Socioeconomic patterns and COVID-19 outcomes before, during and after the lockdown in Italy (2020)

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A B S T R A C T

The objective was to investigate the association between deprivation and COVID-19 outcomes in Italy during pre-lockdown, lockdown and post-lockdown periods using a retrospective cohort study with 38,534,169 citizens and 222,875 COVID-19 cases. Multilevel negative binomial regression models, adjusting for age, sex, population-density and region of residence were conducted to evaluate the association between area-level deprivation and COVID-19 incidence, case-hospitalisation rate and case-fatality. During lockdown and post-lockdown, but not during pre-lockdown, 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.

1. 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 (Riccardo et al., 2020). By the December 15, 2020 over 1,500,000 people had been diagnosed with the disease and over 60,000 had died from it (Istituto Superiore di San, 2020). 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 4th of March, primary and secondary education centres were closed, followed by a national lockdown implemented on the March 10, 2020, by which citizens were only allowed outside their homes for work -if considered essential workers- and to acquire basic need items (Consiglio dei Ministri. D, 2020; Presidenza del Consiglio, 2020a). This measure was eased on the 18th of May, when non-essential work was resumed (Presidenza del Consiglio, 2020b). The full measure was lifted, including travel restrictions between regions, on the 3rd of June. Other measures implemented during this period include the need to keep 1-m distance between people and the mandatory use of face masks indoors and in places where social distancing may not be possible (Presidenza del Consiglio, 2020a). 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 (Presidenza del Consiglio, 2020a).

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 (Grantz et al., 2016), but others have reported no differences by socioeconomic status in New Zealand during the same pandemic (Summers et al., 1918). Similarly, the impact of the 2009 pandemic influenza has been found to be higher in lower socioeconomic groups in England

(Rutter et al., 2020), but not in France (Mansiaux et al., 2015). 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 (Bambra et al., 2020; Di Girolamo et al., 2021). 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 (Bambra et al., 2020; The Health Foundation. Wi, 2020; Patel et al., 2020a). 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 crowed housing, among other factors (The Health Foundation. Wi, 2020; Patel et al., 2020a). 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 (Mamo et al., 2020). 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 (Bambra et al., 2020). Yet, the published literature shows inconsistent results (Wachtler et al., 2020). 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 (Williamson et al., 2020; Niedzwiedz et al., 2020; Nayak et al., 2020), but other studies have not found such association (Pollán et al., 2020; Carrat et al., 2020); and others have found that it is actually the wealthier groups who have been hit harder by COVID-19 (Abedi et al., 2020; Mukherji, 2020).

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.

2. Methods

2.1. 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 out 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) (Benchimol et al., 2015).

2.2. 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 (National Health Institute, 2020). 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) (Istituto Nazionale di Sta, 2020). As a measure of deprivation, we used the Italian municipality index of deprivation (Rosano et al., 2020).

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 January 1, 2020 through the Italian institute of statistics (ISTAT) (Istituto Nazionale di Sta, 2020), assuming these remained unchanged during the study period.

2.3. 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 (Rosano et al., 2020). In the analysis, we categorized 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 (Istituto Superiore di San, 2020). Population density was categorized into three levels (<54 people per km^2, 54–106 people per km^2 and >106 people per km^2).

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 10th of March and was lifted on the 18th 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 (Guan et al., 2020)-. Therefore, cases were assigned to the pre-lockdown period if they had a date of sampling/diagnosis between the February 20, 2020 and the March 16, 2020, to the lockdown period if the date was between the March 17, 2020 and the 24th of May; and to the post-lockdown if between the May 25, 2020 and the 15th of October.

2.4. Statistical analysis

The analysis was conducted using surveillance data extracted on the December 9, 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 (Minichilli et al., 2017). 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 Fig. 1), which represented 54.1 % of the total cases (ranging from 33.6 % to 91.9 % across the different regions). Cases were aggregated by 7624 municipalities, which represented a population of 38,534,169 (64.0 % of the total italian population).

