

VIEWPOINT

Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy

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Video

Only 3 cases of coronavirus disease 2019 (COVID-19) were identified in Italy in the first half of February 2020 and all involved people who had recently traveled to China. On February 20, 2020, a severe case of pneumonia due to SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) was diagnosed in northern Italy's Lombardy region in a man in his 30s who had no history of possible exposure abroad. Within 14 days, many other cases of COVID-19 in the surrounding area were diagnosed, including a substantial number of critically ill patients.¹ On the basis of the number of cases and of the advanced stage of the disease it was hypothesized that the virus had been circulating within the population since January.

Another cluster of patients with COVID-19 was simultaneously identified in Veneto, which borders Lombardy. Since then, the number of cases identified in Italy has rapidly increased, mainly in northern Italy, but all regions of the country have reported having patients with COVID-19. After China, Italy now has the second largest number of COVID-19 cases² and also has a very high case-fatality rate.³ This Viewpoint reviews the Italian experience with COVID-19 with an emphasis on fatalities.

Surveillance System and Overall Fatality Rate

At the outset of the COVID-19 outbreak, the Italian National Institute of Health (Istituto Superiore di Sanità [ISS]) launched a surveillance system to collect information on all people with COVID-19 throughout the country. Data on all COVID-19 cases were obtained from all 19 Italian regions and the 2 autonomous provinces of Trento and Bozen. COVID-19 cases were identified by reverse transcriptase-polymerase chain reaction (RT-PCR) testing for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The fatality rate was defined as number of deaths in persons who tested positive for SARS-CoV-2 divided by number of SARS-CoV-2 cases. The overall fatality rate of persons with confirmed COVID-19 in the Italian population, based on data up to March 17, was 7.2% (1625 deaths/22 512 cases).³ This rate is higher than that observed in other countries² and may be related to 3 factors.

Fatality Rate and Population Age

The demographic characteristics of the Italian population differ from other countries. In 2019, approximately 23% of the Italian population was aged 65 years or older. COVID-19 is more lethal in older patients, so the older age distribution in Italy may explain, in part, Italy's higher case-fatality rate compared with that of other countries. The Table shows the age-specific fatality rate in Italy compared with that of China.⁴

The overall case-fatality rate in Italy (7.2%) is substantially higher than in China (2.3%). When data were stratified by age group, the case-fatality rate in Italy and China appear very similar for age groups 0 to 69 years, but rates are higher in Italy among individuals aged 70 years or older, and in particular among those aged 80 years or older. This difference is difficult to explain. The distribution of cases is very different in the 2 countries: individuals aged 70 years or older represent 37.6% of cases in Italy and only 11.9% in China. In addition, a relevant number of cases in Italy are in people aged 90 years or older (n = 687), and this age group has a very high fatality rate (22.7%); data on cases in those aged 90 years or older were not reported in China. In addition, the report from the WHO-China Joint Mission on Coronavirus Disease 2019 Mortality, which presents data on 2114 COVID-19 related deaths among 55 924 laboratory-confirmed cases in China, reported a fatality rate among patients aged 80 years or older that was similar to the rate in the Italian sample (21.9% in China vs 20.2% in Italy).⁵

Thus, the overall older age distribution in Italy relative to that in China may explain, in part, the higher average case-fatality rate in Italy.

Definition of COVID-19-Related Deaths

A second possible explanation for the high Italian case-fatality rate may be how COVID-19-related deaths are identified in Italy. Case-fatality statistics in Italy are based on defining COVID-19-related deaths as those occurring in patients who test positive for SARS-CoV-2 via RT-PCR, independently from preexisting diseases that may have caused death. This method was selected because clear criteria for the definition of COVID-19-related deaths is not available.

Electing to define death from COVID-19 in this way may have resulted in an overestimation of the case-fatality rate. A subsample of 355 patients with COVID-19 who died in Italy underwent detailed chart review. Among these patients, the mean age was 79.5 years (SD, 8.1) and 601 (30.0%) were women. In this sample, 117 patients (30%) had ischemic heart disease, 126 (35.5%) had diabetes, 72 (20.3%) had active cancer, 87 (24.5%) had atrial fibrillation, 24 (6.8%) had dementia, and 34 (9.6%) had a history of stroke. The mean number of preexisting diseases was 2.7 (SD, 1.6). Overall, only 3 patients (0.8%) had no diseases, 89 (25.1%) had a single disease, 91 (25.6%) had 2 diseases, and 172 (48.5%) had 3 or more underlying diseases. The presence of these comorbidities might have increased the risk of mortality independent of COVID-19 infection.

