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The Italian Outbreak of COVID-19: Conditions, Contributors, and Concerns

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In late December 2019, several cases of interstitial pneumonia of unknown origin were reported in Wuhan, China, and on January 9, 2020, a novel coronavirus was identified as the causative infective agent, named *2019 novel coronavirus* (2019-nCoV); the disease was termed *COVID-19*.^{1,2}

Since then, the contagion has spread exponentially through China, South Korea, and many other countries, and the presence of asymptomatic cases together with the ease of modern travel allowed the virus to reach every continent, with the sole exception of Antarctica. On March 11, the World Health Organization declared a state of pandemic. Herein, we discuss possible factors that may contribute to the differences in Italy's COVID-19 outbreak compared with other countries and the differences among regions within Italy.

Italy was one of the first European countries that dealt with COVID-19, with first cases detected in January 2020. In mid-February, cases of community spread were detected in the region of Lombardy, and the outbreak soon involved all of northern Italy, eventually appearing elsewhere in the country.

At first, the fatality rates in Italy and China were comparable, approximating 2.3%. However, over the past weeks, the Italian situation has worsened, with mortality rates reaching as high as 8% to 12%, and with the total number of deaths surpassing those in China.³

As a consequence, and similar to Chinese emergency policy, restrictive measures were then adopted in Italy, including general lockdown, measures shown to check the contagion in Wuhan.

The grave situation in Italy raises 2 salient questions: “Why have there been so

many cases and deaths?” and “Why are there these differences among regions?” There are no answers to these questions, but we offer the following speculations (Figure).

Why Have There Been So Many Cases and Deaths?

1. A first point of discussion is that in other countries, including South Korea, a wider sample of the population was tested, whereas in Italy and especially in the north, diagnostic tests were mainly reserved for symptomatic cases seen in the emergency department or symptomatic cases at home with recent contact with a confirmed case. Therefore, the actual number of positive patients could be even 10-fold higher than the estimated number, thus considerably reducing the percentage of fatal cases. However, this assumption cannot be confirmed until extended population testing is done.
2. Epidemiological and demographic differences should also be considered. For instance, mortality rates have been higher in the elderly as well as in men than in women. This could be because men are more frequent smokers and have more cardiovascular comorbidities than do women. In both China and South Korea, life expectancy is lower than that in Western countries. In South Korea, most infected patients are young, nonsmoking women, who, generally and in the absence of COVID-19, have a lower overall risk of death. This argument may partially explain the differences between Italy on the one hand and South Korea or China, on the other, but not with the rest of Europe or the United States. An additional hypothesis is that Italian grandparents