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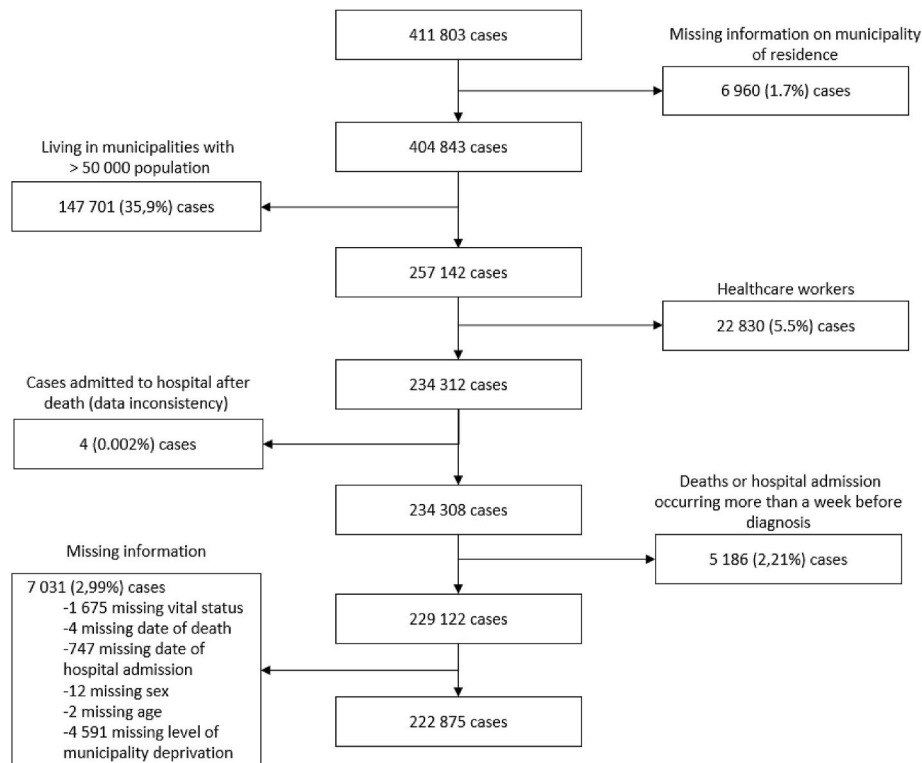
Fig. 1. Flow chart showing the selection of cases included in the analysis.

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 (Pace et al., 2013). 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 (Nakagawa et al., 2017).

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) (The, 2018; tudio Team.tudio: In, 2015). 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 February 27, 2020 (Ordinance n. 640).

3. 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.

3.1. 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 Fig. 2).

