

**Title:** Socio-economic patterns of COVID-19 during the pandemic in Italy

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## Abstract

**Objective:** To investigate the association between deprivation and COVID-19 outcomes in Italy during pre-lockdown, lockdown and post-lockdown periods.

**Design:** Retrospective cohort study.

**Setting:** All municipalities in Italy with less than 50,000 population.

**Participants:** 38,534,169 citizens and 222,875 COVID-19 cases reported to the Italian epidemiological surveillance were assigned to quintiles based on the deprivation index of their municipality of residence.

**Interventions:** The COVID-19 pandemic during pre-lockdown, lockdown and post-lockdown from the 20th of February to the 15th of October of 2020.

**Main outcome measures:** Multilevel negative binomial regression models, adjusting for age, sex, population-density and region of residence were conducted to evaluate the association between deprivation and COVID-19 incidence, case-hospitalisation rate and case-fatality. The association measure was the rate ratio.

**Results:** During pre-lockdown, lockdown and post-lockdown, the incidence rate ratios (IRR) with 95% confidence interval (CI) in the most deprived quintile with respect to the least deprived quintile were 1.17 (95% CI 0.98 to 1.41), 1.14 (1.03 to 1.27) and 1.47 (1.32 to 1.63), respectively. In those three periods, the case-hospitalization IRR were 0.68 (0.51 to 0.92), 0.89 (0.72 to 1.11) and 0.99 (0.81 to 1.22) and the case-fatality IRR were 0.92 (0.75 to 1.13), 0.95 (0.85 to 1.07) and 1.02 (0.73 to 1.41), respectively.

**Conclusions:** During lockdown and post-lockdown, but not during pre-lockdown, a higher incidence of cases was observed in the most deprived municipalities compared with the least deprived ones. No differences in case-hospitalisation and case-fatality according to deprivation were observed in any period under study.

## Introduction

Italy has been one of the most affected European countries by the coronavirus disease 2019 (COVID-19) pandemic which spread out of Hubei (China) in the early months of 2020 (1). By the 15<sup>th</sup> of December 2020 over 1,500,000 people had been diagnosed with the disease and over 60,000 had died from it (2). In order to control the spread of the infection and safeguard the national health system, the Italian government implemented a series of social distancing measures. On the 4<sup>th</sup> of March, primary and secondary education centres were closed, followed by a national lockdown implemented on the 10<sup>th</sup> of March 2020, by which citizens were only allowed outside their homes for work -if considered essential workers- and to acquire basic need items (3,4). This measure was eased on the 18<sup>th</sup> of May, when non-essential work was resumed (5). The full measure was lifted, including travel restrictions between regions, on the 3<sup>rd</sup> of June. Other measures implemented during this period include the need to keep 1-meter distance between people and the mandatory use of face masks indoors and in places where social distancing may not be possible (4). Employers were asked to keep remote working where possible and, if not possible, to ensure the safety of employees by enforcing social distancing and providing face masks (4).

These measures have caused severe social and economic disruption across the country. Yet, it is not yet known whether the different periods of the pandemic, and the measures implemented, could have modulated the risk exposure to SARS-CoV-2 across the different socioeconomic groups in Italy. Studies analysing the impact of previous pandemics on the different socioeconomic groups have found contradictory results. For example, some authors found higher illiteracy rates to be associated with an increased risk of mortality during the 1918 pandemic in the US (6), but others have reported no differences by socioeconomic status in New Zealand during the same pandemic (7). Similarly, the impact of the 2009 pandemic influenza has been found to be higher in lower socioeconomic groups in England (8), but not in France (9). With regards to COVID-19, it has been suggested that those living in the most deprived areas could be at higher risk of morbidity and mortality from COVID-19 (10,11). This increased risk could be the consequence of a greater exposure to the virus mediated by the working and living conditions of those who suffer deprivation (10,12,13). It has been proposed that low-paid workers and those in manual occupations may be at increased exposure to SARS-CoV-2 compared with other occupations given that they are less likely to be able to work remotely, more likely to suffer from poor working conditions and more likely to live in crowded housing, among other factors (12,13). Besides the increased risk in exposure, there is evidence that Non-Communicable Diseases (NCD), such as diabetes, cardiovascular and chronic respiratory diseases, are associated with deprivation (14). As these diseases are risk factors for hospitalisation and mortality from COVID-19, it is plausible that rates of these outcomes are higher in the most deprived areas (10). Yet, the published literature shows inconsistent results

(15). Ecological studies carried out in the UK and US have found a positive association between deprivation and incidence, hospitalisation and mortality from SARS-CoV-2 infection (16–18), but other studies have not found such association (19,20); and others have found that it is actually the wealthier groups who have been hit harder by COVID-19 (21,22).

It is likely that the association between COVID-19 outcomes and socioeconomic variables is influenced by different social, cultural, economic and policy factors; as well as by epidemic dynamics that vary from country to country and within countries. For example, in Italy, incidence has been particularly high in the northern areas, which are wealthier than the centre and south of the country, especially during the first periods of the pandemic.

In this study, we aimed to investigate the association between COVID-19 related outcomes and the level of deprivation of the municipality of residence in the Italian population; and how this association changed throughout the different epidemic periods.

## **Methods**

### *Study design*

We conducted a retrospective cohort study using a contextual approach to evaluate the association between deprivation and COVID-19 incidence, as well as between deprivation and the risk of hospitalisation and death among COVID-19 cases; across Italian municipalities in the different periods of the epidemic (pre-lockdown, lockdown and post-lockdown). The study was carried by analysing individual data and using the Italian deprivation index of the municipality of residence as a contextual measure of deprivation.

We described the methods and presented findings according to the reporting guidelines for observational studies that are based on routinely collected health data (The RECORD statement –checklist of items extended from the STROBE statement) (Supplementary Material 1) (23).

### *Data sources*

We obtained individual data on cases, hospitalisations and deaths from the Italian integrated epidemiological surveillance system of COVID-19, which collects demographic, clinical and epidemiological data on all PCR confirmed cases of COVID-19 in the country (24). From every case, we extracted information on age, sex, vital status, history of hospitalisation, whether or not they were healthcare workers, and their municipality of residence. For this last variable we used the 2020 list of Italian municipalities as reported by the national institute of statistics (ISTAT) (25). As a measure of deprivation, we used the Italian municipality index of deprivation (26).

We obtained estimates of the Italian population (stratified by region, municipality, age and sex) as well as the population density of Italian municipalities updated on the 1<sup>st</sup> of January 2020 through the Italian institute of statistics (ISTAT) (25), assuming these remained unchanged during the study period.

#### *Exposure, outcomes and potential confounders*

We analysed the association between deprivation (exposure) and COVID-19 incidence, case-hospitalisation rate and case-fatality (outcomes). We used the index of deprivation as a contextual measure of deprivation. This index was built using information from the 2011 census on unemployment, educational attainment, percentage of rented housing, house overcrowding and percentage of single-parent families (26). In the analysis, we categorised the index according to quintiles of its distribution among municipalities, with “one” being the least deprived and “five” the most deprived.

We considered as COVID-19 cases those who were tested positive for of SARS-CoV-2 infection by RT-PCR. Among these, we considered hospitalisations and deaths occurring within 40 days of the date of sampling/diagnosis.

We considered age, sex, population density and region of residence, as potential confounders of the associations between the exposure and outcomes in each epidemic period. Age was categorized into three groups (0-49, 50-69 and over 70 years old). We used these cut-offs based on the observed changes in age’s case-fatality as reported by routine surveillance data (2). Population density was categorized into three levels (<54 people per km<sup>2</sup>, 54-106 people per km<sup>2</sup> and >106 people per km<sup>2</sup>).

We used the date of sampling/diagnosis of cases to assign them to each period studied (pre-lockdown, lockdown and post-lockdown). The lockdown in Italy was implemented on the 10<sup>th</sup> of March and was lifted on the 18<sup>th</sup> of May. We added seven days to these dates to account for the median time between infection and diagnosis -four days of incubation period and three days between symptom onset and diagnosis (27)-.

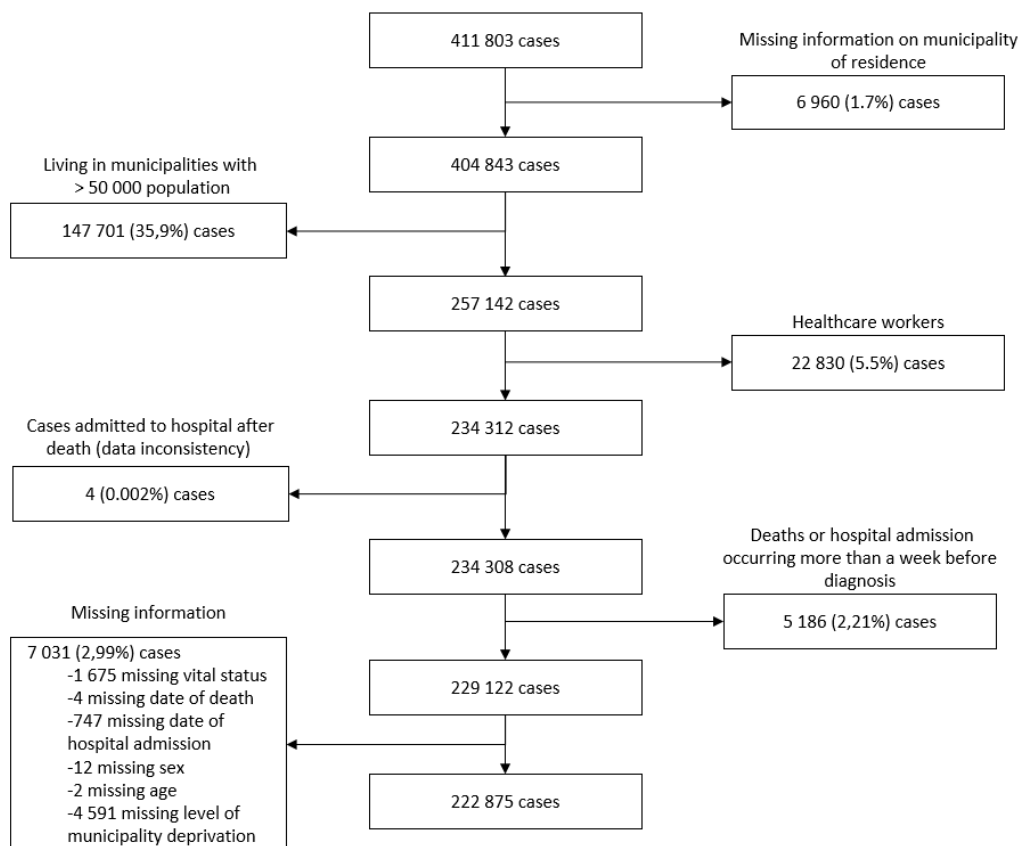
Therefore, cases were assigned to the pre-lockdown period if they had a date of sampling/diagnosis between the 20<sup>th</sup> of February 2020 and the 16<sup>th</sup> of March 2020, to the lockdown period if the date was between the 17<sup>th</sup> of March 2020 and the 24<sup>th</sup> of May; and to the post-lockdown if between the 25<sup>th</sup> of May 2020 and the 15<sup>th</sup> of October.

