced the Italian Government and regional authorities to adopt extraordinary measures to contain the spread of the disease. On March 8 a full lockdown was imposed in the whole Lombardy region, lasting until the beginning of “phase 2,” dated May 4, when in correspondence of a flattening of the epidemic curve the Government allowed a gradual slackening of the containment measures previously adopted (Figure 1).

Within this framework, our work is aimed at assessing if neighborhood SES, in terms of socioeconomic characteristics of the areas involved, may have played a role in the geographic patterning of the disease in the study area. Early studies clearly show that in Lombardy the disease occurred mostly in the elderly, in males, and in subjects with at least one comorbidity,¹ similarly to what has been observed in Wuhan and China, in general,^{2,3} and that preexisting conditions were associated with a major risk of severe progression, hospitalization, and mortality.^{4–10} However, knowledge about the presence of a possible social gradient at the onset of the disease is scant. According to the literature on the social shaping of health and disease, those with less equipment of economic, social, and cultural resources are generally more prone to experience worse health

conditions and lower quality of life throughout their life, in light of a wide range of materials and psychosocial pathways linking SES to health conditions.^{11–14} This framework, however, found less application in relation to contagious diseases as compared to chronic ones, likely because of the predominance of the latter over the former as the leading causes of death after the epidemiological transition.¹⁵ Moreover, another strand of literature has focused on the influence of the local environment in which people live in determining health outcomes.^{16–18} In this view, health conditions are not exclusively the product of individual characteristics and resources, but also the outcome of processes and mechanisms proper of the contextual dimension in which people are embedded.

In light of the above, our objective is to examine the possible association between neighborhood SES and the risk of COVID-19 contagion. Our hypothesis is that—even controlling for individual characteristics—living in areas characterized by social and economic disadvantages may increase the risk of contagion. Our study is focused on the territory covered by the ATS of Milan, namely the provinces of Milan and Lodi. The study area is of considerable interest in relation to the main research question and the outcome investigated, given that it includes the 10 municipalities where the outbreak took place in Lombardy, as well as the municipality of Milan and its hinterland, the most productive area of the country, characterized by high-population density and mobility, both of which have been hypothesized to increase the risk of COVID-19 contagion elsewhere.^{19–21} On the contrary, the adjacent territory of Lodi is

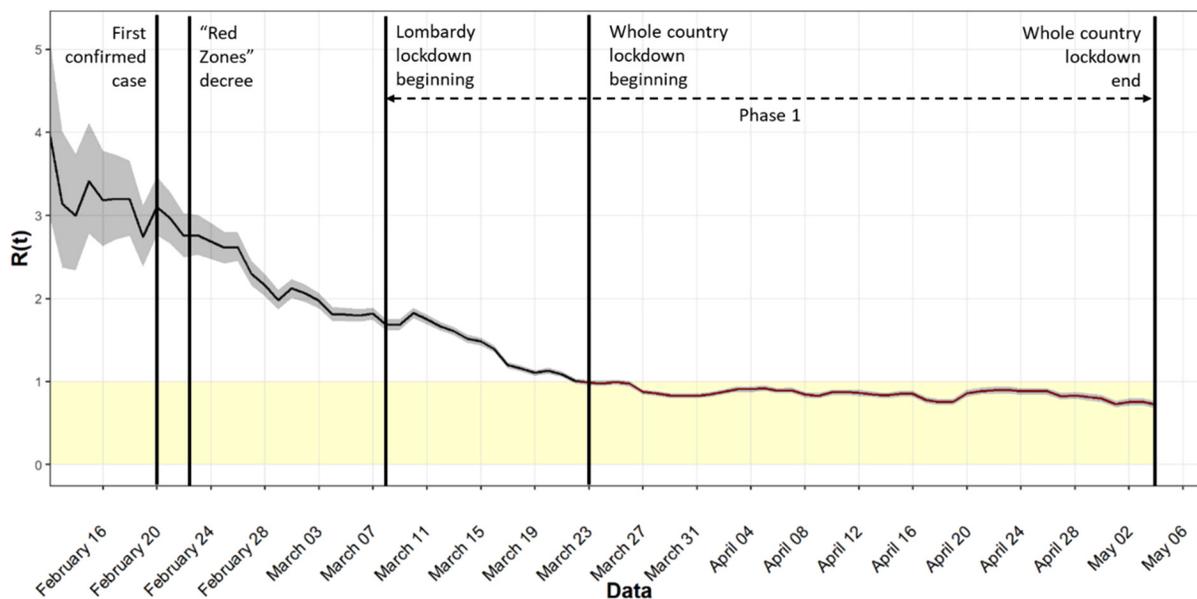


Figure 1. Institutional decrees and evolution of the effective reproduction number (R_t). R_t values below 1 indicate that the epidemic is slowing down (each patient infects, on average, less than 1 person). R_t values above 1 indicate that the epidemic is progressing (each patient infects, on average, more than 1 person).

characterized by a far lower population density, mobility, and gross domestic product (GDP).

Multilevel regression models were used to assess simultaneously the effect of individual and contextual characteristics, enabling to disentangle compositional and contextual influences on the contagion. Specifically, we aim at assessing the impact of 5 census block-level measures, which represent specific characteristics of the residence context: low education, unemployment, housing crowding, mobility, and population density. Here, we evaluate their potential role in shaping the territorial heterogeneity in the distribution of the disease.

Materials and Methods

Study Population

The study included all COVID-19 cases (32 588) in the study area with diagnosis based either on nasopharyngeal swab positive results (20 364; 62.5%) or on symptoms (12 224; 37.5%), identified from February 20 to May 3, 2020. A confirmed case is defined as a person who tested positive for SARS-CoV-2, irrespective of clinical signs and symptoms. Symptomatic cases that did not undergo a nasopharyngeal swab were reported by General Practitioners (GPs).

The study was conducted on the total population of the study area (3.48 million subjects), as extracted from the Health Service Register (HSR) of the Lombardy Region. Approximately 154 300 subjects (4.43%) were excluded, as they were not in the register or had missing information on the place of residence. Hence, the study was performed on 3 325 675 subjects, 0.98% of which were COVID-19 cases. Individual-level administrative data on COVID-19 cases from the ATS of Milan were matched with area-level data from the latest Italian census.²²

Measures

From the *Integrated Datawarehouse for COVID Analysis* in Milan, we extracted all subjects with nasopharyngeal swabs confirmed SARS-CoV-2 infection and all symptomatic cases reported by the GPs as of May 3, 2020. We equally considered swab confirmed and symptomatic subjects as COVID-19 cases. From census data, the area-level measure of educational disadvantage was computed as the percentage of people with at most primary education on the overall population for each census block; the area-level measure of unemployment was computed as the percentage of unemployed or people looking for their first job in the workforce for each census block, the area-level measure of housing crowding was computed as the average number of persons per 100 m² in residential buildings for each census block. The area-level index of mobility was computed summing the overall incoming and outgoing movements of people in each census block for any reason (job, study, leisure time,

etc) and with any mode of transport (foot, car, bike, train, public transports, etc) in an average weekday. Data came from the 2011 census-based origin–destination matrix, projected to 2020 with the integration of survey data for the Lombardy region. Original data came at a higher level of aggregation (municipalities or sub-municipalities) and were attributed to the census block level with areal interpolation methods.²³ Census block level population density was obtained accessing to geo-referenced demographic data present in the HSR and computed as the number of residents per square kilometer. All the area-level predictors were categorized in quartiles to simplify issues of nonlinearity, becoming categorical variables in 4 categories, each identifying the 25% of the census blocks falling in low, medium–low, medium–high, and high rates of the indicators. The geographical distribution of the 5 indicators within the study area is shown in Supplemental Figures A5 to A9 in the Appendix. The study included 14 099 census blocks with an average dimension of 0.15 km² (min: <0.1 km²; max: 10.9 km²) and an average of 236 subjects for each (min: 1; max: 2274).

Data on age, sex, country of birth (aggregated for macro-areas), and province of residence were obtained from the HSR and used as covariates. The models were adjusted also for the number of chronic diseases for each individual, obtained by querying the Administrative Healthcare Databases of the ATS.

Statistical Analysis

We performed a population-based unmatched case–control study, with swab confirmed and symptomatic subjects as cases, and all the other subjects in the study area not affected by the disease as controls. Having available the entire list of the population from the civil register, this type of design minimizes selection bias and, due to the large sample size, has great statistical power, making it possible to study rare exposures and outcomes.²⁴ Given the hierarchical structure of the data, with individuals nested in census blocks, multilevel regression models were used to assess simultaneously the effect of individual and contextual characteristics, enabling the estimation of the effect of neighborhood SES on the odds of contracting SARS-CoV-2, adjusting for individual characteristics. A detailed explanation of how multilevel models work can be found elsewhere, both generally^{25–27} and focusing specifically on health research.^{28–30} Here, we followed a procedure well established in the literature, adopting a bottom-up strategy in which different models are developed incrementally.^{31–36} Given that our outcome is dichotomous (having contracted SARS-CoV-2 or not), multilevel binary logistic regression was used. First, the territorial heterogeneity in COVID-19 was assessed through an “empty” model, which enabled measurement of the extent to which the probability of contracting SARS-CoV-2 varies from one census block to another. The variance partition