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

Table 1

Distribution (column %) 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)**
Females					
Age group					
0–49	701,820	1,493,434	2,080,147	2,475,434	3,562,867
	(49.0 %)	(51 %)	(51.6 %)	(51.7 %)	(55.3 %)
50–69	419,544	840,618	1,139,603	1,356,866	1,787,085
	(29.3 %)	(28.7 %)	(28.3 %)	(28.3 %)	(27.8 %)
70 and over	309,753	596,217	807,980	957,769	1,089,894
	(21.6 %)	(20.3 %)	(20.1 %)	(20 %)	(16.9 %)
	1,431,117	2,930,269	4,027,730	4,790,069	6,439,846
	(100.0 %)	(100.0 %)	(100.0 %)	(100.0 %)	(100.0 %)
Population density					
<54.6 ppkm2	266,933	299,537	274,120	319,201	330,982
	(18.7 %)	(10.2 %)	(6.8 %)	(6.7 %)	(5.1 %)
54.6–106 ppkm2	243,517	386,368	465,022	498,064	603,154
	(17 %)	(13.2 %)	(11.5 %)	(10.4 %)	(9.4 %)
>106 ppkm2	920,667	2,244,364	3,288,588	3,972,804	5,505,710
	(64.3 %)	(76.6 %)	(81.6 %)	(82.9 %)	(85.5 %)
	1,431,117	2,930,269	4,027,730	4,790,069	6,439,846
	(100.0 %)	(100.0 %)	(100.0 %)	(100.0 %)	(100.0 %)
Regions' grouped by geographical area					
North[1]	1,312,378	2,327,889	2,709,840	2,543,374	840,279
	(91.7 %)	(79.5 %)	(67.2 %)	(53.0 %)	(13.0 %)
Centre[2]	63,446	432,369	876,548	870,667	875,738
	(4.4 %)	(14.8 %)	(21.8 %)	(18.2 %)	(13.6 %)
South and Islands[3]	55,293	170,011	441,342	1,376,028	4,723,829
	(3.9 %)	(5.8 %)	(11 %)	(28.7 %)	(73.4 %)
	1,431,117	2,930,269	4,027,730	4,790,069	6,439,846
	(100.0 %)	(100.0 %)	(100.0 %)	(100.0 %)	(100.0 %)
Males					
Age group					
0–49	735,841	1,558,283	2,165,134	2,575,729	3,682,631
	(52.5 %)	(54.9 %)	(55.8 %)	(56.2 %)	(59.3 %)
50–69	424,539	828,766	1,107,808	1,300,344	1,689,939
	(30.3 %)	(29.2 %)	(28.6 %)	(28.3 %)	(27.2 %)
70 and over	239,932	453,733	606,423	711,007	835,029
	(17.1 %)	(16 %)	(15.6 %)	(15.5 %)	(13.5 %)
	1,400,312	2,840,782	3,879,365	4,587,080	6.207.599
	(100.0 %)	(100.0 %)	(100.0 %)	(100.0 %)	(100.0 %)
Population density					
<54.6 ppkm2	267,081	294,422	269,540	313,750	327,828
	(19.1 %)	(10.4 %)	(6.9 %)	(6.8 %)	(5.3 %)
54.6–106 ppkm2	239,837	376,023	450,146	480,715	591,378
	(17.1 %)	(13.2 %)	(11.6 %)	(10.5 %)	(9.5 %)
>106 ppkm2	893,394	2,170,337	3,159,679	3,792,615	5,288,393
	(63.8 %)	(76.4 %)	(81.4 %)	(82.7 %)	(85.2 %)
	1,400,312	2,840,782	3,879,365	4,587,080	6.207.599
	(100.0 %)	(100.0 %)	(100.0 %)	(100.0 %)	(100.0 %)
Regions' grouped by geographical area					
North[1]	1,285,354	2,261,555	2,628,251	2,435,911	808,554
	(91.8 %)	(79.6 %)	(67.8 %)	(53.1 %)	(13.1 %)
Centre[2]	61,693	413,442	828,163	830,278	846,282
	(4.4 %)	(14.6 %)	(21.3 %)	(18.1 %)	(13.6 %)
South and Islands[3]	53,265	165,785	422,951	1,320,891	4,552,763
	(3.8 %)	(5.8 %)	(10.9 %)	(28.8 %)	(73.3 %)
	1,400,312	2,840,782	3,879,365	4,587,080	6.207.599
	(100.0 %)	(100.0 %)	(100.0 %)	(100.0 %)	(100.0 %)

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

incidence was somewhat 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.

4. Results from the multivariable analysis

Table 3 shows the main results from multilevel model adjusted for sex, age, population density and region of residence. The full results of the models, including the ICC, can be found in the Supplementary Material 4. 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.

5. Discussion

5.1. 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-hospitalisation or case-fatality in any period according to deprivation of the municipality of residence.