### Statistical analysis

The analysis was conducted using surveillance data extracted on the 9<sup>th</sup> of December 2020.

We excluded from the analysis individuals living in municipalities with a population larger than 50,000 people, as we considered that the social deprivation index could not represent the reality of large municipalities. The threshold of 50,000 was set up based on previous studies who have analysed data at the level of Italian municipalities (28). We also excluded healthcare workers because, as they have a greater risk of being exposed to the virus than the general population and they are less likely to suffer from socioeconomic deprivation, they could confound the associations tested in this study. Finally, we excluded cases with incomplete information for the analysis. At the end, we included 222,875 cases (see Figure 1), which represented 54.1% of the total cases (ranging from 33.6% to 91.9% across the different regions). Cases were aggregated by 7,624 municipalities, which represented a population of 38,534,169 (64.0% of the total Italian population).

**Figure 1. Flow chart showing the selection of cases included in the analysis.**



We described the main demographic characteristics by level of deprivation of the area of residence with counts and percentages. We conducted a descriptive analysis of the distribution of deprivation and COVID-19 related outcomes. We calculated age-adjusted rates for each outcome by deprivation quintile, stratifying the results by sex and epidemic period. To adjust rates by age we used direct standardisation using the European Standard Population 2013 as reference (29). To calculate rates, we included in the denominator the number of person-days at risk in each period. When calculating incidence, persons living in municipalities included in the study were considered at risk until they were diagnosed with the infection or until the end of the period under study, whichever came first. When calculating case-hospitalisation and case-fatality rates, cases were considered at risk until their recovery/death. If the event did not happen, they were considered as exposed for 40 days.

Then, we carried out a multivariable analysis using negative-binomial regression models for each outcome to measure its association with the level of deprivation of the municipality of residence. We deemed this as the most appropriate method given the significant level of overdispersion ( $>1$ ).

We calculated one model for each outcome and period, in which the number of cases/hospitalisations/deaths was included as the dependent variable. We included the independent variables in three steps. First, we calculated the models including deprivation of the municipality of residence (exposure of interest) together with sex and age group. Then, we added the level of population density of the municipality of residence and in the final step we added the region of residence. We also included in the model random effects accounting for clustering at municipality level (random intercept only). The offset was the person-days at risk. The Intraclass Correlation Coefficient (ICC) (i.e., the proportion of variance explained by random effects) was used to evaluate the need to use multilevel models. To this purpose, we used the formula suggested by Nakagawa et al. for negative binomial models (30).

Estimates are presented with the 95% confidence intervals (CI). The analysis was carried out in R (version 4.0.2), using Rstudio (version 1.3.959) (31,32). We used the package glmmTMB for the multivariable analysis. The formula used for the calculation of the models alongside the full list of the R packages used can be found in the Supplementary Material 2.

#### *Ethical statement*

This study was conducted using data from the Italian national integrated COVID-19 surveillance routinely collected and analysed within the mandate of the Italian National Institute of Health. The scientific dissemination of COVID-19 surveillance data was authorised by the Italian Presidency of the Council of Ministers on the 27th of February 2020 (Ordinance n. 640).

## Results

Table 1 shows the demographic characteristics of the included population according to the variables of interest, a map with the geographical position of each Italian region can be found in the Supplementary Material 3.



**Table 1 Distribution of the Italian population included in the study (38,534,169 population) according to the characteristics of interest.**