coefficient (VPC) revealed the proportion of variability in the outcome at each level of analysis, providing a first description of the geographic distribution of the disease in the study area and highlighting the existence of a possible contextual dimension for the phenomenon studied. Second, the model was integrated with level-1 predictors (age, sex, country of birth, comorbidities, province of residence) to investigate the extent to which area-level differences were explained by individual characteristics. Third, the level-2 predictors were added (educational disadvantage, unemployment, housing crowding, mobility, and population density) to check if they were associated with contagion adjusting for individual characteristics. In all the main analyses, random intercept models were fitted; multicollinearity was also checked. Additional analyses were performed to test for a cross-level interaction between the province of residence and mobility, and between the province of residence and population density. With the aim to assess whether the effect of the area-level predictors varied before and after the full lockdown measure, we fitted models among COVID-19 cases only and distinguishing them between cases diagnosed before and after March 23 as outcome measure. This date was chosen as the full lockdown measure was imposed in Lombardy on March 8, but to unfold its effects, it is necessary to consider the maximum incubation period of 14 days in the normal range.³⁷ Moreover, in the study area, the chosen date coincides with the shift from an effective reproduction number (R_t) above 1 to values below this threshold (Figure 1), indicating a slowdown in the spread of the disease,³⁸ likely because of the effectiveness of interventions aimed at reducing social interactions.³⁹ Thus, in relation to each predictor, the odds ratios (ORs) express the relative impact of each indicator on the risk of contagion in the second time interval compared to the first one. Accordingly, we warn that the ORs of the 2 sets of models should not be compared between themselves, as they refer to different outcomes and are subject to different interpretations.

Concerning the interpretation of the multivariable model parameters, the fixed effects of the predictors on the outcome variable were conditional, that is, they represented the expected outcome variation (in OR terms) per unit increase of a predictor, keeping fixed the others in the built-in model. The model parameters were tested by z -tests and the statistical significance was set by P -values $<.05$ (2-sided). All the models were estimated with the quasi-maximum-likelihood estimation method using MLwiN software.⁴⁰

Results

Supplemental Figures A1 to A4 in the Appendix show the territorial division and the satellite imagery of the study area, the geographic distribution, and the proportion of COVID-19 cases in each census block, respectively. Descriptive statistics are reported in Table 1. Table 2

shows the main results of the analyses performed. In the “empty” model (Model 1.1), the VPC informed us that 20% of the variability in the outcomes was found at the census block level, suggesting the usefulness of investigating the risk of infection in a multilevel framework. Fitting the model with individual-level covariates (Model 1.2) it is possible to explore the association between individual characteristics and COVID-19. Each additional year of age was associated with 2% increased odds of contagion (OR = 1.02), whilst sex did not result statistically associated with COVID-19. Looking at the country of birth, the association was statistically significant for most of the categories. Compared to being Italian, a protective effect was found for those born in North Africa (OR = 0.67), Centre-Southern Asia (OR = 0.80), Western Asia (OR = 0.71), East Asia (OR = 0.53), and North America (OR = 0.59). Conversely, small increased ORs were found for those born in other European countries (OR = 1.09) or in Eastern Europe (OR = 1.11), whilst those born in Centre-South America (OR = 2.97) showed an almost 3-fold probability of contracting the disease rather than not contracting it compared to Italians. A gradient was found in relation to the presence of chronic diseases, with increased ORs of contagion in correspondence with a higher number of diseases (ORs = 1.11, 1.15, 1.47). With regard to the province of residence, those living in the Lodi area faced a 2-fold probability of contagion as compared to those living in the Milanese area (OR = 2.01). Moving to Model 1.3, with the addition of area-level predictors it is possible to check for the existence of a contextual effect in the contagion. After controlling for individual-level covariates, 3 out of 5 area-level predictors were statistically significant. Specifically, living in areas with higher percentages of low-educated people appeared to be a risk factor for contagion at all levels (ORs = 1.05; 1.06; 1.18); living in medium-high (OR = 1.08) and high (OR = 1.15) instead of low-housing crowding was associated with increased ORs of COVID-19; whereas living in higher unemployment areas appeared to be protective against contagion at all levels (ORs = 0.94, 0.91, 0.90). The effects of mobility and population density, instead, were not statistically significant at any level. However, suspecting that these indicators may be influenced by their different distribution across the 2 provinces (see Supplemental Figures A8 and A9 in the Appendix), we tested models with a cross-level interaction between them and the province of residence. The interaction terms between the province and mobility in Model 1.4 show that the inhabitants of the province of Lodi living in high-mobility areas reported increased ORs of contagion compared with those living in the reference category of both province and mobility (OR = 1.26). The interaction between the province and population density was not statistically significant.

