



Coronavirus Disease Mortality: Understanding Regional Differences

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ABSTRACT

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Since the emergence of the coronavirus disease (COVID-19) pandemic, the world has struggled to contain it and deal with the increasing number of deaths. There have been reported variations in the incidence, prevalence, and fatality rates. These variations were thought to be multifactorial rather than due solely to unique characteristics or interventions. This work reviews data publicly available regarding COVID-19 and discusses the possible reasons for the regional variabilities of prevalence and mortality.

Keywords: COVID-19, SARS-CoV-2, disparity, mortality

INTRODUCTION

Since the emergence of the coronavirus disease (COVID-19) pandemic, the world has struggled to contain it and deal with the increasing number of deaths (1). There have been reported variations in the incidence, prevalence, and case fatality rates (2, 3). These variations were thought to be multifactorial rather than due solely to unique characteristics or interventions. This work reviews data publicly available regarding COVID-19 and discusses the possible reasons for the regional variabilities of prevalence and mortality. Herein, we present data from a large population encompassing the province of Brescia, with the assistance of the Health Protection Company (ATS Brescia). This review provides possible explanations for the regional differences.

Background of Brescia, Italy

According to the data from ATS Brescia, on December 31, 2019, the province of Brescia had a population of 1,179,966 people (4). The average age was 44.7 years. The number of people aged ≥ 65 years was 254,947 (21.61% of the total population). In the last 10 years, the birth rate decreased by 31.2%. The elderly populations aged ≥ 65 and ≥ 85 years increased by 18.4% and 41.5%, respectively (5).

Decreased birth rate and aging population are generalized phenomena in Italy, a trend particularly seen in the Northern Italy. Nevertheless, in Italy, the life expectancy at birth according to the Office of Child Support Enforcement data is the second highest in the EU (6). During the pandemic, various measures were taken, such as strict public health measures aimed at reducing the spread of the contagion, including home isolation, travel restrictions, crowd avoidance via social distancing, universal masking, and lockdown (7–9). Countries that adopted strict measures (China and Singapore) were more successful than those that applied mitigating measures (Italy) (10). Italy later implemented a national lockdown and followed social containments, but these measures were too late (11).

The number of hospital beds in Italy according to the World Bank was 3.4 beds per 1,000 people (12). The number of hospital beds (in public and private affiliated facilities) in the province of Brescia was 5,401 on December 31, 2019, corresponding to a ratio of 4.5 beds per 1,000 people (12). In Italy, according to an extensive study of long-term care facilities, the prevalence of elderly people in institutional care was 19.8 per 1,000 inhabitants aged ≥ 65 years (13). This average conceals a huge interregional variability, from approximately 4 to 49 per 1000 elderly people in Northern Italy.

The province of Brescia has 68 nursing homes with 6,787 long-term beds (26 per 1,000 inhabitants aged ≥ 65 years) (5). As the occupancy rate of the beds in the LTC facilities is close to 100%, we can assume that the prevalence of elderly residents in LTC facilities is 0.58% of the total population (and 2.66% of people aged ≥ 65 years) of the province of Brescia.

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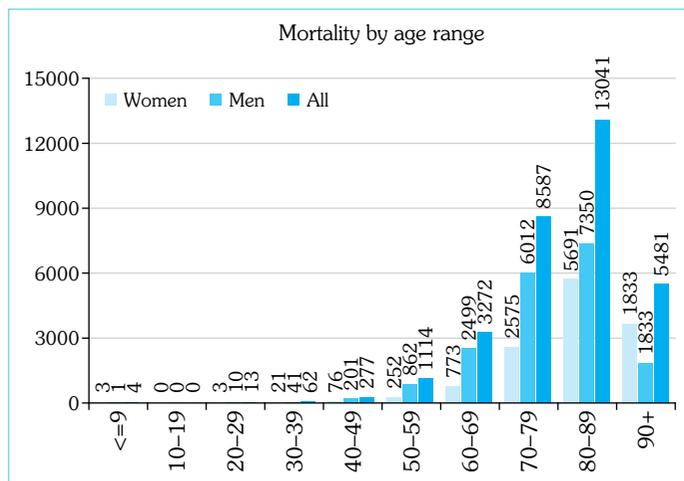