	Index of deprivation				
	Q1 (least deprived)	Q2	Q3	Q4	Q5 (most deprived)
<b>Females</b>					
<b>Age group</b>					
0-49	701,820 (49%)	1,493,434 (51%)	2,080,147 (51.6%)	2,475,434 (51.7%)	3,562,867 (55.3%)
50-69	419,544 (29.3%)	840,618 (28.7%)	1,139,603 (28.3%)	1,356,866 (28.3%)	1,787,085 (27.8%)
70 and over	309,753 (21.6%)	596,217 (20.3%)	807,980 (20.1%)	957,769 (20%)	1,089,894 (16.9%)
<b>Population density</b>					
<54.6 ppkm <sup>2</sup>	266,933 (18.7%)	299,537 (10.2%)	274,120 (6.8%)	319,201 (6.7%)	330,982 (5.1%)
54.6-106 ppkm <sup>2</sup>	243,517 (17%)	386,368 (13.2%)	465,022 (11.5%)	498,064 (10.4%)	603,154 (9.4%)
>106 ppkm <sup>2</sup>	920,667 (64.3%)	2,244,364 (76.6%)	3,288,588 (81.6%)	3,972,804 (82.9%)	5,505,710 (85.5%)
<b>Regions' grouped by geographical area</b>					
North <sup>1</sup>	1,312,378 (91.7%)	2,327,889 (79.5%)	2,709,840 (67.2%)	2,543,374 (53.0%)	840,279 (13.0%)
Centre <sup>2</sup>	63,446 (4.4%)	432,369 (14.8%)	876,548 (21.8%)	870,667 (18.2%)	875,738 (13.6%)
South and Islands <sup>3</sup>	55,293 (3.9%)	170,011 (5.8%)	441,342 (11%)	1,376,028 (28.7%)	4,723,829 (73.4%)
<b>Males</b>					
<b>Age group</b>					
0-49	735,841 (52.5%)	1,558,283 (54.9%)	2,165,134 (55.8%)	2,575,729 (56.2%)	3,682,631 (59.3%)
50-69	424,539 (30.3%)	828,766 (29.2%)	1,107,808 (28.6%)	1,300,344 (28.3%)	1,689,939 (27.2%)
70 and over	239,932 (17.1%)	453,733 (16%)	606,423 (15.6%)	711,007 (15.5%)	835,029 (13.5%)
<b>Population density</b>					
<54.6 ppkm <sup>2</sup>	267,081 (19.1%)	294,422 (10.4%)	269,540 (6.9%)	313,750 (6.8%)	327,828 (5.3%)
54.6-106 ppkm <sup>2</sup>	239,837 (17.1%)	376,023 (13.2%)	450,146 (11.6%)	480,715 (10.5%)	591,378 (9.5%)
>106 ppkm <sup>2</sup>	893,394 (63.8%)	2,170,337 (76.4%)	3,159,679 (81.4%)	3,792,615 (82.7%)	5,288,393 (85.2%)
<b>Regions' grouped by geographical area</b>					
North <sup>1</sup>	1,285,354 (91.8%)	2,261,555 (79.6%)	2,628,251 (67.8%)	2,435,911 (53.1%)	808,554 (13.1%)
Centre <sup>2</sup>	61,693 (4.4%)	413,442 (14.6%)	828,163 (21.3%)	830,278 (18.1%)	846,282 (13.6%)
South and Islands <sup>3</sup>	53,265 (3.8%)	165,785 (5.8%)	422,951 (10.9%)	1,320,891 (28.8%)	4,552,763 (73.3%)

<sup>1</sup>Includes Regions of: Piemonte, Valle d'Aosta, Liguria and Lombardia, Trentino-Alto Adige, Veneto, Friuli-Venezia Giulia and Emilia-Romagna; <sup>2</sup>Includes Regions of: Toscana, Umbria, Marche and Lazio; <sup>3</sup>Includes Regions of: Abruzzo, Molise, Campania, Puglia, Basilicata, Calabria, Sicilia and Sardegna

### Distribution of COVID-19 outcomes according to deprivation

In Italy, deprivation follows a north-south gradient, with the south concentrating a larger number of municipalities in the most deprived quintiles compared to the north. On the contrary, incidence of COVID-19 was higher in the north of the country, particularly during the pre-lockdown period, spreading more widely during the lockdown and post-lockdown periods (See Figure 2).

**Figure 2. Geographical distribution of the cumulative number of cases per 100,000 persons during the periods of the epidemic in Italian municipalities with less than 50 000 population (n = 7,624), and distribution of quantiles of the index of deprivation.**

