SHORT COMMUNICATION

Case fatality rate analysis of Italian COVID-19 outbreak

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Abstract
The Italian outbreak of COVID-19 cases is a public health emergency and there is a worldwide tremendous interest in the evaluation of the Italian epidemic evolution. Indeed, from February 2020, Italy is facing an explosion of COVID-19 cases. In particular, the Italian observed case fatality rate (CFR) is much higher than the other countries. Recently, it has been hypothesized that the extensive number of intergenerational contacts—typical of Italian culture—could contribute to explain the high number of deaths observed in Italy. However, through an analysis performed for all the Italian regions, here it is shown that the deaths are localized in specific regions and that the CFRs of different Italian regions are overlapping with the rates of European countries. Moreover, through correlation analyses between CFRs and different social habits, it is shown that no positive correlation is observed between social behaviors and CFRs. In conclusion, this analysis clearly rejects the possibility that social habits and intergenerational contacts can contribute to explaining such a profound effect on the number of deaths observed in Italy during the COVID-19 outbreak and more effort should be addressed to evaluate the real amount of positive cases.

KEYWORDS
case fatality rate, COVID-19, Italy, outbreak, SARS-CoV-2, social behavior

1 | INTRODUCTION
At the end of 2019, a novel beta-coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was observed in the city of Wuhan, Hubei province, China. This virus is able to cause serious respiratory infections (namely Coronavirus Disease 2019, COVID-19) with a case fatality rate between 1% and 5%. From February 2020, Italy has been the first European country to face a massive outbreak of cases. There is a huge concern for the Italian situation since the data show a tremendous high case fatality rate (CFR) compared to the other nations. In particular, Germany and South Korea—although with similar population and age distribution—have a much lower CFR compared to the Italian data. Recently, it was reported that CFR analyzed by age is similar between Italy and other nations and it was hypothesized that the CFR could be explained by a higher number of intergenerational interactions, co-residence, and commuting patterns typical of Italian culture, that may have accelerated the outbreak through social networks that increased the proximity of elderly to initial cases.

Social habits, at country level, are described by a complex mixture of different variables, and intergenerational contacts between people is one of these variables, often used as a proxy to evaluate the social behavior of different populations.

This manuscript analyses the CFR of different countries to evaluate if the social behavior of the different populations can contribute to explaining the observed differences.

2 | MATERIALS AND METHODS

2.1 | Data availability

Italian data of positive patients and deaths were obtained from the Italian Department of Civil Protection updated at the 31st March 2020.
The South Korean data of positive patients and deaths were obtained from the Korea Centers for Disease Control and Prevention updated at the 31st March 2020 (https://www.cdc.go.kr/cdc_eng/).

The German data of positive patients and deaths were obtained from the Robert Koch Institute updated at the 31st of March 2020 (https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/Situationsberichte/Archiv.html).

The French data of positive patients and deaths were obtained from the France Public Health Ministry updated at the 31st March 2020 (https://www.santepubliquefrance.fr/maladies-et-traumatismes/maladies-et-infections-respiratoires/infection-a-coronavirus/articles/infection-au-nouveau-coronavirus-sars-cov-2-covid-19-france-et-monde).

The Spanish data of positive patients and deaths were obtained from the Spanish Ministry of Health updated at the 31st March 2020 (https://www.mscbs.gob.es/en/profesionales/saludPublica/ccayes/alertasActual/nCov-China/situacionActual.htm).

The UK data of positive patients and deaths were obtained from the UK Department of Health and Social Care updated at the 31st of March 2020 (https://www.gov.uk/guidance/coronavirus-covid-19-information-for-the-public#number-of-cases-and-deaths).

The Italian national and regional population numbers (updated at 2019), the percentage of people which have daily contact with friends (updated at 2018) and the percentage of young people (18-34 years old) that live with at least one parent (updated at 2018) were obtained from the Italian Institute of Statistics (http://dati.istat.it/#). The other national population numbers were obtained from the United Nations database updated at the 2019 (https://population.un.org/wpp).

2.2 | Data analysis

For CFR calculation, the number of deaths for each country/region was divided for the total number of SARS-CoV-2 positive cases and shown as a percentage. For the correlation analysis, the square of the Pearson coefficient ($R^2$) and the P-value of two-tailed Student’s t distribution were calculated using Excel software.

3 | RESULTS

To analyze the CFR, data of positive cases and deaths (updated at the 31st of March 2020) from South Korea, Italy, Spain, UK, France, and Germany outbreaks have been compared. Interestingly, Italy and Spain show a strong increase in both positive cases and deaths compared to the others (Figure 1A,B). To analyze the CFRs, the percentage of deaths over the number of positive cases was calculated (Figure 1C): South Korea and Germany show around 1% of CFR, while Italy, Spain, UK, and France definitely more. In particular, Italy shows a CFR around eight times more than South Korea and Germany.

To evaluate if the hypothesis of a high number of intergenerational contacts between people could contribute to explain the high Italian CFR, a more detailed analysis of all the Italian regions has been performed. Indeed, it is known that also within Italy there are different social habits.

For this reason, the number of positive cases and deaths have been analyzed also for all the Italian regions (Figure 1D,E): similar to the high differences between Italy and South Korea or Germany, also within the Italian country, there is huge variability between different regions, with Northern territories more hit by the SARS-CoV-2 infection. The comparison of the CFRs shows that the CFR of Northern regions ranges from 5% to 17%, while Southern regions have CFRs from 3% to 6%, similar to other European countries (Spain, France, and UK) and comparable with the ones of South Korea or Germany (around 1%) (Figure 1F).