Figure 1. Mortality by age and sex [graph from (15)]

Data ISS on 28 May 2020. ISS: Istituto Superiore di Sanità

COVID-19 in Italy

Italy was the first European country affected by the COVID-19 pandemic, which initially affected the Northern part of the country (11). According to the official data from the Lombardy Region on May 31, 2020, in the province of Brescia, the total number of confirmed COVID-19 cases was 14,768, corresponding to a prevalence of 1.25% in the province population, with a little overestimation due to the lack of updated data of the total province population and a trend of continuous increase in the last few years.

According to the latest data from the Italian Istituto Superiore di Sanità (ISS) on May 28, 2020, the total mortality rate in Italy was 13.96% (31,851 deaths among the infected people). The average age of the deceased people was 80 years. Of the people who died, 1,470 were younger than 60 years; 30,381 deceased people were ≥ 60 years of age (95.38%), of whom 27,109 were aged ≥ 70 years (85.11%) (14) (Fig. 1). On the basis of the data from ATS Brescia, on May 26, 2020, 2,474 people (17.08% of infected people at that time) died in the province of Brescia (15). Although these percentages are already alarming, the actual number of fatalities due to COVID-19 might be underestimated. The official figures in Italy mostly include hospital deaths. Few of the elderly in long-term care homes were tested, and the number of deaths from the virus in the community is unknown. Since the day of the first death from severe acute respiratory syndrome coronavirus 2 infection was reported, from February 20 to March 31, the number of deaths across Italy increased from an average of 65,592 in the period 2015–2019 to 90,946 in 2020.

According to the national statistics from the Italian National Institute of Statistics (reporting date May 4, 2020), from February 20 to March 31, in the province of Brescia, the number of deaths increased by 291% as compared with that in the same period in the previous years, thus proving Brescia to be the fourth most affected by the pandemic among the Italian provinces (11).

Possible Explanations for the Mortality Disparity

The difference in mortality rate has been attributed to different factors, including differences in preventative measures and healthcare systems, testing and definitions of death, and demographics (16,

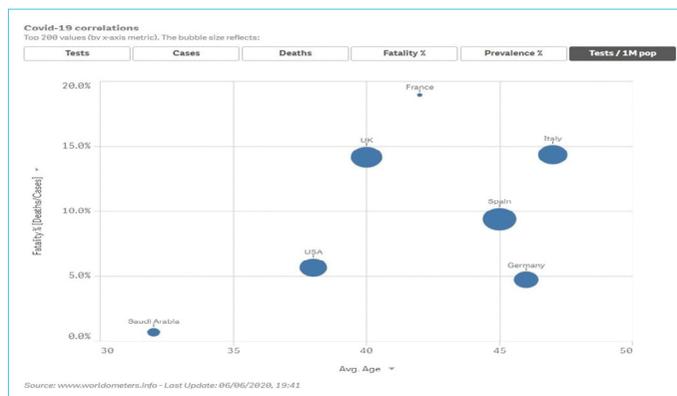


Figure 2. Graph showing the relationship between average age and mortality

17). It would be tempting to believe that the difference in mortality rate depends on the average age of any COVID-19 population. Data from Worldometer updated on June 6, 2020, do not seem to clearly support this hypothesis on the difference in the ages of the patients in Italy (18) (Fig. 2). However, in a prospective study from China, the case fatality rate was 3.76 (95% confidence interval [CI]: 1.14–17.39) in those aged >65 years (19). Moreover, a study from Italy showed that the contributing factors to mortality include age, cancer, obesity, and smoking (20). The fatality rate was particularly higher among the elderly in Italy than in China. Among those aged >80 years, the fatality rate was 20.2% in Italy and 14.8% in China (21).