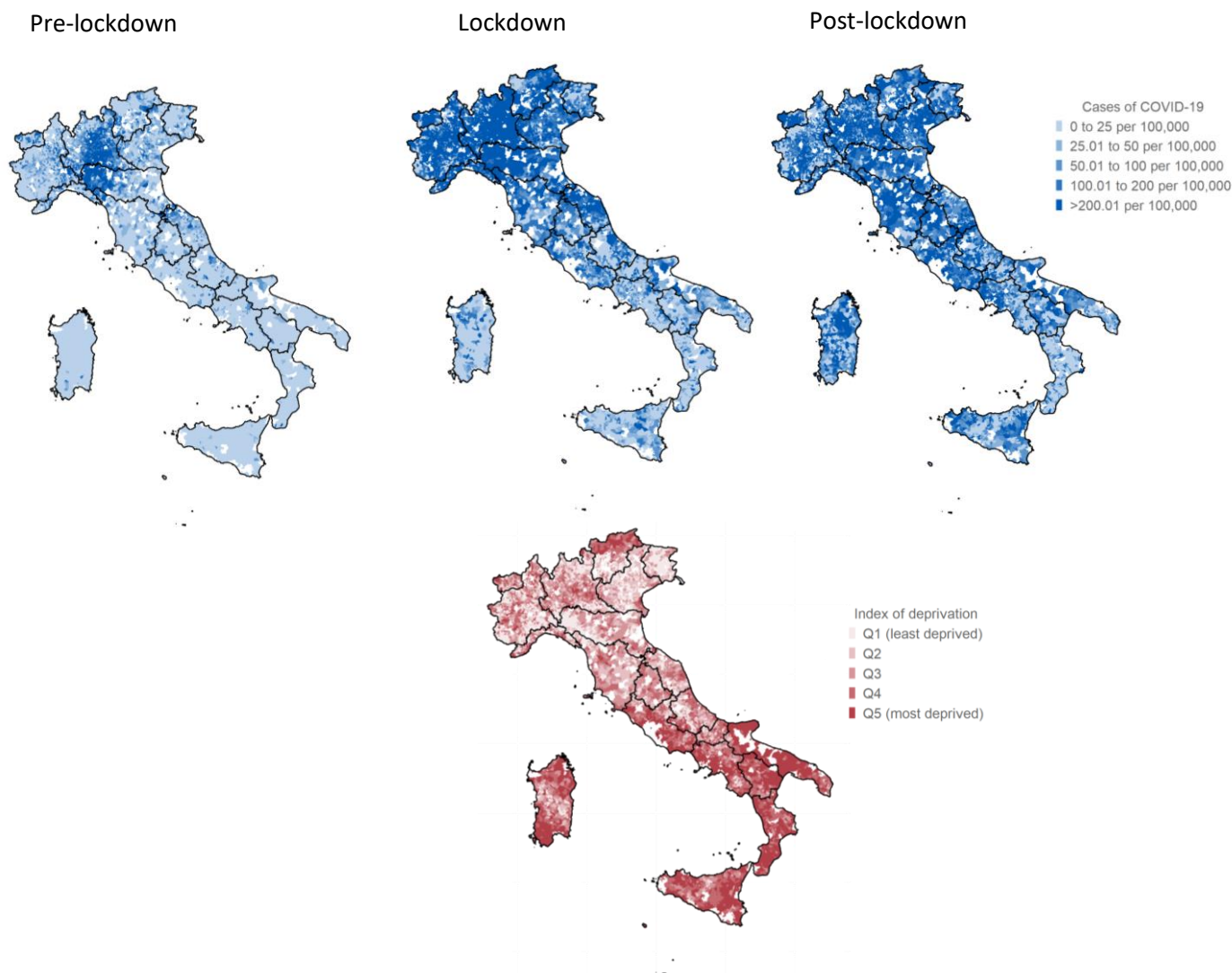


Table 2 summarises the number of cases, hospitalisations and deaths by municipalities' deprivation quintiles, with their respective age-adjusted rates; stratified by sex and epidemic period. Incidence peaked during the lockdown period and decreased afterwards. During pre-lockdown and lockdown periods, higher incidence was observed in the municipalities belonging to the least deprived quintile (Q1) compared with those in the most deprived ones (Q5), in both females and males. However, this gradient inverted during the post-lockdown period, when incidence was higher in municipalities belonging to the most deprived quintile than in the least deprived ones, in females and males.

Case-hospitalisations rates were higher during the pre-lockdown period, decreased during lockdown and reaching its lowest level during the post-lockdown period, in females and males and in all deprivation groups. In the pre-lockdown period, the most and least deprived quintiles (Q1 and Q5) had the lowest case-hospitalisation rates. During lockdown, case-hospitalisation rate was lowest in municipalities belonging to the least deprived quintile, but no clear gradient was observed. In the post-lockdown, similar rates were observed across deprivation groups.

Case-fatality rates also peaked during the pre-lockdown period and decreased afterwards, reaching its lowest levels during post-lockdown. No clear socioeconomic gradient was observed in any period. During pre-lockdown, cases living in the least and most deprived municipalities had the lowest case-fatality rates. During lockdown and post-lockdown, case-fatality rates were similar across all groups.

**Table 2. Age-adjusted rates (AAR) of cases, hospitalisations and deaths from SARS-CoV-2 infection in Italian municipalities by level of deprivation (Q1 least deprived, Q5 most deprived). Stratified by sex and epidemic period\*.**

		Pre-lockdown		Lockdown		Post-lockdown	
Incidence							
ID	Sex	Number	AAR	Number	AAR	Number	AAR
Q1	Females	844	19.9	6023	51.8	2896	14.8
Q2		1,412	16.7	10,949	47.1	7357	18.2
Q3		2,198	18.6	15,459	48.5	9840	17.6
Q4		2,136	15.4	18,257	48.2	11025	16.6
Q5		918	5.3	8,364	17.9	14475	16.0
Q1	Males	1,258	31.6	4,674	44.3	3277	16.9
Q2		2,441	31.2	8,858	42.7	8090	20.4
Q3		3,958	37.6	12,761	45.6	10773	19.9
Q4		3,831	31.0	14291	43.3	11795	18.3
Q5		1539	9.9	7,379	17.4	15797	17.8
Case-hospitalisation (within 40 days of diagnosis)							
ID	Sex	Number	AAR	Number	AAR	Number	AAR
Q1	Females	409	17.3	1314	4.9	284	2.8
Q2		844	28.4	2772	6.2	643	2.5
Q3		1363	29.6	4340	7.1	921	2.6
Q4		1381	34.5	4389	6.2	1094	2.8
Q5		512	24.9	2197	6.5	1151	2.5
Q1	Males	854	39.3	1740	10.5	359	3.9
Q2		1843	57.9	3975	15.0	802	3.6
Q3		2975	57.5	6037	16.6	1129	3.8
Q4		2898	59.2	6101	14.4	1366	4.1
Q5		1009	38.8	2886	13.0	1583	3.8
Case-fatality (within 40 days of diagnosis)							
ID	Sex	Number	AAR	Number	AAR	Number	AAR
Q1	Females	163	2.3	766	1.2	37	0.3
Q2		292	2.7	1266	1.1	94	0.3
Q3		515	3.0	1854	1.2	213	0.5
Q4		487	3.1	2280	1.2	194	0.4
Q5		156	2.4	807	1.1	161	0.3
Q1	Males	342	3.9	813	2.2	59	0.6
Q2		749	4.9	1553	2.4	112	0.5
Q3		1252	4.9	2342	2.5	179	0.6
Q4		1228	5.0	2598	2.5	199	0.6
Q5		396	4.2	1101	2.4	266	0.6