Models 2.1 to 2.3 represent, exclusively for COVID-19 cases, the odds of having contracted the virus after the

Table 1. Descriptive Statistics.

	n	Overall, n 3 325 675	Controls 3 293 087	Cases, overall 32 588	Cases, pre lockdown 15 191	Cases, post lockdown 17 397
Sex						
Male		1 608 616	48.39	46.24	53.47	39.93
Female		1 717 059	51.61	53.76	46.53	60.07
Age, mean (std. dev.)		45.89 (23.53)	45.76 (23.51)	58.83 (21.06)	58.95 (18.51)	58.72 (23.05)
Country of birth						
Italy		2 856 202	85.88	85.72	88.45	83.34
European Union		77 916	2.34	2.18	1.99	2.33
Eastern Europe		64 940	1.95	1.76	1.48	2.01
Other European		6370	0.19	0.19	0.16	0.22
Centre-Southern Africa		2034	0.06	0.06	0.06	0.06
West Africa		12 977	0.39	0.29	0.24	0.33
East Africa		8355	0.25	0.25	0.22	0.28
North Africa		82 816	2.50	1.32	1.01	1.59
Centre-Southern Asia		39 517	1.19	0.71	0.49	0.90
Western Asia		6317	0.19	0.11	0.10	0.13
East Asia		65 679	1.99	0.83	0.66	0.98
Centre-South America		94 971	2.82	6.49	5.06	7.74
North America		4298	0.13	0.06	0.05	0.06
Oceania		729	0.02	0.02	0.03	0.02
Other/not specified		2554	0.08	0.00	0.00	0.00
Chronic diseases						
0		2 242 654	67.61	49.54	46.78	51.94
1		542 211	16.27	20.21	21.32	19.24
2		255 693	7.65	11.66	12.57	10.87
3 or more		285 117	8.47	18.59	19.32	17.95
Province of residence						
Milan		3 117 684	93.79	88.82	83.32	93.63
Lodi		207 991	6.21	11.18	16.68	6.37
Educational disadvantage (quartiles)						
Low		831 644	25.03	22.20	22.72	21.73
Medium–low		831 337	25.01	23.55	23.24	23.83
Medium–high		831 651	25.01	24.69	24.77	24.62
High		831 043	24.94	29.56	29.27	29.81
Unemployment (quartiles)						
Low		832 167	25.02	25.04	25.99	24.21
Medium–low		832 127	25.02	24.79	24.99	24.61
Medium–high		831 867	25.02	24.65	25.00	24.35
High		829 514	24.94	25.53	24.03	26.84
Housing crowding (quartiles)						
Low		831 547	25.01	24.29	26.17	22.64
Medium–low		831 541	25.01	24.84	25.92	23.89
Medium–high		831 337	24.99	25.37	25.18	25.54
High		831 250	24.99	25.50	22.74	27.92
Mobility (quartiles)						
Low		831 712	24.98	27.98	29.78	26.41
Medium–low		831 188	24.99	25.71	25.46	25.92
Medium–high		831 727	25.03	23.21	22.45	23.88
High		831 048	25.01	23.10	22.32	23.79
Population density (quartiles)						
Low		831 468	24.98	26.98	30.58	23.84
Medium–low		831 411	25.01	24.45	24.15	24.72
Medium–high		831 435	25.01	24.09	23.03	25.01
High		831 361	25.00	24.48	22.25	26.43

Table 2. Multilevel Logistic Regression on the Risk of Infection with COVID-19 (N = 3 325 675; Groups = 14 099).

	Model 1.1 (VPC = 0.20)		Model 1.2 (VPC = 0.13)		Model 1.3 (VPC = 0.12)		Model 1.4 (VPC = 0.13)	
	OR	P-value	OR	P-value	OR	P-value	OR	P-value
Age			1.02	<.001	1.02	<.001	1.02	<.001
Sex								
Male (ref.)				—		—		—
Female			0.98	.068	0.98	.068	0.98	.068
Country of birth								
Italy (ref.)				—		—		—
European Union			1.09	.033	1.09	.034	1.08	.035
Eastern Europe			1.11	.013	1.11	.016	1.11	.016
Other European			1.13	.318	1.14	.299	1.14	.300
Centre-Southern Africa			1.22	.380	1.22	.384	1.21	.390
West Africa			0.93	.514	0.92	.454	0.92	.455
East Africa			1.01	.932	1.00	.997	1.00	1.000
North Africa			0.67	<.001	0.66	<.001	0.66	<.001
Centre-Southern Asia			0.80	.001	0.80	.001	0.80	.001
Western Asia			0.71	.040	0.72	.045	0.72	.045
East Asia			0.53	<.001	0.53	<.001	0.53	<.001
Centre-South America			2.97	<.001	2.95	<.001	2.95	<.001
North America			0.59	.021	0.59	.027	0.60	.027
Oceania			1.03	.945	1.04	.930	1.04	.927
Other/not specified			0.03	<.001	0.03	<.001	0.03	<.001
Chronic diseases								
0 (ref.)				—		—		—
1			1.11	<.001	1.11	<.001	1.11	<.001
2			1.15	<.001	1.15	<.001	1.15	<.001
3 or more			1.47	<.001	1.47	<.001	1.47	<.001
Province of residence								
Milan (ref.)				—		—		—
Lodi			2.01	<.001	2.00	<.001	1.94	<.001
Educational disadvantage								
Low (ref.)						—		—
Medium–low					1.05	.054	1.05	.055
Medium–high					1.06	.040	1.06	.043
High					1.18	<.001	1.19	<.001
Unemployment								
Low (ref.)						—		—
Medium–low					0.94	.020	0.94	.026
Medium–high					0.91	<.001	0.91	<.001
High					0.90	<.001	0.90	<.001
Housing crowding								
Low (ref.)						—		—
Medium–low					1.03	.347	1.02	.382
Medium–high					1.08	.008	1.07	.014
High					1.15	<.001	1.14	<.001
Mobility								
Low (ref.)						—		—
Medium–low					1.04	.115	1.04	.114
Medium–high					1.01	.776	1.00	.966
High					1.05	.058	1.04	.148
Population density								
Low (ref.)						—		—
Medium–low					0.96	.111	0.96	.137
Medium–high					0.96	.092	0.96	.100
High					1.00	.892	1.00	.910