5.2. Comparison with other studies and possible explanations

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 (Niedzwiedz et al., 2020; Disparities in the risk a, 2020; Liu et al., 2020; Ho et al., 2020; Whittle and Diaz-Artiles, 2020; Baena-Díez et al., 2020). Our findings suggest that, in Italy, municipality-level deprivation was only associated
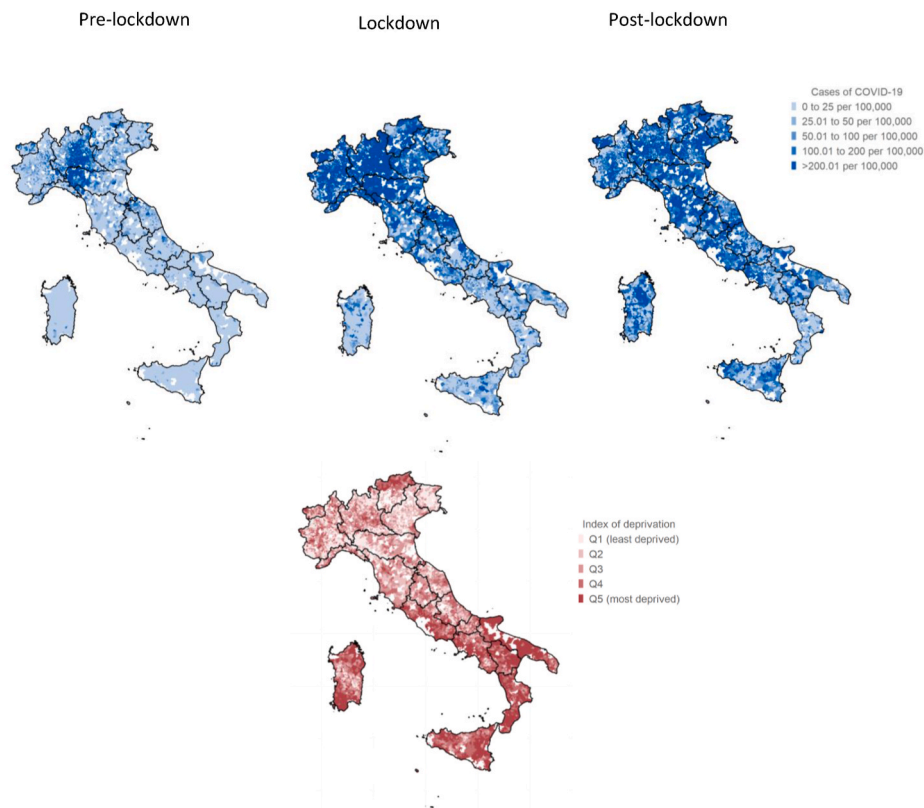
Fig. 2. Geographical distribution of the cumulative number of cases per 100,000 persons during the periods of the epidemic in Italian municipalities with less than 50,000 population (n = 7624), and distribution of quantiles of the index of deprivation.

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 (Spiteri et al., 2019). 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 (Coronavirus and firmato il D, 2020). 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 (Di Girolamo et al., 2021; Stivanello et al., 2020). On the other hand, during March 2020, the relative differences in mortality according to citizens' educational level showed greater magnitude than the differences observed in March 2019 (apporto annuale 2, 2020). This finding suggests a higher incidence of COVID-19 in people of low socioeconomic position. The higher incidence in these citizens could explain the findings observed here during the lockdown and post-lockdown, since the proportion of people of low socioeconomic position is higher in the municipalities with greater deprivation.

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 (Socioeconomic inequalitie, 2020); 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 (Office for National Stati, 2020a). 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 (Hallal et al., 2020).

There are several mechanisms that could explain the slightly 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 (Bambra et al., 2020; The Health Foundation. Wi, 2020; Patel et al., 2020a); especially in a context where family transmission is the main setting of exposure (Signorelli et al., 2020). Equally, it has been proposed that those living in the most deprived areas are less likely to be able to work remotely (Bambra et al., 2020), and that they carry out manual jobs that may increase their exposure risk compared to those living in wealthier areas (The Health Foundation. Wi, 2020), which could explain why incidence inequalities were higher particularly during the post-lockdown period. It is also possible that, as prevalence of

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		1412	16.7	10,949	47.1	7357	18.2
Q3		2198	18.6	15,459	48.5	9840	17.6
Q4		2136	15.4	18,257	48.2	11,025	16.6
Q5		918	5.3	8364	17.9	14,475	16.0
Q1	Males	1258	31.6	4674	44.3	3277	16.9
Q2		2441	31.2	8858	42.7	8090	20.4
Q3		3958	37.6	12,761	45.6	10,773	19.9
Q4		3831	31.0	14,291	43.3	11,795	18.3
Q5		1539	9.9	7379	17.4	15,797	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 1000 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 20th of February and the 16th of March, to the lockdown period if their date of sampling/diagnosis was between the 17th of March and the 24th of May and to the post-lockdown period if that date was between the 25th of May and the 15th of October. Cases were classified as hospitalized or dead if they had a date of recovery/death within 40 days of sampling/diagnosis.