COVID-19-related deaths are not clearly defined in the international reports available so far, and differences

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Table. Case-Fatality Rate by Age Group in Italy and China^a

	Italy as of March 17, 2020		China as of February 11, 2020	
	No. of deaths (% of total)	Case-fatality rate, % ^b	No. of deaths (% of total)	Case-fatality rate, % ^b
All	1625 (100)	7.2	1023 (100)	2.3
Age groups, y				
0-9	0	0	0	0
10-19	0	0	1 (0.1)	0.2
20-29	0	0	7 (0.7)	0.2
30-39	4 (0.3)	0.3	18 (1.8)	0.2
40-49	10 (0.6)	0.4	38 (3.7)	0.4
50-59	43 (2.7)	1.0	130 (12.7)	1.3
60-69	139 (8.6)	3.5	309 (30.2)	3.6
70-79	578 (35.6)	12.8	312 (30.5)	8.0
≥80	850 (52.3)	20.2	208 (20.3)	14.8

^a Data from China are from Chinese Center for Disease Control and Prevention.⁴ Age was not available for 1 patient.

^b Case-fatality rate calculated as number of deaths/number of cases.

in definitions of what is or is not a COVID-19–related death might explain variation in case-fatality rates among different countries. To better understand the actual causes of death, the ISS is now reviewing the complete medical records of all patients with positive RT-PCR results who have died in Italy.

Testing Strategies

A third possible explanation for variation in country-specific case-fatality rates are the differing strategies used for SARS-CoV-2 RT-PCR testing. After an initial, extensive testing strategy of both symptomatic and asymptomatic contacts of infected patients in a very early phase of the epidemic, on February 25, the Italian Ministry of Health issued more stringent testing policies. This recommendation prioritized testing for patients with more severe clinical symptoms who were suspected of having COVID-19 and required hospitalization. Testing was limited for asymptomatic people or those who had limited, mild symptoms. This testing strategy resulted in a high proportion of positive results, ie, 19.3% (positive cases, 21 157 of 109 170 tested as of March 14, 2020), and an apparent increase in the case-fatality rate because patients who presented with less severe clinical disease (and therefore with lower fatality rate) were no longer tested (case-fatality rate changed from 3.1% on February 24 to 7.2% on March 17). These more mild cases, with low fatality rate, were thus no longer counted in the denominator.

Other countries have different testing strategies. For example, the Republic of Korea has adopted a strategy of widely testing for

SARS-CoV-2. This may have led to the identification of a large number of individuals who had mild or limited symptoms, but a much lower case-fatality rate compared with Italy (1.0% vs 7.2%) because many patients with mild disease who would not be tested in Italy were included in the denominator in Korea.²

Conclusions

In conclusion, the current data illustrate that Italy has a high proportion of older patients with confirmed COVID-19 infection and that the older population in Italy may partly explain differences in cases and case-fatality rates among countries. Within Italy, COVID-19 deaths are mainly observed among older, male patients who also have multiple comorbidities. However, these data are limited and were derived from the first month of documented COVID-19 cases in Italy. In addition, some patients who are currently infected may die in the near future, which may change the mortality pattern.

From a research perspective, the comparisons discussed highlight the need for transparency in reporting testing policies, with clear reporting of the denominators used to calculate case-fatality rates and the age, sex, and clinical comorbid status of affected persons when comparing COVID-19 case and mortality rates between different countries and regions. Finally, because the outbreak is new, continued surveillance, with transparent and accurate reporting of patient characteristics and testing policies, is needed from multiple countries to better understand the global epidemiology of COVID-19.

ARTICLE INFORMATION

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REFERENCES

1. Grasselli G, Pesenti A, Cecconi M. Critical care utilization for the COVID-19 outbreak in Lombardy, Italy: early experience and forecast during an emergency response. *JAMA*. Published online March 13, 2020. doi:10.1001/jama.2020.4031
2. Coronavirus disease 2019 (COVID-19): situation report-57. Published March 17, 2020. Accessed March 18, 2020. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200317-sitrep-57-covid-19.pdf?sfvrsn=a26922f2_2
3. Livingston E, Bucher K. Coronavirus disease 2019 (COVID-19) in Italy. *JAMA*. Published online March 17, 2020. doi:10.1001/jama.2020.4344
4. Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. Vital surveillances:

the epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China, 2020. *China CDC Weekly*. 2020;2(8):113-122. Accessed March 18, 2020. <http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51>

5. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). Published February 16, 2020. Accessed March 18, 2020. <https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf>