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Health and healthcare variables associated with Italy's excess mortality during the first wave of the COVID-19 pandemic: An ecological study



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ABSTRACT

Background: Healthcare factors have strongly influenced the propagation of COVID-19. This study aims to examine whether excess mortality during the first phase of the COVID-19 outbreak in Italy was associated with health, healthcare, demographic, and socioeconomic, provincial-level indicators.

Methods: This ecological study concerns the raw number of deaths reported from February 1 to April 30, 2020 and the mean number of deaths occurred during the same months from 2015 to 2019, per province. Information on socioeconomic factors and healthcare settings was extracted from updated databases on the Italian National Institute of Statistics (ISTAT) website. A multivariate model and four multilevel models were constructed to test the association between excess mortality and the analysed indicators across 107 Italian provinces.

Results: The hospitalization rate in long-term care wards and the cardiovascular disease mortality rate correlate positively with excess mortality (p < 0.05), while higher densities of licensed physicians and of general practitioners are associated with lower excess mortality (p < 0.05). After controlling for the COVID-19 cumulative incidence in each province, only the density of licensed physicians remains negatively associated with excess mortality (p < 0.01).

Conclusion: Some health and healthcare variables (in particular, the density of physicians) are strongly associated with excess mortality during the first wave of the COVID-19 pandemic in Italy and should be targeted to increase the resilience of health systems.

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1. Introduction

Pandemics are natural disasters that affect global health for prolonged periods [1]. Depending on their impact on healthcare systems, pandemics prompt varying degrees of public health interventions to contain the contagion. The availability of resources – in terms of staff, stuff, and structures – plays a fundamental part in expanding a healthcare system capacity to cope with the increasing demand [2]. When a healthcare system is overwhelmed, the level of care delivered to the population gradually declines until the crisis capacity threshold is reached [3]. Beyond that point, se-

vere disruptions in the chain of care affect not only infected patients but also those suffering from chronic illnesses or presenting with acute conditions that need prompt or urgent treatment, leading to a worsening of the population health.

Excess mortality is an essential epidemiological indicator to monitor the capability of healthcare systems. It gives us a comprehensive picture of the death toll attributable to a pandemic. Rapid surveillance systems can effectively track deaths due directly to the disease as well as indirect fatalities caused by the impact of a pandemic on healthcare systems [4]. The result is a better mortality estimate, less affected by errors in the certification of the cause of death, that enables before–after comparisons within the same country [5].

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As seen previously with the influenza pandemic of 1918 [6], COVID-19 has brought the healthcare systems of every country to the brink of failure. The first wave of the disease dramatically increased mortality rates across countries. Italy registered over 45,000 total deaths in March and April 2020, corresponding to an excess mortality due to any cause of 50% in March and 36% in April, compared with average deaths in the same months in the years from 2015 to 2019 [7,8]. There were marked differences between regions and provinces, with most excess deaths occurring in the north of Italy. Strict nationwide lockdown policies, which included restrictions on movement between regions from the beginning of March until early May, probably helped contain the infection and the consequent excess mortality in the country's central and southern regions [9]. The pandemic's impact on different countries and regions varied [10], but the spread of COVID-19 followed much the same trend in 24 European nations early in the first wave [11]. Social, environmental, and economic factors strongly influenced the transmission of the disease (especially in the complex scenario of the European continent [10,12]), with a far from negligible impact on cumulative excess deaths.

The present study aims to identify health, healthcare, environmental, demographic, and socioeconomic indicators associated with the province-level excess mortality during the first wave of the COVID-19 outbreak in Italy. This might reveal underlying "predisposing" factors to be considered when implementing effective policies to mitigate the effects of a pandemic.

2. Materials and methods

2.1. Context

The National Health Service (NHS) in Italy is a regionally-based healthcare system. It provides universal coverage free of charge at the point of service. The country's central government ensures compliance with the general objectives and fundamental principles of the NHS, defines a national statutory benefits package of "essential levels of care" for the population, and allocates national funds to the regional authorities. The regional governments (19 regions and two autonomous provinces) are responsible for organizing and delivering healthcare services through a network of local health authorities. The latter have catchment areas that are often defined by the boundaries of provinces (institutional entities that group together several municipalities in a given region). Depending on the region, public funds are allocated by local health authorities to public hospitals and accredited private clinics.

2.2. Study design and data sources

The present ecological study includes mortality data for each Italian province. Data on mortality were obtained from the IS-TAT demographic database [13] as the raw number of deaths from February 1 to April 30, 2020 and the mean number of deaths during the same months in the years 2015 to 2019.

Information on the provinces' socioeconomic, demographic, health, and healthcare variables was extracted from the most recently updated databases available on the Italian Ministry of Health's and ISTAT's websites [7], and the ISTAT's "Health for All" database [14]. As regards provincial COVID-19 confirmed cases and deceases, the data were drawn from the Italian Civil Protection Department's official database, which was updated daily [15]. Besides the target variable (excess mortality), the independent variables included in the analysis (75 predictive indicators: 66 at provincial level and nine at regional level) are divided into seven categories (demographic, socioeconomic, environmental, health, healthcare activity, healthcare resources, healthcare human resources) and are presented in detail in Appendix 1.

2.3. Statistical analysis

The excess mortality was first calculated for each of the 107 Italian provinces. Given the total number of deaths in February–April 2020 for each province (D_1) and the mean number of deaths during the same period in the years 2015 to 2019 (D_0), the excess mortality E_i for every province *i* was computed as the following percentage:

$$E_i = [(D_{1i} - D_{0i})/D_{0i}] \cdot 100$$

The Pearson correlation coefficient was then calculated for each pair of the 75 analysed predictive indicators, both at provincial and regional level, to inspect collinearity. The obtained correlation matrix is depicted in Fig. 1. Setting a maximum Pearson's coefficient threshold to 0.8 in absolute value, the highly correlated indicators were dropped as redundant variables, comparing firstly the indicators falling into the same category (e.g., health, socioeconomic variables, etc.).

At a second stage, considering only the indicators at the provincial level, the least absolute shrinkage and selection operator (LASSO) method was adopted to select the most relevant predictors to include in the analysis. Firstly, the optimum shrinkage parameter λ was determined by performing a 10-fold cross-validation. Then, the more relevant covariates were determined as the variables with a LASSO regression coefficient >0.05 in absolute terms. Subsequently, a univariate linear model was constructed for each of the returned predictors to estimate the effect of each predictor with the outcome.

The following nine provincial variables regarding healthcare, health, and socioeconomic indicators were selected:

- local public transport facility availability: the number of buses and metro facilities per person;
- acquired immunodeficiency syndrome (AIDS) mortality rate: number of deaths due to AIDS per 10,000 people;
- cardiovascular disease mortality rate: number of deaths due to cardiovascular diseases per 10,000 people;
- tuberculosis mortality rate: number of deaths due to tuberculosis per 10,000 people;
- long-term care hospitalization rate: number of hospital admissions in long-term care wards per 1,000 people;
- average density of long-term care beds in private hospitals: number of private hospitals long-term care beds in per 10,000 people;
- average density of long-term care beds in public and private hospitals: number of public and private hospitals long-term care beds in per 10,000 people;
- average density of physicians licensed to practise: number of doctors (both practising and non-practising) registered with the National Board of Physicians per 10,000 people;
- average density of GPs: number of GPs per 1,000 people.

Five different multivariate models were developed to analyse the association of excess mortality with the previously described factors. First, a simple multivariate regression model was developed which considered the nine most relevant indicators at provincial level against the excess mortality (Model 1). Then, a multilevel generalization of the previous model was tested, with the region considered as a grouping variable and a random intercept introduced for each Italian region (Model 2). Subsequently, as the regional effect was significant, Model 3 was implemented, introducing the following seven indicators which were available only at the regional level (two regional indicators were not considered to be highly correlated):

 relative poverty index: percentage of individuals that have a consumption expenditure below the poverty line (individuals



Fig. 1. Correlation matrix of the analysed indicators sorted by category.

with a consumption expenditure level lower than 50% of the mean per-capita consumption expenditure);

- average density of hypertensive subjects aged 65 or more: number of hypertensive subjects aged 65 or more per 1,000 people;
- population rate with at least one chronic disease: number of subjects with at least one chronic disease per 1,000 people;
- respiratory system and intrathoracic organs malignant cancer mortality rate: number of deaths due to respiratory system and intrathoracic organs malignant cancers per 1,000 people;
- ischaemic heart disease mortality rate: number of deaths due to ischaemic heart disease per 1,000 people;
- respiratory system disease mortality rate: number of deaths due to respiratory system diseases per 1,000 people;
- COPD mortality rate: number of deaths due to chronic obstructive pulmonary disease (COPD) per 1,000 people.

Finally, the province's COVID-19 cumulative incidence on 30 April 2020 (COVID-19 confirmed cases per 10,000 people) was computed and included in the analysis. Since this indicator measures the rate of COVID-19 spread in each province, we can expect it to capture most of the variability in the outcome, enabling us to understand the role of the other covariates independently of the

effect of spread of infection on excess mortality risk factors. In this way, it was also possible to represent the different rates of transmission of the infection between different areas. Models 4 and 5 are the adjusted version of Models 2 and 3, respectively, where the cumulative incidence is added as a covariate.

For all the presented models, it is worth mentioning that the response variable was log-transformed prior to the fitting in order to normalize its originally skewed distribution and produce more reliable estimates. This operation turned out to improve the models' performance scores in terms of residual standard error (RSE) or (for Model 1 only) adjusted R².

The data analysis was performed with RStudio statistical software (RStudio, Inc., Boston).

3. Results

In the period considered, excess mortality ranged from -11.59% (for Cagliari, a province of southern Sardinia) to 237.30% (for Bergamo, in the Lombardy region of northern Italy), with a mean value of 27.58% and a median of 12.31% across Italy as a whole. The five provinces with the highest excess mortality are all in Northern Italy: four in Lombardy, and one (Piacenza) in the Emilia-Romagna region on Lombardy's southern border, while the five with the low-

Excess mortality by Provinces



Fig. 2. Choropleth map representing excess mortality by province.

est excess mortality are scattered between the centre, south, and islands. Fig. 2 shows how the excess mortality is distributed across the Italian territory.

Table 1 shows the descriptive statistics for the selected predictive indicators, 10 at provincial level and seven at regional level.

Table 2 shows the estimates of the designed models. The first column reports the regression coefficients of the univariate linear model for all the indicators selected with the LASSO method, while the other columns report the coefficients of the five multivariate models.

In Model 1, the multivariate analysis with the nine LASSOselected province-related indicators, the hospitalization rate in long-term care wards is positively associated with excess mortality (0.108, p value <0.001), while the density of GPs, as well as the density of physicians licensed to practise, is negatively associated with the outcome (respectively -1.578, -0.013; p values 0.022 and <0.001). Model 2 – the multilevel version of the previous model with the region as a grouping variable - shows similar results to those of Model 1. Therefore, it seems that the introduction of the regional random effect does not affect the association of the indicators under study, even if it results in a lower RSE (0.487). The estimation results of Model 3 confirm the significant negative correlation between the density of GPs and physicians licensed to practice and excess mortality (respectively 1.702, -0.009; p values <0.05). After introducing the additional regional indicators (with Model 3), the hospitalization rate in long-term care wards is no longer significant, while the cardiovascular disease mortality rate correlates significantly with the outcome variable (0.019; p value 0.048). Moreover, it is worth noting that both the regional poverty index and other health variables at the regional level are not significant in explaining excess mortality. Finally, Models 4 and 5 adjusted versions of Models 2 and 3, respectively, after controlling for the rate at which COVID-19 spread in each province – show, as expected, a strongly significant positive association between excess mortality and a province's COVID-19 cumulative incidence (0.016, 0.015, respectively; p value <0.001). In both these models, only the density of physicians licensed to practice is confirmed to be significant in explaining the excess mortality (p value <0.01), while, once again, the hospitalization rate in long-term care wards appears significantly (and positively) associated with the outcome variable only when additional covariates at regional level are not considered (Model 4; p value <0.10).

4. Discussion

Since the outbreak of COVID-19 in Europe, strict public health measures have gradually been introduced to contain the contagion. Decision-makers have mainly relied on daily updates regarding new cases of COVID-19, COVID-19 mortality, the numbers of those infected being admitted to general wards and intensive care units, and the number of patients who have recovered. Unfortunately, the under-reporting of cases has hindered the proper interpretation of these data. On the other hand, excess mortality can be more useful in describing pandemic trends in relation to other variables affecting local and national health systems [16].

This ecological study found that some health and healthcare variables were associated with excess mortality at a provincial level during the first wave of the COVID-19 outbreak in Italy (February–April 2020). Our analysis confirmed that most excess deaths occurred in northern provinces in or adjacent to Lombardy, the region most overwhelmed by the pandemic [9].

The results that emerged from our analysis show that, overall, the availability of physicians in the various provincial territories

Table 1

Descriptive statistics for the explanatory variables included in the models.