chronic diseases is highest in deprived areas (Gnavi et al., 2020), people living in these municipalities are more likely to suffer from symptomatic COVID-19 and therefore seek testing than those living in the least deprived ones. Some studies have found higher hospitalisation and mortality rates in the most deprived areas of the UK (Williamson et al., 2020; Patel et al., 2020b; Rose et al., 2020; Office for National Stati, 2020b; Lone et al., 2020), as well as in the US (Nayak et al., 2020; Azar et al., 2020). 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 hospitalized patients with COVID-19 infection did not find differences in case-fatality according to deprivation in the area of residence (Khan et al., 2020a). 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 (Mackenbach et al., 2008; Regidor et al., 2015). It is also possible that inequalities in mortality for COVID-19 are mainly driven by individual socioeconomic status, or that they occur mainly in big urban areas and (Baena-Díez et al., 2020), given that we measured deprivation as a contextual variable and excluded large municipalities, that our study did not capture this pattern.

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 (Guha et al., 2020; Apea et al., 2021; Khan et al., 2020b). Further studies would help in clarifying the individual and contextual influence of deprivation on COVID-19 outcomes.

5.3. 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.

The association between deprivation and COVID-19 is complex and is likely to be influenced by contextual and individual factors. One of the limitations of our study is that we did not have an individual measure of deprivation and, thus, we could not test the interaction between deprivation at the contextual and individual levels. In any case, we included municipalities with very different population sizes. It is likely that the deprivation index represents better the context in those with smaller population than in the larger ones, where different realities may exist

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. Adjusted for sex, age, population density and region of residence.

	Pre-lockdown	Lockdown	Post-lockdown
Incidence IRR [95%CI]			
Q1 (least deprived)	Ref	Ref	Ref
Q2	0.80 [0.71–0.91]	0.95 [0.88–1.03]	1.12 [1.03–1.21]
Q3	0.92 [0.80–1.05]	1.01 [0.93–1.09]	1.11 [1.02–1.20]
Q4	1.00 [0.87–1.16]	1.18 [1.08–1.29]	1.16 [1.06–1.27]
Q5 (most deprived)	1.17 [0.98–1.41]	1.14 [1.03–1.27]	1.47 [1.32–1.63]
Case-hospitalisation (within 40 days of diagnosis) IRR [95%CI]			
Q1 (least deprived)	Ref	Ref	Ref
Q2	0.88 [0.71–1.09]	1.00 [0.85–1.16]	0.92 [0.77–1.08]
Q3	0.88 [0.71–1.09]	0.93 [0.79–1.09]	0.95 [0.81–1.13]
Q4	0.81 [0.65–1.03]	0.86 [0.73–1.03]	0.99 [0.83–1.19]
Q5 (most deprived)	0.68 [0.51–0.92]	0.89 [0.72–1.1]	0.99 [0.81–1.22]
Case-fatality (within 40 days of diagnosis) IRR [95%CI]			
Q1 (least deprived)	Ref	Ref	Ref
Q2	0.96 [0.82–1.12]	0.94 [0.86–1.02]	0.94 [0.71–1.25]
Q3	1.01 [0.86–1.17]	0.94 [0.86–1.02]	1.26 [0.96–1.66]
Q4	1.06 [0.90–1.24]	0.94 [0.86–1.02]	1.20 [0.90–1.59]
Q5 (most deprived)	0.92 [0.75–1.13]	0.95 [0.85–1.07]	1.02 [0.73–1.41]
ICC	0.522**	0.389**	0.384**

ICC: Intra Class Correlation Coefficient.

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

[**] Likelihood Ratio test < 0.05.

inside the same municipality. On the other hand, we cannot infer the findings at the individual level since we would incur the ecological fallacy bias, by assuming that socioeconomic status is homogeneous in all residents living in the same municipality. 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. During the pre-lockdown and lockdown periods, particularly, there was a limited COVID-19 testing capacity in Italy affecting to a greater extent the areas with higher incidence. It is possible that access to testing varied according to deprivation, with those living in the most deprived areas being less likely to access testing than those living in more affluent municipalities, which could confound our results towards underestimation of inequalities during these 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.

6. 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.

Declaration of competing interest

All authors declare no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.healthplace.2021.102642.

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