Another factor is related to the capacities and capability of the healthcare facilities. The province of Brescia appeared to be well equipped. However, especially in the first 2 months of the COVID-19 epidemic, the determining factor was the availability of intensive care unit (ICU) beds. In Brescia, the number of beds proved insufficient to cope with the massive influx of patients with acute respiratory distress syndrome caused by COVID-19. Other more resource-rich organizations were able to accommodate the influx of new patients, by requisitioning hotels for patients with mild symptoms (9).

The large availability of beds in LTC homes in the province of Brescia is secondary to a sustained demand due to cultural and socioeconomic reasons. Their occupancy rate was so high that approximately 6,700 frail elders live in these facilities. This turned out to be a death trap. In a study from the USA, long-term care home residents accounted for 47.3% of all COVID-19 deaths (22).

Regarding the prevalence of COVID-19, it is particularly important to consider the different initial strategies of the various nations to confirm the diagnosis of COVID-19 infection. These differences have huge repercussions on estimates of disease prevalence, cure, and mortality. The prevalence of confirmed cases was 1.25% in the province of Brescia, which falls within the maximum value of the range published by the WHO (23). The Potential Risk Index, which indicates the relationship between actual patients at a given time and the overall population, by attributing the data to a base of 10,000 inhabitants, the rate in the Lombardy region (to which the province of Brescia belongs) is the worst in Italy (18) (Fig. 3).

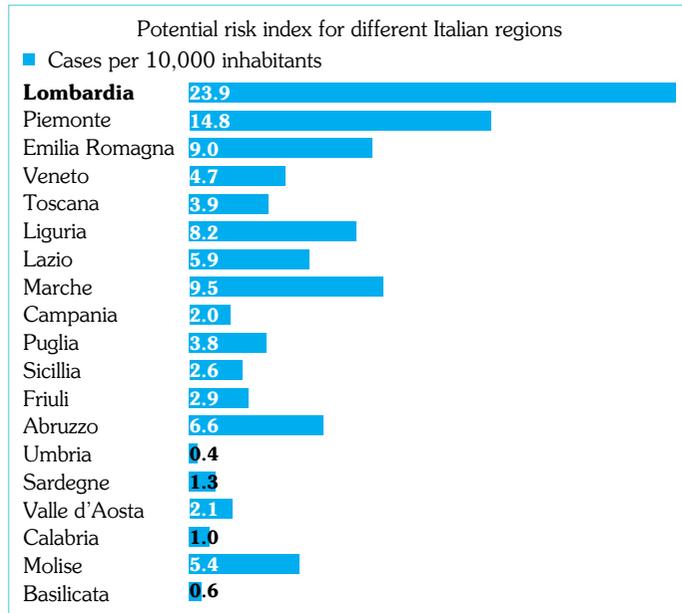


Figure 3. Graph showing the Potential Risk Index for different Italian regions, with Lombardy carrying the highest risk
Data from Protezione/ISTAT updated to 27 May 2020

By analyzing data from the WHO on June 6, 2020, concerning some European countries, the USA, the UK, Singapore, Saudi Arabia, Japan, Australia, and New Zealand, there is a gradient of COVID-19 prevalence with the highest rate in Singapore (0.63% of the entire population), followed by Spain (0.61%), the USA (0.59%), the UK (0.41%), Italy (0.38%), Saudi Arabia (0.27%), France (0.23%), and Germany (0.22%). We find at the lower end of the prevalence rate countries such as New Zealand (0.03%), Australia, and South Korea (0.02%), and Japan (0.01%) (18). The distribution of the confirmed COVID-19 cases shows that in the selected European countries, the USA, and Singapore, the prevalence of confirmed cases is one order of magnitude greater than in South Korea/Japan and Australia/New Zealand.

At the lowest end of the spectrum was China (0.006%), while at the highest end of the spectrum were cities close to the epicenter of Italy, such as Brescia (1.25%), indicating a 167-fold higher rate than that in China.