Variable	Minimum	Maximum	Mean	Median	Standard Deviation	Interquartile Range
Local public transport facility availability	14.460	210.060	70.960	67.280	36.880	45.108
AIDS mortality rate	0.000	0.270	0.065	0.060	0.051	0.070
Cardiovascular disease mortality rate	19.410	60.100	41.350	42.230	6.986	9.458
Tuberculosis mortality rate	0.000	0.060	0.045	0.040	0.040	0.050
Hospitalization rate in long-term care wards	0.000	34.410	7.112	6.340	5.093	6.358
Density of long-term care beds in private hospitals	0.000	11.630	2.671	1.885	2.525	3.753
Density of long-term care beds in hospitals	0.000	30.520	5.590	4.975	4.165	4.543
Physicians registered with the National Board of Physicians per 10,000 people	34.220	160.880	63.480	59.120	18.498	21.615
GPs per 1,000 people	0.700	1.300	0.936	0.900	0.116	0.1
Provincial COVID-19 cumulative incidence on 30 April 2020	2.688	169.565	34.496	21.174	32.285	44.849
Relative poverty index	5.600	34.600	14.720	10.200	8.495	14.350
No. of hypertensive subjects aged 65 or more per 1,000 people	400.100	543.400	483.800	488.200	39.614	50.965
Population with at least one chronic disease per 1,000 people	118.600	202.400	157.700	162.000	14.814	17.460
Respiratory system and intrathoracic organs malignant cancer mortality rate	4.400	8.380	6.086	6.160	0.941	1.345
Ischaemic heart disease mortality rate	8.450	17.060	11.380	10.580	1.863	1.700
Respiratory system disease mortality rate	6.260	12.060	9.082	8.780	1.346	1.970
COPD mortality rate	2.810	6.210	4.370	4.530	0.659	0.590
	Variable Local public transport facility availability AIDS mortality rate Cardiovascular disease mortality rate Tuberculosis mortality rate Hospitalization rate in long-term care wards Density of long-term care beds in private hospitals Density of long-term care beds in hospitals Density of long-term care beds in hospitals Physicians registered with the National Board of Physicians per 10,000 people GPs per 1,000 people Provincial COVID-19 cumulative incidence on 30 April 2020 Relative poverty index No. of hypertensive subjects aged 65 or more per 1,000 people Population with at least one chronic disease per 1,000 people Respiratory system and intrathoracic organs malignant cancer mortality rate Ischaemic heart disease mortality rate Respiratory system disease mortality rate COPD mortality rate	VariableMinimumLocal public transport facility availability14.460AIDS mortality rate0.000Cardiovascular disease mortality rate19.410Tuberculosis mortality rate0.000Hospitalization rate in long-term care wards0.000Density of long-term care beds in private hospitals0.000Density of long-term care beds in hospitals0.000Physicians registered with the National Board of Physicians per 10,000 people34.220CPs per 1,000 people0.700Provincial COVID-19 cumulative incidence on 30 April 20202.688Relative poverty index5.600No. of hypertensive subjects aged 65 or more per 1,000 people118.600Population with at least one chronic disease per 1,000 people118.600Respiratory system and intrathoracic organs malignant cancer mortality rate4.400Ischaemic heart disease mortality rate8.450Respiratory system disease mortality rate2.260COPD mortality rate2.810	VariableMinimumMaximumLocal public transport facility availability14.460210.060AIDS mortality rate0.0000.270Cardiovascular disease mortality rate19.41060.100Tuberculosis mortality rate0.0000.060Hospitalization rate in long-term care wards0.00034.410Density of long-term care beds in private hospitals0.00031.630Density of long-term care beds in hospitals0.00030.520Physicians registered with the National Board of Physicians per 10,000 people34.220160.880CPs per 1,000 people0.7001.300Provincial COVID-19 cumulative incidence on 30 April 20202.688169.565Relative poverty index5.60034.600No. of hypertensive subjects aged 65 or more per 1,000 people118.600202.400Respiratory system and intrathoracic organs malignant cancer mortality rate8.45017.060Respiratory system disease mortality rate6.26012.0602.060COPD mortality rate2.8106.2101.000	VariableMinimumMaximumMeanLocal public transport facility availability14.460210.06070.960AIDS mortality rate0.0000.2700.065Cardiovascular disease mortality rate19.41060.10041.350Tuberculosis mortality rate0.0000.0600.045Hospitalization rate in long-term care wards0.00034.4107.112Density of long-term care beds in private hospitals0.00034.220160.880Optimizer rate beds in hospitals0.00030.5205.590Physicians registered with the National Board of Physicians per 10,000 people34.220160.88063.480GPs per 1,000 people0.7001.3000.936Provincial COVID-19 cumulative incidence on 30 April 20202.688169.56534.496Relative poverty index5.60034.60014.720No. of hypertensive subjects aged 65 or more per 1,000 people118.600202.400157.700Respiratory system and intrathoracic organs malignant cancer mortality rate8.45017.06011.380Respiratory system disease mortality rate6.26012.0609.082COPD mortality rate2.8106.2104.370	Variable Minimum Maximum Mean Median Local public transport facility availability 14.460 210.060 70.960 67.280 AIDS mortality rate 0.000 0.270 0.065 0.060 Cardiovascular disease mortality rate 19.410 60.100 41.350 42.230 Tuberculosis mortality rate 0.000 0.060 0.045 0.040 Hospitalization rate in long-term care wards 0.000 34.410 7.112 6.340 Density of long-term care beds in private hospitals 0.000 30.520 5.590 4.975 Physicians registered with the National Board of Physicians per 10,000 people 34.220 160.880 63.480 59.120 GPs per 1,000 people 0.700 1.300 0.936 0.900 Provincial COVID-19 cumulative incidence on 30 April 2020 2.688 169.565 34.496 21.174 Relative poverty index 5.600 34.600 14.720 10.200 No. of hypertensive subjects aged 65 or more per 1,000 people 118.600 202.400 157.700 162.000	Variable Minimum Maximum Mean Median Standard Deviation Local public transport facility availability 14.460 210.060 70.960 67.280 36.880 AIDS mortality rate 0.000 0.270 0.065 0.060 0.051 Cardiovascular disease mortality rate 19.410 60.100 41.350 42.230 6.986 Tuberculosis mortality rate 0.000 0.060 0.045 0.040 0.040 Hospitalization rate in long-term care wards 0.000 34.410 7.112 6.340 5.093 Density of long-term care beds in private hospitals 0.000 30.520 5.590 4.975 4.165 Physicians registered with the National Board of Physicians per 10,000 people 34.220 160.880 63.480 59.120 18.498 GPs per 1,000 people 0.700 1.300 0.936 0.900 0.116 Provincial COVID-19 cumulative incidence on 30 April 2020 2.688 169.565 34.496 21.174 32.285 Relative poverty index 5.600 34.600

Table 2

egression coefficients for variables explaining excess mortality.

	Variable	Univariate Model	Model 1 Multivariate model	Model 2 Multilevel model	Model 3 Multilevel model with regional indicators	Model 4 Incidence adjusted Multilevel model	Model 5 Incidence adjusted Multilevel model with regional indicators
Province							
	Local public transport facility availability	0.244 (0.022)	0.002 (0.320)	0.001 (0.356)	0.001 (0.375)	0.00002 (0.992)	-0.00002 (0.986)
	AIDS mortality rate	249.892 (0.001)	0.990 (0.423)	0.161 (0.888)	0.196 (0.870)	-0.128 (0.889)	0.174 (0.860)
	Cardiovascular disease mortality rate	-1.692 (0.003)	0.006 (0.500)	0.015 (0.094)	0.019 (0.048)	0.006 (0.338)	0.012 (0.140)
	Tuberculosis mortality rate	271.621 (0.006)	1.407 (0.363)	1.171 (0.383)	1.117 (0.412)	-0.140 (0.900)	0.113 (0.922)
	Hospitalization rate in long-term care wards	3.656 (<0.001)	0.108 (<0.001)	0.066 (0.022)	0.047 (0.124)	0.039 (0.090)	0.033 (0.187)
	Density of long-term care beds in private hospitals	4.327 (0.006)	-0.045 (0.174)	-0.034 (0.267)	-0.032 (0.318)	-0.031 (0.210)	-0.032 (0.218)
	Density of long-term care beds in hospitals	3.139 (<0.001)	-0.041 (0.227)	-0.025 (0.415)	-0.015 (0.636)	-0.011 (0.659)	-0.008 (0.755)
	Physicians registered with the National Board of Physicians per 10,000	-0.645 (0.002)	-0.013 (<0.001)	-0.010 (0.002)	-0.009 (0.013)	-0.009 (0.001)	-0.008 (0.008)
	people						
	GPs per 1,000 people	-175.835 (<0.001)	-1.578 (0.022)	-1.758 (0.014)	-1.702 (0.036)	-0.169 (0.761)	-0.520 (0.425)
	Provincial COVID-19 cumulative incidence on 30 April 2020	1.086 (<0.001)	-	-	-	0.016 (<0.001)	0.015 (<0.001)
Region							
	Relative poverty index	-1.670 (<0.001)	-	-	-0.025 (0.365)	-	-0.012 (0.503)
	No. of hypertensive subjects aged 65 or more per 1,000 people	-0.200 (0.045)	-	-	-0.002 (0.632)	-	-0.0002 (0.904)
	Population with at least one chronic disease per 1,000 people	-0.932 (<0.001)	-	-	-0.003 (0.745)	-	0.0003 (0.955)
	Respiratory system and intrathoracic organs malignant cancer mortality rate	9.200 (0.028)	-	-	-0.124 (0.405)	-	-0.082 (0.386)
	Ischaemic heart disease mortality rate	-5.581 (0.008)	-	-	-0.034 (0.627)	-	-0.008 (0.853)
	Respiratory system disease mortality rate	-0.478 (0.872)	-	-	-0.048 (0.801)	-	-0.082 (0.485)
	COPD mortality rate	-17.031 (0.004)	-	-	0.176 (0.522)	-	0.111 (0.520)
	adjR ²	-	0.473	-	-	-	-
	RSE	-	0.588	0.487	0.485	0.407	0.409

proved to be an important protective factor in limiting excess mortality.

In particular, Models 1, 2, and 3 show that a higher density of GPs was significantly associated with a lower COVID-19 excess mortality. This indicator could be seen as a measure of the accessibility of primary care. Its negative association with the outcome variable suggests that provinces with fewer GPs per 1,000 people may have experienced a higher COVID-19 excess mortality because GPs faced an excessive workload at the onset of the pandemic, making them less able to meet their patients' needs. Primary care plays a crucial role in minimizing the burden of COVID-19 cases in hospitals. GPs can help prevent healthcare system overload, but they need appropriate engagement and training to work effectively as gatekeepers to acute care facilities [17]. Primary care services should have response mechanisms and systems in place well before there is widespread community transmission to ensure the continued availability of services and enable a rapid upscaling of services as required. People exposed to COVID-19 and seeking a test or medical advice may have had great difficulty accessing primary care. When people cannot access a primary care provider for routine or COVID-19-related care, they may flood emergency departments and urgent care facilities, contributing to overwhelming the hospital system and potentially increasing the transmission of COVID-19. Besides, patients with complex medical needs (such as multiple chronic conditions, functional limitations, and other health issues) may have been told only to seek care for urgent problems, but their delayed management may have worsened their condition. Several policies could help primary care to build capacity in the short term and mitigate the effects of future crises. For instance, policymakers can help primary care providers develop an adequate telehealth infrastructure and offer them fair reimbursement. A more robust and better-functioning primary care system is now needed more than ever to save lives in an increasingly daunting health crisis [18].

Models 4 and 5 include the provincial COVID-19 cumulative incidence, an indicator which represents a measure of different rates of COVID-19 transmission across Italian provinces and captures most of the variability in excess mortality at provincial level. After controlling for the COVID-19 cumulative incidence in each province, the density of GPs loses its significance in explaining a lower excess mortality. This result may be explained by the specific role played by GPs in preventing patients' risk of contracting the COVID-19 disease. Primary care, as stated by the World Health Organization (WHO), plays a significant role in gatekeeping and clinical responses by differentiating patients with respiratory symptoms from those with COVID-19, making an early diagnosis, helping vulnerable people cope with their anxiety about the virus, strengthening risk communication and community engagement, maintaining delivery of essential health services, and reducing the demand for hospital services [19-21].

Models 4 and 5 nonetheless confirm the significance of the density of physicians registered with the National Board as an explanatory variable. The available literature exploring possible relationships between physician density and population mortality draws different conclusions, ranging from negative connections to lack of association [22]. One of the most frequently proposed explanations for this inconsistency is the lack of disease-specific analysis. Similarly to our work, Xie and coll [23]. and Tchicaya and coll [24]. focused on COVID-19, finding a negative association between the availability of medical personnel and mortality in Hubei province in China and France, respectively. It is worth noting that the density of doctors indicator includes both practising and nonpractising physicians who were registered and entitled to practise as healthcare professionals. In particular, the availability of physicians licensed to practise but who, for various reasons (e.g., retirement or unemployment) were not active before the COVID-19 pandemic appears to have been an important factor in containing excess mortality. This evidence seems to indicate that those provinces with a larger pool of inactive licensed doctors may have had less difficulty in rapidly activating the extraordinary procedures adopted by the Italian NHS, from March 2020, for the recruitment of medical personnel (e.g., through the recall of doctors who had just retired) to deal with the COVID-19 emergency during the first wave and that this this may have proved an important factor in limiting excess mortality. Such a conclusion corroborates the need to increase staff, along with stuff and structures, to ensure that healthcare systems have the necessary capability to manage the overwhelming number of patients during pandemics [25].

Considering only the multivariate models which do not include regional indicators (Models 1, 2, and 4), the long-term care hospitalization rate is significantly and positively associated with excess mortality. This result may mean that, even after controlling for the rate of COVID-19 transmission across provinces (with Model 4), excess mortality still remained associated with the rates of elderly patients admitted to long-term care wards. Such patients are typically frailer (owing to pre-existing conditions and chronic diseases, or specific rehabilitation needs) and at substantial risk of dying once infected, as are nursing home residents [26]. This factor contributed to the excess mortality seen in several European countries during the first wave of COVID-19, when specific measures to control the spread of the disease (personal protective equipment, proper isolation of infected cases, and training of personnel on infectious disease management) were poor, and the likelihood of nosocomial transmission of COVID-19 was still high [27]. Moreover, even if they were not infected with COVID-19, patients in long-term care settings had to be abruptly isolated, losing contact with families and caregivers. Such a situation may have led to depression and a decline in their psychological and physical health [28]. Solutions targeting these specific issues and ways to improve the community health training of long-term care personnel and administrators should be investigated in the future. From this perspective, it also appears vital to strengthen primary care services. There are currently too few intermediate services (community hospitals and rehabilitation facilities), home care services, and telecare solutions in Italy to cope with the needs of the frail elderly, which often leads to inappropriate admissions to acute care hospitals. The hospitalization rate in long-term care wards loses its significance as an explanatory variable in Models 3 and 5, which include further regional indicators, probably because these models include variables on the regional prevalence of pathologies typical of patients admitted to long-term wards. This observation is also supported, to some extent, by the evidence that Model 3 shows a significant and positive correlation between the cardiovascular disease mortality rate and the variable of interest.

Moreover, our analysis does not find a significant correlation between socioeconomic variables (in particular the poverty index at regional level included in Models 3 and 5) and excess mortality. This may stem from the fact that, within health systems characterized by universal coverage of the population, socioeconomic factors (capturing economic interactions and levels of deprivation) tend to be more significantly related to COVID-19 incidence than to excess mortality [12,29], while health and healthcare variables could become more relevantly associated with excess mortality directly and indirectly caused by COVID-19 across territories.

4.1. Limitations

The main limitation of this study lies in the relatively small number of provinces taken into consideration, which could lend a low power to the statistical analyses. Moreover, our findings only regard the Italian context and may not hold for other countries. Another possible shortcoming of the adopted approach is that, due to the lack of available data, our analysis was able to consider intra-regional influences but could not represent inter-regional interactions, especially between adjoining provinces. Finally, it is worth mentioning that any correlation emerging from ecological studies does not necessarily imply causality between two events. In fact, in health services research, where healthcare organizations rather than individual patients are often the focus of inquiry, ecological studies are often an appealing tool. Nevertheless, the ecological study aimed only to generate hypotheses exploring associations between one or more variables and a specific health outcome; the results need to be confirmed with high validity observational studies, conducted at individual level, or experimental studies.