(continued)

Table 2. Continued.

	Model 1.1 (VPC = 0.20)		Model 1.2 (VPC = 0.13)		Model 1.3 (VPC = 0.12)		Model 1.4 (VPC = 0.13)	
	OR	P-value	OR	P-value	OR	P-value	OR	P-value
Province × Mobility								
Lodi × low (ref.)							1	—
Lodi × medium–low							0.93	.372
Lodi × medium–high							1.28	.057
Lodi × high							1.26	.033
Province × population density								
Lodi × low (ref.)							1	—
Lodi × medium–low							1.01	.926
Lodi × medium–high							0.87	.158
Lodi × high							0.91	.804

Note: Model 1.1: empty model; Model 1.2: individual-level predictors only; Model 1.3: individual- and area-level predictors; Model 1.4: individual- and area-level predictor plus interaction.

Abbreviations: VPC, variance partition coefficient; OR, odds ratio.

lockdown rather than before it. The aim is to assess whether the effects of the predictors on the risk of contagion have changed after the lockdown. The results of these analyses are shown in Table 3. The VPC of the “empty” model (Model 2.1; VPC = 0.09) suggests the presence of a territorial heterogeneity in the phenomenon investigated. With the addition of individual-level covariates, it is possible to assess which characteristics are associated with a change in risk profile between the two time intervals (Model 2.2). The change in the effect of age after the lockdown was negligible (OR = 1.00). Being female rather than male was associated with a considerable increased ORs of contagion after the containment measure (OR = 1.66). Compared with Italians, statistically significant increased ORs of contracting the virus after the lockdown were found for those born in Eastern Europe (OR = 1.33), West and North Africa (ORs = 1.56 and 1.81, respectively), Centre-Southern and East Asia (ORs = 1.96 and 1.39, respectively), and Centre-South America (OR = 1.39). Compared to those with no chronic disease, those having at least one chronic disease resulted to be at lower risk after the lockdown rather than before it (ORs = 0.80, 0.79, and 0.89); similarly, living in the Lodi rather than the Milan area was associated with reduced odds of contagion after the lockdown (OR = 0.36).

Finally, fitting the model with area-level predictors, it is possible to observe how the full lockdown changed the role of area characteristics in shaping contagion (Model 2.3). Specifically, living in areas with medium–high (OR = 1.11) and high (OR = 1.18) percentages of low-educated people, as well as higher levels of housing crowding (ORs = 1.10, 1.09, and 1.16) and higher population density (ORs = 1.10, 1.12, and 1.16) were found to be more important risk factors after the lockdown rather than before it, whilst the effect of area unemployment and mobility did not change significantly between the two time intervals.

Discussion

Our study reported a nonnegligible territorial heterogeneity in the spread of COVID-19, which was not entirely explained by the differences in individual characteristics, with a class gradient emerging in relation to contagion.

Educational Disadvantage

The association between area-level educational deprivation and COVID-19 contagion may reflect the situation of disadvantage experienced by people inhabiting these contexts, with the typical mechanisms driving class inequalities in relation to chronic diseases unfolding their effects also on the novel virus. The less educated, for instance, in light of their lower level of health literacy^{41,42} may be less prone to adhere to institutional recommendations disseminated in the first instance to avoid contagion, such as wearing protective masks and gloves and maintaining social distancing.⁴³ This conjecture seems to be supported by the fact that the role played by the area educational disadvantage increased after the full lockdown, in correspondence of an overall decrease in the numbers of infected. However, pathways other than those involving cognitive skills, behaviors, and explicit choices may be involved in the association between poor education and COVID-19 risk. Increased ORs of COVID-19 in low-education areas may have emerged also as a consequence of the kind of jobs (eg, personal services, logistics, cleaning, retail, etc) in which the most disadvantaged are typically employed, putting them at higher risk of contagion as compared to people employed in skilled jobs. Again, the increased ORs of educational disadvantage in the second time interval might support this interpretation, whereby those working in the service sector may have benefitted extensively from the possibility of

Table 3. Multilevel Logistic Regression on the Post- vs Prelockdown Risk of Infection with COVID-19 (N = 32 588; Groups = 9085).