The average age of the population does not necessarily correlate with the prevalence, as Japan has the highest median age (47.8 years) in the entire group and South Korea (44 years) falls in the middle of the European countries (Germany, 46 years; Italy, 47 years; Spain, 45 years; France, 42 years; the UK, 40 years) (14). The population densities in the countries previously examined for prevalence analysis were not related to the total numbers of infected people (24) (Fig. 4a, b).

The province of Brescia is in an area of high environmental pollution. In addition, it is characterized by numerous companies and factories with a high density of employees working closely together. Finally, owing to the high entrepreneurship rate, the inhabitants of Brescia often travel abroad, and the consequent economic wealth favors tourist travel. All these factors contribute to the increased prevalence. Unexpectedly, population density correlated weakly with fatality (Fig. 5) (24).

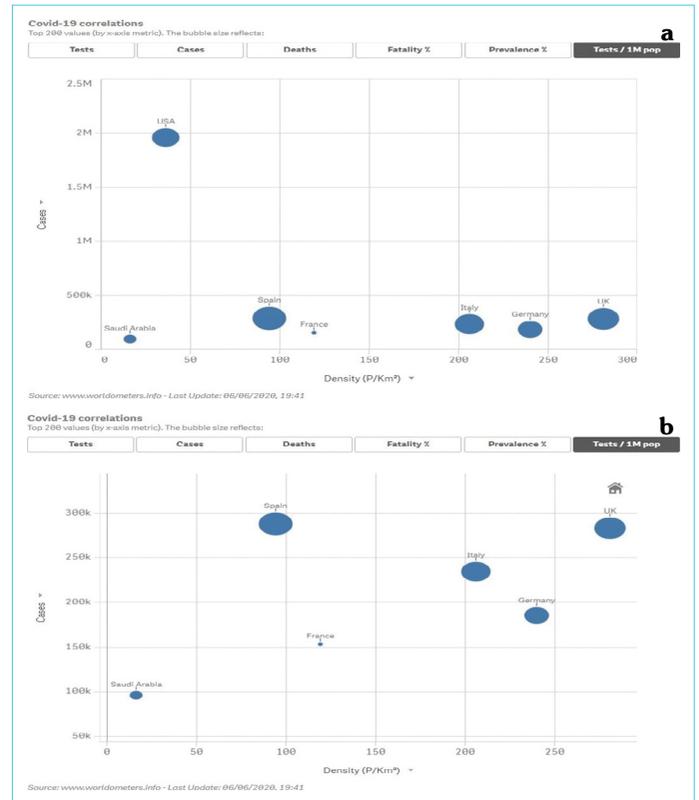


Figure 4. (a) Graph showing no relationship between population density and prevalence. (b) Graph showing no relationship between population density and prevalence (without the USA, outlier)

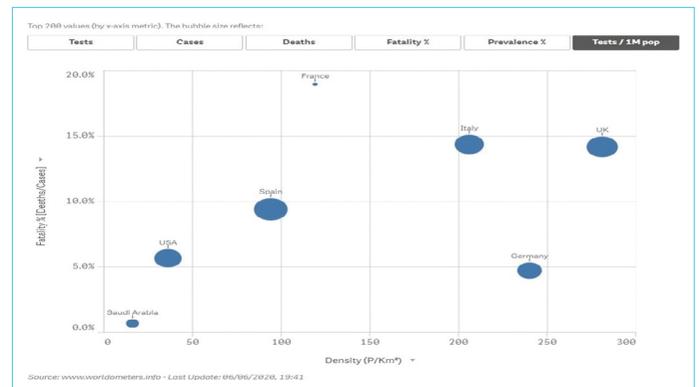


Figure 5. Graph showing a weak correlation between population density and fatality

The mortality figure was 17.08% in the province of Brescia (15). Fatality is defined as the number of deaths as compared with the total number of cases. However, the counting criteria of deaths and cases widely differ between countries and even between hospitals. This fact is relevant when performing a comparative analysis. Extensive use of swab test tends to reduce the fatality rate, as it identifies more cases. On the other hand, the different definitions of deceased patients due to COVID-19 may be died in hospital only, with COVID-19 only; died in hospital only, with COVID-19 and other diseases; died from symptoms compatible with COVID-19, either in hospital or at home (with or without a swab test). More inclusive definitions tend to increase the fatality rate. The defini-

tion of death might also change over time. For example, the UK changed the definition of death due to COVID-19 to be death due to laboratory-confirmed COVID-19 and death at 28 days or 28 days from the first positive sample or other definitions (25, 26).