5. Conclusions

This ecological study indicates that some health and healthcare variables were strongly associated with the excess mortality caused directly and indirectly by the COVID-19 outbreak in Italy during the first wave of the pandemic (February–April 2020). These variables may be seen as drivers behind the spatially uneven spread of COVID-19, with most excess deaths occurring in some parts of northern Italy. They should be taken into account when implementing effective mitigation policies and making health systems more resilient to COVID-19 and other crises by reshaping the organization of healthcare resources and services.

Our results suggest that knowing more about different territories' susceptibility to the diffusion of viruses (which is linked to their propensity for prevention) may help the preparation of locally-tailored mitigation strategies in countries like Italy, which are characterized by a marked heterogeneity across local communities.

Our findings also provide important input for the design of policies aiming to improve a health system's resilience by drawing on the Italian NHS's experience during the first wave of COVID-19. This study shows that the excess mortality due to COVID-19 may have been fuelled by limited response capacity on the part of primary and community care and, in particular, by a shortage in the density of physicians. These issues seem particularly relevant in the case of the Italian NHS, which has seen reduced investment in primary and community care, a rapid ageing of the medical workforce, and a long period of constraints on the dynamics of personnel recruitment, with a shortage of specialist physicians, in particular, in some areas [30]. Therefore, it seems crucial to readjust the balance in the allocation of resources, strengthen the areas of primary and community healthcare, and plan an adequate supply of medical personnel for future years.

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Data availability

Data used in this study are available on the referenced public datasets.

Declaration of Competing Interest

The authors declare no conflicts of interest.

CRediT authorship contribution statement

Alessandra Buja: Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing original draft, Writing - review & editing. Matteo Paganini: Writing – original draft, Writing – review & editing. Riccardo Fusinato: Formal analysis, Investigation. Claudia Cozzolino: Data curation, Formal analysis, Investigation. Silvia Cocchio: Data curation, Formal analysis, Investigation. Manuela Scioni: Data curation, Formal analysis, Investigation. Vincenzo Rebba: Data curation, Funding acquisition, Resources, Supervision, Validation, Writing - original draft, Writing - review & editing. Vincenzo Baldo: Funding acquisition, Resources, Supervision, Validation, Writing - original draft, Writing - review & editing. Giovanna Boccuzzo: Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.healthpol.2022.03.002.

References

- Hick JL, Einav S, Hanfling D, Kissoon N, Dichter JR, Devereaux AV, et al. Surge capacity principles. Chest 2014;146(4) e1S-e16S. doi:10.1378/chest.14-0733.
- [2] Kaji A, Koenig KL, Bey T. Surge capacity for healthcare systems: a conceptual framework. Acad Emerg Med 2006;13(11):1157–9. doi:10.1197/j.aem.2006.06. 032.
- [3] Hick JL, Barbera JA, Kelen GD. Refining surge capacity: conventional, contingency, and crisis capacity. Disaster Med Public Health Prep 2009;3(S1):S59–67. doi:10.1097/DMP.0b013e31819f1ae2.
- [4] Vestergaard LS, Nielsen J, Krause TG, Espenhain L, Tersago K, Bustos Sierra N, et al. Excess all-cause and influenza-attributable mortality in Europe, December 2016 to February 2017. Eurosurveillance 2017;22(14). doi:10.2807/ 1560-7917.ES.2017.22.14.30506.
- [5] Beaney T, Clarke JM, Jain V, Golestaneh AK, Lyons G, Salman D, et al. Excess mortality: the gold standard in measuring the impact of COVID-19 worldwide? J R Soc Med 2020;113(9):329–34. doi:10.1177/0141076820956802.
- [6] Schoch-Spana M. Hospital's full-up": the 1918 influenza pandemic. Public Health Rep 2001;116(2_suppl):32-3. doi:10.1093/phr/116.52.32.
- [7] Statistiche istat; 2020. [citato 15 dicembre 2020]Accessed: December 15Available at: http://dati.istat.it/Index.aspx .
- [8] Alicandro G, Remuzzi G, La Vecchia C. Italy's first wave of the COVID-19 pandemic has ended: no excess mortality in May, 2020. Lancet 2020;396(10253):e27–8. doi:10.1016/S0140-6736(20)31865-1.
- [9] Scortichini M, Schneider Dos Santos R, De' Donato F, De Sario M, Michelozzi P, Davoli M, et al. Excess mortality during the COVID-19 outbreak in Italy: a two-stage interrupted time-series analysis. Int J Epidemiol 2021;49(6):1909– 17. doi:10.1093/ije/dyaa169.
- [10] Kapitsinis N. The underlying factors of the COVID-19 spatially uneven spread. Initial evidence from regions in nine EU countries. Reg Sci Policy Pract 2020;12(6):1027-45. doi:10.1111/rsp3.12340.
- [11] Vestergaard LS, Nielsen J, Richter L, Schmid D, Bustos N, Braeye T, et al. Excess all-cause mortality during the COVID-19 pandemic in Europe preliminary pooled estimates from the EuroMOMO network, March to April 2020. Eurosurveillance 2020;25(26). doi:10.2807/1560-7917.ES.2020.25.26.2001214.
- [12] Buja A, Paganini M, Cocchio S, Scioni M, Rebba V, Baldo V. Demographic and socio-economic factors, and healthcare resource indicators associated with the rapid spread of COVID-19 in Northern Italy: an ecological study. PLoS ONE 2020;15(12):e0244535. doi:10.1371/journal.pone.0244535.
- [13] Mappe, Popolazione, Statistiche Demografiche dell'ISTAT. Accessed: December 15, 2020. Available at: http://demo.istat.it/.
- [14] Health for all Italia. Accessed: December 15, 2020. Available at: https://www.istat.it/it/archivio/14562.
- [15] Italian civil protection contagion rates. Accessed January 21, 2020. Available from: https://github.com/pcm-dpc/COVID-19/tree/master/dati-province.
- [16] Woolf SH, Chapman DA, Sabo RT, Weinberger DM, Hill L. Excess deaths from COVID-19 and other causes, March-April 2020. JAMA 2020;324(5):510–13. doi:10.1001/jama.2020.11787.