ID = Index of deprivation; AAR = Age Adjusted Rate per 1,000,000 person-days for incidence and per 1,000 person-days for case-hospitalisations and case-fatality

\*Cases were allocated to the pre-lockdown period if they had a date of sampling/diagnosis between the 20<sup>th</sup> of February and the 16<sup>th</sup> of March, to the lockdown period if their date of sampling/diagnosis was between the 17<sup>th</sup> of March and the 24<sup>th</sup> of May and to the post-lockdown period if that date was between the 25<sup>th</sup> of May and the 15<sup>th</sup> of October. Cases were classified as hospitalized or dead if they had a date of recovery/death within 40 days of sampling/diagnosis.

### *Results from the multivariable analysis*

Table 3 shows the main results from multilevel models, the full results of the models, including the ICC, can be found in the Supplementary Material 4. After adjusting for age and sex (model 1), the incidence was lower in the municipalities belonging to the least deprived quintile. The inclusion of population density (model 2) hardly altered the results. In the full model (Model 3), after adjusting for region of residence, during the pre-lockdown period, there was not a clear socioeconomic gradient in the incidence of COVID-19. Incidence was 20% lower in municipalities belonging to the second least deprived quintile (Q2) compared with the least deprived one (Q1, IRR 0.80, 95% CI: 0.70 to 0.91); and it was 17% higher in municipalities belonging to the most deprived quintile, but not statistically significant (Q5, IRR 1.17, 95% CI: 0.98 to 1.41). During lockdown, incidence was significantly higher in the most deprived quintile (Q5, IRR: 1.14, 95% CI: 1.03 to 1.27) and in the second most deprived quintile (Q4, IRR: 1.18, 95% CI: 1.08 to 1.29) compared with the least deprived one. These differences increased during post-lockdown, when municipalities in the most deprived quintile had 47% higher incidence compared with the least deprived one (Q5, IRR: 1.47, 95% CI: 1.32 to 1.63).

The results of the models using case-hospitalisation as the dependent variable show no gradient according to deprivation after full adjustment. During the pre-lockdown, cases living in the most deprived municipalities had the lowest hospitalisation rate (IRR: 0.68, 95% CI: 0.51 to 0.92). No statistically significant differences with cases living in least deprived municipalities were observed in any other group and in any other period studied.

No differences in case-fatality rates were observed across groups during the pre-lockdown or lockdown periods after full adjustment. During the post-lockdown, compared with cases living in least deprived municipalities, case-fatality rates were higher in cases from municipalities belonging to the third quintile (Q3, IRR: 1.26, 95% CI: 0.96 to 1.66), as well as in those from the most deprived municipalities (Q4, IRR: 1.20, 95% CI: 0.90 to 1.59; Q5, IRR: 1.02, 95% CI: 0.73 to 1.41), but these differences were not statistically significant.

**Table 3. Incidence Rate Ratios (IRR) and 95% confidence interval (95% CI) of the results of the multilevel negative binomial regression analysis for the association between COVID-19 related outcomes and deprivation in Italian municipalities**