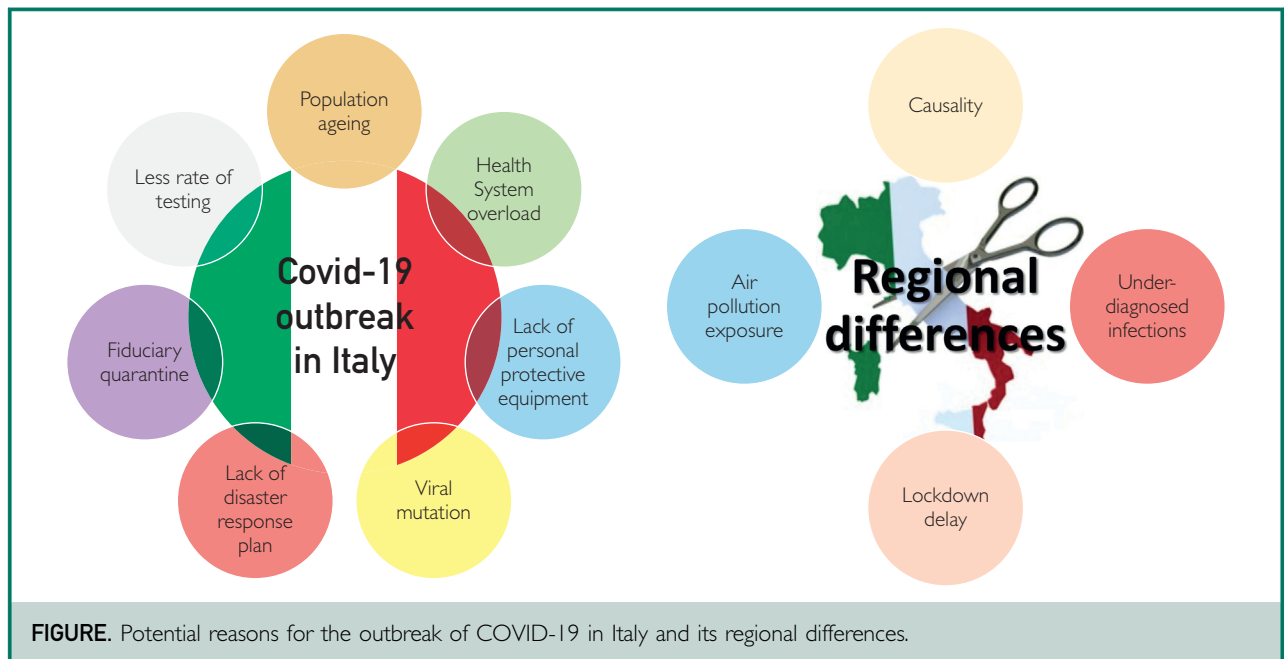


FIGURE. Potential reasons for the outbreak of COVID-19 in Italy and its regional differences.

spend more time with their young grandchildren, the latter possibly representing asymptomatic carriers of the infection. Further epidemiological research is needed with regard to this issue.

3. A relevant issue is that the Italian health system, which experienced financial cuts in the past years, was poorly positioned and resourced to deal with the emergency imposed by the COVID-19 crisis. The lack of an appropriate number of intensive care units, managed care organization, and lifesaving devices such as ventilators may have compromised the care of patients. The paucity of personal protective equipment throughout the country caused a spread of the contagion among medical staff and consequently patients.⁴ Furthermore, the lack of renovation in health care facilities with inappropriate air ducts could have facilitated virus circulation in compromised patients.
4. The Chinese “disaster response plan” allowed the construction of 2 dedicated hospitals in only 10 days, whereas Italy was unprepared to face emergency conditions.
5. The Chinese experience emphasized not just the quarantine of asymptomatic and

mildly symptomatic cases but also follow-up of possible contacts and of the infectious status so as to attenuate viral spread.

Finally, virus mutation and the appearance of more virulent genotypes may contribute to geographic differences in morbidity and mortality caused by COVID-19. Different genotypes for 2019-nCoV exist, and it is thus intriguing whether genotypes determine the infectivity of and mortality caused by 2019-nCoV.⁵

Why Are There These Differences Among Regions?

Substantial differences occur throughout Italy, with the north of the country, predominantly Lombardy, exhibiting the highest rates of spread and mortality.

1. One possible explanation is that the above-mentioned Italian regions represent a central driver of the Italian economy, being the headquarters of several major industries; individuals from other regions and other countries who are involved with such industries may spread the virus elsewhere. Nevertheless, other Italian cities that are overcrowded because of

- business and tourism, such as Rome, have not experienced the same prevalence and spread of COVID-19. A supposition could be that the northern experience led to severe restrictive measures throughout the country, thereby containing the outbreak.
- Climate conditions may also be relevant to the differences reported among Italian regions. Higher temperature and humidity may block virus diffusion and reduce its persistence in the air and on the objects.⁶ This explanation has been given to the unequal distribution of the contagion among the continents. In Italy, however, differences in climate among regions are less than what exists between Italy and other parts of the world such as China.
 - More recently, there is increasing attention on the possible role of air pollution in virus diffusion. The correlation between the air pollution index and increased fatality was previously hypothesized for the severe acute respiratory syndrome caused by a virus member of the Coronaviridae family; subsequent evidence supported this hypothesis for the severe acute respiratory syndrome. In particular, atmospheric particulate seems to act as a carrier of the virus, facilitating its diffusion and dissemination and allowing its survival in active form for hours and even days. Indeed, air pollution imposes an increased vulnerability of the population to respiratory syndromes, even in the absence of microbial causative agents. A recently published position paper of the Italian Society of Environmental Medicine in collaboration with 2 Italian universities compared COVID-19 case distribution (updated to March 3) and air pollution levels in the past 20 days. Interestingly, northern Italy had both the most polluted area and the highest number of cases of COVID-19, thereby supporting the possibility that the degree of air pollution may contribute to regional differences in cases of COVID-19.⁷

In sum, there is no single explanation that accounts for the severity and catastrophic consequences of the COVID-19

outbreak in Italy. Intense and sustained effort is needed to optimize strategies that prevent the spread of infection and to devise targeted therapies for the disease. In the meantime, severe restrictive measures and strict social distancing are crucial to contain the contagion among the population. Hospitals should be provided with appropriate personal protective equipment, ventilators, and further intensive care unit equipment to preserve the medical staff and to optimize care for all patients.

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