	Model 2.1 (VPC = 0.09)		Model 2.2 (VPC = 0.07)		Model 2.3 (VPC = 0.07)	
	OR	P-value	OR	P-value	OR	P-value
Age			1.00	.003	1.00	.003
Sex						
Male (ref.)			1.00	—	1.00	—
Female			1.66	<.001	1.66	<.001
Country of birth						
Italy (ref.)			1.00	—	1.00	—
European Union			1.10	.232	1.08	.329
Eastern Europe			1.33	.002	1.28	.007
Other European			1.54	.113	1.52	.121
Centre-Southern Africa			1.02	.972	0.96	.940
West Africa			1.56	.045	1.49	.072
East Africa			1.18	.483	1.12	.618
North Africa			1.81	<.001	1.70	<.001
Centre-Southern Asia			1.96	.000	1.87	<.001
Western Asia			1.19	.620	1.21	.589
East Asia			1.39	.013	1.35	.024
Centre-South America			1.39	.000	1.32	<.001
North America			1.03	.959	1.08	.880
Oceania			0.74	.710	0.80	.781
Other/not specified			—	—	—	—
Chronic diseases						
0 (ref.)			1.00	—	1.00	—
1			0.80	<.001	0.80	<.001
2			0.79	<.001	0.78	<.001
3 or more			0.89	.002	0.87	<.001
Province of residence						
Milan (ref.)			1.00	—	1.00	—
Lodi			0.36	<.001	0.38	<.001
Educational disadvantage						
Low (ref.)					1.00	—
Medium–low					1.05	.210
Medium–high					1.11	.016
High					1.18	<.001
Unemployment						
Low (ref.)					1.00	—
Medium–low					1.06	.130
Medium–high					1.02	.535
High					1.06	.153
Housing crowding						
Low (ref.)					1.00	—
Medium–low					1.10	.011
Medium–high					1.09	.030
High					1.16	.001
Mobility						
Low (ref.)					1.00	—
Medium–low					1.02	.582
Medium–high					1.02	.606
High					1.01	.776
Population density						
Low (ref.)					1.00	—
Medium–low					1.10	.011
Medium–high					1.12	.007
High					1.16	<.001

Note: Model 2.1: empty model; Model 2.2: individual-level predictors only; Model 2.3: individual- and area-level predictors.
Abbreviations: VPC, variance partition coefficient; OR, odds ratio.

working remotely, with reduced possibility of being infected. Conversely, being the less-educated more commonly employed in sectors which have been touched to a lesser extent by the decree's measures, their isolation may have been limited due to their working activities and work-related mobility, as well as their stronger need to receive their salary. However, though education and occupation are known to be associated, having included in our analyses only a measure for the former, we may be cautious in extending our interpretation to occupational class.

Unemployment

At the census block level, only an indicator of employment status—and not occupational class—was available, which turned out to be inversely associated with COVID-19 risk. This may be due to the higher patterns of social isolation/exclusion and reduced mobility already experienced before the containment measures by the subjects living in a context where the share of unemployment is higher. Hence, joblessness may have acted as a protective factor against the virus since the beginning of the outbreak, as the unemployed are more prone to stay at home. Indeed, the effect of this indicator did not change after the lockdown, suggesting that in the areas characterized by higher unemployment, restricting social interactions may have had less impact than elsewhere.

Housing Crowding

Living in areas characterized by higher values of housing crowding was found to be positively associated with COVID-19 risk, with larger effects after the lockdown. Having less space available in dwellings implies more possibility of person-to-person transmission if one household member is infected, a mechanism that gains importance when the members are forced to spend most of—if not all of—the day in their houses. The different results coming from the area-level measures of education and housing crowding on one side, and unemployment on the other, grasp the multidimensionality of socioeconomic disadvantage, with different indicators representing diverse facets of the concept, supporting the choice not to collapse the separate measures into a single deprivation index.