	Model 1. Adjusted for sex and age			Model 2. Adjusted for sex, age and population density			Model 3. Adjusted for sex, age, population density and region of residence		
	Pre-lockdown	Lockdown	Post-lockdown	Pre-lockdown	Lockdown	Post-lockdown	Pre-lockdown	Lockdown	Post-lockdown
<b>Incidence IRR [95%CI]</b>									
Q1 (least deprived)	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Q2	0.97 [0.83-1.14]	0.92 [0.84-1.02]	1.19 [1.09-1.29]	0.81 [0.69-0.95]	0.81 [0.73-0.89]	1.11 [1.02-1.21]	0.80 [0.71-0.91]	0.95 [0.88-1.03]	1.12 [1.03-1.21]
Q3	1.09 [0.93-1.27]	0.89 [0.80-0.98]	1.15 [1.06-1.25]	0.83 [0.71-0.97]	0.72 [0.65-0.80]	1.03 [0.95-1.13]	0.92 [0.80-1.05]	1.01 [0.93-1.09]	1.11 [1.02-1.20]
Q4	0.67 [0.57-0.78]	0.64 [0.57-0.71]	0.99 [0.91-1.08]	0.50 [0.43-0.59]	0.52 [0.47-0.58]	0.90 [0.83-0.98]	1.00 [0.87-1.16]	1.18 [1.08-1.29]	1.16 [1.06-1.27]
Q5 (most deprived)	0.21 [0.18-0.25]	0.23 [0.21-0.26]	0.85 [0.78-0.92]	0.15 [0.13-0.18]	0.18 [0.16-0.20]	0.74 [0.68-0.81]	1.17 [0.98-1.41]	1.14 [1.03-1.27]	1.47 [1.32-1.63]
<b>Case-hospitalisation (within 40 days of diagnosis) IRR [95%CI]</b>									
Q1 (least deprived)	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Q2	1.11 [0.88-1.40]	1.59 [1.32-1.91]	0.97 [0.82-1.16]	1.09 [0.86-1.38]	1.49 [1.24-1.80]	0.97 [0.81-1.15]	0.88 [0.71-1.09]	1.00 [0.85-1.16]	0.92 [0.77-1.08]
Q3	1.15 [0.92-1.44]	1.63 [1.36-1.96]	1.07 [0.90-1.27]	1.12 [0.89-1.42]	1.49 [1.24-1.80]	1.06 [0.89-1.26]	0.88 [0.71-1.09]	0.93 [0.79-1.09]	0.95 [0.81-1.13]
Q4	0.99 [0.78-1.25]	1.39 [1.15-1.67]	1.10 [0.93-1.30]	0.96 [0.75-1.23]	1.27 [1.04-1.53]	1.09 [0.92-1.29]	0.81 [0.65-1.03]	0.86 [0.73-1.03]	0.99 [0.83-1.19]
Q5 (most deprived)	0.82 [0.63-1.07]	1.58 [1.29-1.92]	1.02 [0.86-1.21]	0.80 [0.61-1.05]	1.42 [1.16-1.73]	1.01 [0.85-1.20]	0.68 [0.51-0.92]	0.89 [0.72-1.1]	0.99 [0.81-1.22]
<b>Case-fatality (within 40 days of diagnosis) IRR [95%CI]</b>									
Q1 (least deprived)	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Q2	1.03 [0.88-1.20]	1.00 [0.91-1.08]	0.93 [0.70-1.22]	1.04 [0.89-1.22]	0.97 [0.89-1.06]	0.95 [0.72-1.26]	0.96 [0.82-1.12]	0.94 [0.86-1.02]	0.94 [0.71-1.25]
Q3	1.14 [0.99-1.32]	1.04 [0.96-1.13]	1.16 [0.89-1.51]	1.15 [0.99-1.35]	1.00 [0.92-1.09]	1.21 [0.93-1.57]	1.01 [0.86-1.17]	0.94 [0.86-1.02]	1.26 [0.96-1.66]
Q4	1.22 [1.05-1.42]	1.04 [0.96-1.13]	1.17 [0.90-1.52]	1.24 [1.06-1.45]	1.00 [0.92-1.09]	1.22 [0.94-1.58]	1.06 [0.90-1.24]	0.94 [0.86-1.02]	1.20 [0.90-1.59]
Q5 (most deprived)	1.01 [0.84-1.21]	1.00 [0.91-1.10]	1.26 [0.97-1.62]	1.02 [0.85-1.23]	0.96 [0.87-1.06]	1.31 [1.01-1.70]	0.92 [0.75-1.13]	0.95 [0.85-1.07]	1.02 [0.73-1.41]

\*Random intercepts were included in the models to account for clustering of observations at the municipality level.

## Discussion

### *Statement of principal findings*

Incidence of COVID-19 did not vary according to deprivation of the municipality of residence in the pre-lockdown, but as the epidemic affected more regions of Italy during the lockdown and post-lockdown, the incidence increased more during the lockdown and decreased less during the post-lockdown in the municipalities with the greatest deprivation. On the other hand, we did not observe differences in case-hospitalization or case-fatality in any period according to deprivation of the municipality of residence.

### *Strengths and weaknesses of the study*

This is the first study analysing the relation between COVID-19 and inequalities in Italy. To the best of our knowledge, it is also the first study analysing the association between deprivation and various COVID-19 outcomes through the various epidemic periods. Using individual data allowed us to classify each case according to the variables studied and to keep the maximum possible disaggregation level, as well to adjust the analysis for several individual characteristics and contextual factors other than level of deprivation of the municipality of residence.

One of the limitations of our study is that, as we did not have an individual measure of deprivation, we could not test the interaction between deprivation at the contextual and individual levels. Another limitation is that we did not have data on the number of COVID-19 tests done by municipality, or the number of cases ascertained out of the total estimated. We know that this changed through time, thereby, the number of cases in each period should be taken with caution. We do not know if this under ascertainment was associated with deprivation and, therefore, if it acted as a confounder, particularly during the pre-lockdown and lockdown periods. Also, we measured the level of deprivation of the cases' municipality of residence. However, we do not know if cases acquired the infection in these municipalities or elsewhere. There are, also, other factors which could confound of the association between deprivation and the outcomes for which we did not have data to adjust, such as ethnicity or occupation.

Finally, deprivation is a complex concept difficult to measure. The deprivation index we used takes into account five characteristics (namely: low level of education, being unemployed, living in rent, living in crowded house, living in a single-parent family), but there may be other important components not captured by the index.