The following European countries in the group, with generally older populations, though with quite different counting strategies, reported fatality rates >10%: France (19%), the UK, Italy (14.2 and 14.4%, respectively), and Spain (9.4%), with the exception of Germany (4.7%) (24).

Published data revealed a concerning correlation between mortality and old age. In a multivariable analysis, older age, coronary artery disease, cancer, low lymphocyte count, and high Radiographic Assessment of Lung Edema score were independently associated with an increased risk of mortality (27). In another study, age (>75 years) and low platelet count ($<150 \times 10^3/\text{mm}^3$) and ferritin levels (>750 ng/mL) were independent predictors of death (28). It was also speculated that the difference in the human leukocyte antigen gene system may contribute to the differences in the severity and outcome of COVID-19 (28).

From February 20 to March 31, the number of deaths across Italy increased from an average of 65,592 in the period 2015–2019 to 90,946 in 2020 (29). The official figures in Italy, mostly counting hospital deaths, including deaths of the elderly in care homes, have been tested, and the number of deaths from the virus in the community was likely underestimated. As mentioned earlier, the number of deaths increased as compared with those in previous years. In Brescia, the number of deaths increased by 291%. As mentioned earlier, death occurred predominantly in the elderly. In Italy, the rapid growth of demand for long-term care services and, more generally, for health and social services for elderly people, reflects both the progressive aging of the Italian population and the changes in the family structure and other cultural and socioeconomic aspects. The structure of LTC service supply varies widely among regions. For instance, the number of elderly persons institutionalized was highest in Northern Italy, where the culture of public service in LTC is diffuse owing to the high female involvement in the labor market. Lombardy, in fact, has 50,668 beds in nursing homes. In a study from the USA, the case fatality rate for affected LTC residents was 33.7% (30). COVID-19 is feared disease in LTC facilities in Italy (31). The possible explanations for the variations in the prevalence and case fatality rate include differences in testing strategy and population (2).

The Italian Corte dei Conti has bitterly criticized the health policy in the last 10–15 years because it provides privileges almost exclusively to the implementation of hospitals of excellence. In fact, many patients with COVID-19 have not been visited by general practitioners at home. Physicians were few, ill-equipped, and easily prone to get infected. Especially in the first 2 months of the pandemic, they could have offered more than the standard therapy for a “bad flu” to their patients. However, compassionate support of physicians for suffering, often dying, patients is a standard of care that a good health system should guarantee.

Anecdotal evidence implies that in the three hospitals of the province of Brescia that were ad hoc reconverted for patients with COVID-19, during the days when beds were no longer available in the hospitals and especially in the ICU, the criteria of

age and associated pathologies excluded the elderly from hospitalization, favoring younger patients.

During the worst days of the pandemic, the elderly rejected by hospitals returned to their homes or those of their closest relatives; it was difficult for everyone in usually small and un-equipped homes to observe the recommended hygiene and prophylactic standards. Alternatively, healthy seniors had to share life in the same conditions with infected younger relatives with mild symptoms who were rejected by hospitals. Thus, the infection spread further.

Moreover, the authorities of the Lombardy Region encouraged some LTC facilities by offering financial incentives, provided that different and separate areas were ensured, to accommodate patients with COVID-19 who have mild or moderate symptoms and could not be hospitalized but also could not be adequately cared for at home. The facts have shown that these initiatives have proved to be shortsighted.

In conclusion, as a vulnerable population without adequate defense, elderly in the province of Brescia, being easy and fatal targets, contracted the infection. Given the social and cultural context, this large-scale fatality was an inevitable tragedy.

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