Mobility and Population Density

Census block mobility and population density were not significant in relation to SARS-CoV-2 diffusion, as initially hypothesized, which led us to further investigate their role during the outbreak. The fact that mobility was not significant in the overall model is apparently a consequence of not distinguishing in the first instance between the diverse territorial profiles of the Milan and the Lodi areas. As Supplemental Figure A8 in the Appendix shows, mobility

is markedly lower in the Lodi area, where the outbreak initially took place, with lower absolute numbers but higher rates compared with the Milan area. Suspecting that this may have influenced the results, we added an interaction term that indeed confirmed that higher levels of mobility were significantly associated with the spread of the virus in the Lodi area, but not in the Milan area. A plausible explanation could be that because the Milanese area is characterized by high mobility, this did not affect the risk of infection. Conversely, in the Lodi area, where mobility is generally lower, the spread of the disease may have been fostered by more incoming and outgoing population movements in certain areas. We also tested an interaction between the province of residence and population density, but this was not significant. However, population density turned out to be relevant when assessing the effect of the containment measure, with more people per square kilometer facilitating the spread of the disease after the lockdown. Reading this finding jointly with those of mobility, we can conclude that in a dynamic context characterized by internal and external flows of people, population density may not account for virus transmission. Contrarily, when mobility is necessarily reduced to the bare minimum, a higher concentration of individuals in the same area may trigger contagion.

Individual-level Covariates

In addition to area-level influences, some individual factors played a role in shaping the risk of contagion, with changing effects before and after the lockdown. Age was found to be positively associated with the risk of contracting the virus, with stable effects in the two time intervals. Whilst, overall, differences in the contagion in relation to sex did not emerge, being female was associated with increased COVID-19 risk in the second time interval, highlighting the emergence of a pattern of gender inequalities. Having no data to investigate this deeply, we can only speculate that this may be primarily due to the preponderance of female employment in jobs that may have been less touched by the restrictions imposed, especially personal and home care services. Similarly, though an overall pattern emerged in relation to the country of birth, it is after the lockdown that being Italian became actually a protective factor against the risk of contagion. Situations of marginality and relative disadvantage of the foreigners as compared to the natives may have contributed to a differentiation in the opportunities to benefit from the measures aimed at reducing social interactions. Migrants from less developed countries cumulate the factors of higher risk, namely overcrowding, employment in low-quality jobs requiring getting in touch with clients or users, a stronger need for a wage that discourages staying home during the lockdown, and movements by public transportation.⁴⁴

With regard to preexisting health conditions, a positive association between the number of chronic diseases and the

risk of contagion was found, but on a time comparison, we can notice that after the lockdown people with at least one chronic disease were less likely to be infected as compared with those without any disease. This may have emerged as a result of an effective communication of the dangers inherent to those in worse health conditions, which may have led to a more rigorous compliance with the rules and the indications to avoid the contagion by those subjects facing greater risks. Nonetheless, it is also plausible that the majority of subjects most exposed to the risk of contagion (those with one or more chronic diseases) were infected in the first time interval.

Findings and Limitations

Though the existing literature assessing the impact of SES on the COVID-19 epidemic is inevitably limited, our findings are mostly in line with the earliest studies on the issue. A study carried out in China found that area factors such as population density, land use, total retail sales of consumer goods and GDP per unit of land area, public green space density, average building scale, and hospital density were significantly associated with COVID-19 morbidity rates.⁴⁵ COVID-19 morbidity and mortality were found to be related to the socioeconomic characteristics of local areas in England and Wales.⁴⁶ A territorial variability in the pandemic severity was found also across different geographic areas in Spain, and this was significantly associated with some sociodemographic variables,⁴⁷ though a study in the municipalities of the Catalonia region led to mixed findings.⁴⁸ A study comparing the 50 largest American cities found that a number of socioeconomic factors, among which being unmarried, not having a computer, and being unemployed were associated with COVID-19 prevalence and/or fatality at the community level.⁴⁹ Moreover, a study at the zip-code level in New York City reported noticeable disparities in the COVID-19 rates according to area-income levels.⁵⁰ Furthermore, the differentials in contagion in the US between different ethnic groups raised public concern in the country,⁵¹ drawing attention to the possible effects of situations of marginality and disadvantage for the most vulnerable groups, such as African Americans and Hispanics.

Accordingly, though the empirical research on this specific issue is at its very beginning, a pattern of socioeconomic inequalities in the ongoing epidemic is clearly emerging, with the most vulnerable being at higher risk of contagion compared to the better off, despite the institutional and public health efforts to contain the outbreak at all levels.

Most of the research on the social determinants of health has been focused on chronic diseases, in light of their predominance over infectious disease as the leading causes of morbidity and mortality in middle- and high-income countries. In public opinion, the ongoing epidemic seems to go ahead ignoring class inequality, potentially hitting everyone notwithstanding his or her socioeconomic background.