These data suggest that intergenerational contacts, as a proxy of the social behavior of a specific country, are not linked to the observed CFRs, since it is known that Italy has more intergenerational contacts not only Germany, but also than UK and France; while the CFRs of Italy, France, and UK are similar.

However, to perform a more reliable and quantitative analysis of the connection of COVID-19 CFR with social habits, two further variables linked have been considered and analyzed for all Italian regions: the percentage of people that have contacts with friends every day (Figure 2A), as an indicator of the contact rates observed in the different Italian regions, and the percentage of young people (18-34 years old) that live with at least one parent (Figure 2B), which is tightly linked to the number of intergenerational contacts between the different Italian regions.

In particular, a correlation between CFR and the two variables has been performed. From this analysis, first of all, it is visible how the Southern Italian regions have an increased number of contacts between people and higher intergenerational connectivity compared to Northern regions (Figure 2A,B). Regarding the correlation between CFR and the percentage of people with every day contacts with friends, no statistically significant correlation has been observed (Figure 2A). Moreover, when it is analyzed the correlation between CFR and the percentage of young people that live with parents, it is observed a slight statistically significant negative correlation ($R^2 = 0.2754$; Figure 2B), which confirms that no link is present between the increased number of intergenerational contacts (typical of Southern regions, as visible from the graph) and the high CFR.

Overall, the data clearly indicate that there is no positive correlation between the increase of CFR and the higher number of contacts.

4 | DISCUSSION

European countries and South Korea are facing similar outbreaks of SARS-CoV-2 positive cases starting from February 2020. However, South Korea and Germany are registering very low CFR compared to other European countries, especially Italy.
Importantly, it has been shown that CFR analyzed by age is similar between Italy and other nations, suggesting that the reason for this observed CFR is not linked to some putative mutation of the Italian viral strain that became more aggressive. There are many possible parameters that can influence the number of deaths, for example, the efficiency of the national health system, the criteria to assess whether a death is due to SARS-CoV-2 infection or not, the strategy to perform tests in the population, which are difficult to be estimated to date and could be very different among nations.

Intergenerational contacts, and more in general contact rates, are an important variable in the evaluation of the COVID-19 outbreak. Indeed, in the absence of vaccines, governments have almost uniformly adopted the strategy to drastically decrease the contact rates to control the pandemic. However, while this

**FIGURE 1** Analyses of SARS-CoV-2 positive cases, deaths, and CFRs. A, Histogram showing the number of SARS-CoV-2 positive cases for South Korea, Italy, Spain, UK, France, and Germany normalized on the population and showed as a number of cases over 100,000 people. B, Histogram showing the case fatality rate for South Korea, Italy, Spain, UK, France, and Germany: percentage of deaths over positive cases was calculated. D, Histogram showing the number of SARS-CoV-2 positive cases for Italian regions normalized on the population and showed as number of cases over 100,000 people. In red are shown Northern regions; in blue Central regions; in yellow are shown Southern regions. E, Histogram showing the number of SARS-CoV-2 deaths for Italian regions normalized on the population and showed as a number of cases over 100,000 people. In red are shown Northern regions; in blue Central regions; in yellow are shown Southern regions. F, Histogram showing the case fatality rate for Italian regions: percentage of deaths over positive cases was calculated. In red are shown Northern regions; in blue Central regions; in yellow are shown Southern regions. AP, autonomous province; CFR, case fatality rate.
strategy is able to strongly and quantitatively decrease the viral spreading, very different is the evaluation of the effect of social behavior (typical of each country and linked to intergenerational contacts, the attitude of a specific population, amount of time spent with other people and family members) during the epidemic.

Interestingly, it was proposed that the Italian outbreak may have been accelerated “through social networks that increased the proximity of elderly to initial cases”\(^4\). Indeed, Italy is among the countries with the highest number of contacts between people,\(^15\) and as such, more social activities may have contributed to the spread of the virus. However, a detailed description of CFR of European countries and of South Korea, reveals—through an analysis performed for all the Italian regions—the deaths are localized in specific regions and do not correlate with any social behavior. Moreover, CFRs of Italian Southern regions are overlapping with the rates of European countries (like UK and France), that do not show the same number of personal contacts.\(^10\) These data suggest that social behavior is probably not implicated with the high number of deaths that are observed in Italy.

Interestingly, here it is shown that—also at the regional level—there are different social habits. Indeed, Southern Italian regions are more socially active, with a higher rate of interconnection between people. To evaluate the effect of the social behavior on the CFR observed for all Italian regions, a correlation analysis of CFR compared with two social habit variables has been performed, indicating once again that there is no positive correlation between the increase of CFR and the social behavior.

Overall, these data clearly indicate that the hypothesis of different social behaviors between Italy and other countries cannot explain the CFR differences.

One other possibility is that the Italian CFR is only apparently more than the other countries and that the real number of positive cases is much higher. To understand if this is the case, governments need to try to implement a concrete surveillance strategy to test the population with higher efficiency. World Health Organization indicates to avoid testing of asymptomatic people.\(^14\) However, these

![FIGURE 2](image-url) Correlation of CFRs and variables of social behavior for Italian regions.

A. Correlation of CFRs and percentage of people that have contacts with friends every day for all Italian regions. \(R^2\) and \(P\)-value of two-tailed Student’s t distribution are shown. B. Correlation of CFRs and percentage of young people (18-34 years of age) that live with at least one parent for all Italian regions. \(R^2\) and \(P\)-value of two-tailed Student’s t distribution are shown. CFR, case fatality rate.
results suggest it is time to implement and to uniform a strategy to increase the surveillance and to immediately identify positive cases and delay the viral spreading at the European level.

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