*Strengths and weaknesses in relation to other studies, discussing important differences in results*

Several studies have analysed the correlation between incidence of COVID-19 and socioeconomic indicators. The majority of those using area-level deprivation indexes as the socioeconomic measure have found higher incidence in the most deprived areas (17,33–37). Our findings suggest that, in Italy, municipality-level deprivation was only associated with incidence in the lockdown and post-lockdown periods. The finding that the association between deprivation and COVID-19 outcomes varied throughout the different epidemic periods might be explained by different epidemiological and policy factors. The first cases reported of SARS-CoV-2 infection in Europe were associated with clusters affecting, generally, young adults and linked to travel to East Asia for work related reasons (38). Infection likely spread through the social networks of these first cases during the pre-lockdown period affecting, at the initial stage, a series of municipalities in the northern region of Lombardy. None of the 11 municipalities which formed part of the first “red zone” in Italy belong to the most deprived quintile, with all but one belonging to the first 3 quintiles (39). Although the epidemic spread outside this initial “red zone”, it remained contained in the north during the pre-lockdown period and did not spread widely to other parts of the country, which could explain the lack of socioeconomic gradient observed.

During lockdown, even if due to the blanket measures implemented the epidemic kept limited to the north and centre of the country, it started to spread to a wider area and population. During this period, we observed that incidence increased more in the most deprived municipalities than in the least deprived ones. This finding coincides two previous studies carried out in the Italian region of Emilia-Romagna (11,40).

During the post-lockdown period the epidemic spread widely through the country, even though at a lower rate of infection in the population and at a much lower rate of hospitalisation and death compared with the previous period. It was in this period when we observed the largest differences in incidence between the most deprived quintile and the least deprived. It is possible that, with the spread of the epidemic, the socio-economic risk factors showed the role they play and the impact of deprivation on the epidemiology of epidemic became more apparent. These findings coincide with those reported in Germany, where it was found that initially incidence was higher in less deprived areas, but that the gradient inverted overtime, with higher incidence in more deprived areas from April to June (41); and differ from what has been observed in the UK, where, during the second wave that started in early September, incidence increased more in the least deprived areas compared with the more deprived ones (42).

There are several mechanisms that could explain the higher incidence observed in the most deprived areas after the early period of the epidemic. People living in deprived areas may be more likely to live in crowded housing, which act as a barrier to isolating effectively positive cases and increases the likelihood of the



infection being spread to other co-habitants (10,12,13); especially in a context where family transmission is the main setting of exposure (43). Equally, it has been proposed that those living in the most deprived areas are less likely to be able to work remotely (10), and that they carry out manual jobs that may increase their exposure risk compared to those living in wealthier areas (12), which could explain why incidence inequalities were higher particularly during the post-lockdown period.

It is likely that the socioeconomic pattern of COVID-19 incidence varies depending on the country. For example, seroprevalence studies in Spain and France have not found a clear correlation between income and prevalence of SARS-CoV-2 infection(19,20), but a clear inverse gradient has been found in Brazil (44).

Some studies have found higher hospitalisation and mortality rates in the most deprived areas of the UK (16,45–48), as well as in the US (18,49). These findings could reflect the known social gradient in co-morbidities and risk factors for COVID-19 severity, such as obesity, diabetes, cardiovascular disease or respiratory diseases, by which those living in the most deprived areas suffer the biggest burden. However, a study in Scotland on mortality in hospitalised patients with COVID-19 infection did not find differences in case-fatality according to deprivation in the area of residence (50). Equally, we did not find an association between the deprivation level of the municipality of residence and the risk of hospitalisation or death. One possible explanation is that, as reported in the literature, the extent of inequalities in mortality is less pronounced in southern Mediterranean countries, like Italy or Spain, than in the US or the UK (51,52). Therefore, it is possible that the factors associated with the severity of COVID-19 cases in Italy do not show a clear socioeconomic gradient and, as a consequence, the present study did not show socioeconomic differences in case-hospitalisation and case-fatality". Another possible explanation may lie in the methodological differences across studies, as there is significant heterogeneity in the indicators used to assess deprivation and the geographical areas studied. This could explain why, for example, other studies carried out in the UK and the US have not found such association (53–55).

### *Conclusions*

The COVID-19 pandemic has had a large impact on the Italian population in terms of morbidity and mortality. The impact, however, has not been homogeneous across the different population subgroups. In terms of deprivation, we found an increased incidence of COVID-19 in the most deprived municipalities during lockdown and post-lockdown. We did not find differences in case-hospitalisation rates or case-fatality rates across deprivation groups in any epidemic period.

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## **Patient involvement**

No patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans for design or implementation of the study. No patients were asked to advise on interpretation or writing up of results. There are no plans to disseminate the results of the research to study participants or the relevant patient community.

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**What is already known on this topic?**

- Several studies from the US and the UK have shown that those living in the most deprived areas may be at higher risk of infection from SARS-CoV-2, as well as to be hospitalised and die from COVID-19.
- Other studies in European countries, however, have not found an association between COVID-19 outcomes and socioeconomic status.
- The association between deprivation and COVID-19 is probably mediated by epidemiological and policy factors that may have changed throughout the different phases of the pandemic.

**What this study adds?**

- In Italy, up to October 2020, incidence of COVID-19 did not vary according to area-level deprivation in the pre-lockdown period, but increased more during the lockdown and decreased less during the post-lockdown in the most deprived areas.
- Area-level deprivation was positively associated with incidence of COVID-19 during the lockdown and post-lockdown, but not during the pre-lockdown period.
- There was no association between area-level deprivation and the risk among cases of being hospitalised or die from COVID-19.

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