- [17] European Centre for Disease Prevention and Control Guidance for health system contingency planning during widespread transmission of SARS-CoV-2 with high impact on healthcare; 2021. Accessed: January 15Available at: https://www.ecdc.europa.eu/en/publications-data/guidance-health-systemcontingency-planning-during-widespread-transmission-sars.
- contingency-planning-during-widespread-transmission-sars.
 [18] Lewis, C., Shah, T., Seervai, S., Abrams, M.K., Zephyrin, L. Primary care and the COVID-19 pandemic. The Commonwealth Fund, 2020. Accessed January 15, 2021. Available at: https://www.commonwealthfund.org/blog/2020/primary-care-and-covid-19-pandemic.
- [19] WHO. Role of primary care in the COVID-19 response. Interim guidance. 2020.
- [20] Rust G, Melbourne M, Truman BI, Daniels E, Fry-Johnson Y, Curtin T. Role of the primary care safety net in pandemic influenza. Am J Public Health 2009;99:S316–23.
- [21] Lee A, Chuh AA. Facing the threat of influenza pandemic roles of and implications to general practitioners. BMC Public Health 2010;10(1):1–7.
- [22] Chen BK, Jindal D, Yang YT, Hair N, Yang CY. Associations between physician supply levels and amenable mortality rates: an analysis of Taiwan over nearly 4 decades. Health Serv Insights 2020;13:1178632920954878 Published 2020 Sep 10. doi:10.1177/1178632920954878.
- [23] Xie L, Yang H, Zheng X, Wu Y, Lin X, Shen Z. Medical resources and coronavirus disease (COVID-19) mortality rate: evidence and implications from Hubei province in China. PLoS ONE 2021;16(1):e0244867 Published 2021 Jan 15. doi:10.1371/journal.pone.0244867.
- [24] Tchicaya A, Lorentz N, Leduc K, de Lanchy G. COVID-19 mortality with regard to healthcare services availability, health risks, and socio-spatial factors at department level in France: a spatial cross-sectional analysis. PLoS ONE 2021;16(9):e0256857 Published 2021 Sep 17. doi:10.1371/journal.pone. 0256857.

- [25] Kelen GD, McCarthy ML. The science of surge. Acad Emerg Med 2006;13(11):1089–94. doi:10.1197/j.aem.2006.07.016.
- [26] Lombardo FL. Adverse events in Italian nursing homes during the COVID-19 epidemic: a national survey. Front Psychiatry 2020;11:9 DOI:. doi:10.3389/ fpsyt.2020.578465.
- [27] European Centre for Disease Prevention and Control Rapid risk assessment: increase in fatal cases of COVID-19 among long-term care facility residents in the EU/EEA and the UK; 2021. Accessed: January 21Available at: https://www.ecdc.europa.eu/en/publications-data/rapid-risk-assessmentincrease-fatal-cases-covid-19-among-long-term-care-facility.
- [28] Meng R, Yu C, Liu N, He M, Lv J, Guo Y, et al. Association of depression with all-cause and cardiovascular disease mortality among adults in China. JAMA Netw Open 2020;5(2):e1921043 3. doi:10.1001/jamanetworkopen.2019.21043.
- [29] Gangemi S, Billeci N, Tonacci A. Rich at risk: socio-economic drivers of COVID-19 pandemic spread. Clin Mol Allergy 2020;18:12 Doi:. doi:10.1186/ s12948-020-00127-4.
- [30] Cicchetti A, Giorgio L, Di Paolo MG, Daugbjerg SB, Laurita R, Morandi F, et al. Sustainability and resilience in the Italian health system. The London School of Economics and Political Science Partnership for Health System Sustainability and Resilience; 2021. Report, March.