This is likely a consequence of the infectious nature of the disease, with physical mechanisms (the transmission of germs) replacing lifestyles and behaviors as prominent risk factors. Our findings suggest instead that the underlying pattern of inequality is still at work shaping the risk of contagion, notwithstanding the change in risk profile, in line with the *Fundamental Causes Theory's* postulates.¹³ This is far from being groundbreaking, since—after years of debate on whether the 1918 epidemic was “socially neutral”—a social patterning in the so-called “Spanish flu” was reported to exist.⁵² Long before the COVID-19 outbreak, Quinn and Kumar⁵³ outlined a list of mechanisms linking SES with infectious disease epidemics, most of which we have already discussed above. The scholars divide them into *structural measures* (eg, working, living in a metro area, living in an apartment building), *work-related measures of inability to social distance* (eg, not able to work remotely, not having sick leave, at risk of job loss if not able to go to work) *other measures of inability to social distance* (eg, difficulty avoiding public transportation), *measures of susceptibility* (chronic conditions such as heart disease, high blood pressure, cancer, diabetes, asthma, lung disease, immunosuppression), and *measures of access to health care* (eg, no regular health care provider, lack of money, experienced discrimination/hassle when seeking health care). Given the presence of several pathways putting the most disadvantaged at higher risk of infection—both because of their *habitus*⁵⁴ and preexisting health conditions—conceiving infectious diseases as more “democratic” than chronic ones may be misleading.

This work is subject to some limitations that should be highlighted. First, due to data unavailability, we did not control our models for individual SES measures, which may have led to lessened effects for the area-level predictors. Related to this, we are aware that there may be other factors intervening in shaping the risk of contagion which have not been included in our analysis. Nonetheless, our models were specified relying on the most pertinent indicators among those available from ATS and census data. Second, because of the *Modifiable Area Unit Problem*,⁵⁵ we are aware that the measurement of contextual effects may be significantly influenced by the geographic scale adopted. We relied on the administrative division of the territory in census blocks, the lowest scale available. Our decision was driven by the inverse relationship between the size of the area unit and the area-level variance,^{56,57} since relying on larger units (which in our case for most of the areas coincide with the municipality) would have implied to neglect most of the territorial heterogeneity in the outcome, especially for Milan. Conversely, the area units we adopted might be too small, and it would be useful to reproduce the study relying on areas of intermediate dimension between the census block and the municipality, as it has been done for phenomena of different kinds in the Milan area.⁵⁸ Third, there is a time mismatch between the data sources, since

ATS information on COVID-19 cases is referred to the year 2020, whereas the census-based indicators we used are referred to 2011. However, these latter represent the most recent data at the time of writing and, consequently, provide the only way to approach the phenomenon using the methodology adopted. Moreover, we have good reasons to think that no big changes happened in terms of the social organization of space in the last 9 years. Indeed, research carried out with different census waves has shown that the composition of urban areas remained stable across years, even in correspondence with remarkable economic changes.^{59–62} Furthermore, the indicator of mobility is based on 2011 data projected to 2020 and came at a different area unit, thus we should be cautious when interpreting its effects. Fourth, not all the subjects included in the study as COVID-19 cases underwent a swab test. Anyway, we equally considered swab tested and symptomatic subjects as COVID-19 cases given that the latter were detected following specific criteria within the context of a systematic reporting system with a strict procedure. This minimized the possibility that not-tested subjects were improperly included in the study as COVID-19 cases.

Conclusion

Our findings highlighted that neighborhood SES was associated with COVID-19 contagion, after controlling for individual-level confounders. Rather than being just a methodological exercise to assess the presence of possible contextual effects on health outcomes, this study has relevant implications. Policies aimed at reducing inequalities are often neglected by decision-makers, but in the case of an infectious disease, this may lead to even more deleterious consequences. Disregarding class differences in risk exposure may foster the spread of the virus, with consequences not limited to the production of health inequities, but also involving higher disease rates among the overall population. Though addressing the root causes of inequalities would be the most effective—yet not simple—strategy, prompt interventions aimed at tackling the mechanisms putting the most vulnerable at higher risk of infection (eg, temporarily sick leaves and/or economic subsidies for those who are not entitled to them) may help in containing the outbreak at its beginning. At a later stage, changes in the vaccination policy based on social conditions in addition to biomedical priorities for pandemic vaccination may be useful.⁶³

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethics Approval and Consent to Participate

Ethics approval and consent to participate were not required, as this is an observational study based on data routinely collected by the

ATS of Milan, a public body of the Regional Health Service—Lombardy Region. The ATS has among its institutional functions, established by the Lombardy Region legislation (R.L. 23/2015), the government of the care pathway at the individual level in the regional social and health care system, the evaluation of the services provided to, and the outcomes of, patients residing in the covered area. This study is also ethically compliant with the National Law (D.Lgs. 101/2018) and the “General Authorisation to Process Personal Data for Scientific Research Purposes” (nos. 8 and 9 of 2016, referred to in the Data Protection Authority action of December 13, 2018). Data were anonymized with a unique identifier in the different datasets before being used for the analyses.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Supplemental material

Supplemental material for this article is available online.

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