Viewpoint

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April 7, 2020

What Other Countries Can Learn From Italy During the COVID-19 Pandemic

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JAMA Intern Med. Published online April 7, 2020. doi:10.1001/jamainternmed.2020.1447

In the coronavirus disease 2019 (COVID-19) pandemic, Italy has been hit very hard,[1] with 110 574 documented cases and 13 155 documented deaths related to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection as of April 1, 2020. The number of cases and deaths cannot be explained simply because of the epidemic starting in Italy earlier compared with other countries besides China. It is important to understand why death rates were so high in Italy to learn how to best prepare and how to plan for optimal actions in other countries. Some contributing factors may be immutable (eg, age structure of the population), but even these need to be laid out carefully in preparedness assessments. Some other contributing factors are potentially modifiable.

Some factors pertain to demographics and background disease in the population. Italy has the most elderly population in Europe and the second most elderly population in the world after Japan. COVID-19 has a strong age dependence for the severity of the infection and the risk of death. The median age of people infected with SARS-CoV-2 who are dying in Italy has been 80 years, and the average age of patients requiring critical care support has been 67 years. Moreover, COVID-19 morbidity and mortality is strongly dependent on the presence of concomitant serious diseases, and Italy has a high proportion of patients with history of smoking and high rates of chronic obstructive pulmonary disease and ischemic heart disease.[2] The corollary is that preparedness for needs of intensive care unit (ICU) beds and estimates of expected deaths should consider the age structure and chronic diseases of the population served by each health care system. Taking this adjustment into account, burden of disease may be expected to be much less in most areas in the United States, with variability across states and hospital catchment areas. For example, the proportion of the population older than 65 years is 9.5% in Alaska as compared with 19.1% in Florida and 23.1% in Italy.

A second set of factors in Italy is the increased burden of cases that presented themselves to the health care system. The proportion of people infected must have been very high in specific areas that were highly affected. In the town of Vò, all 3300 residents were tested the day the first case was detected in the third week of February, and 3% were found to be infected.[3] Following aggressive testing, the epidemic was extinguished. However, elsewhere in Italy, it is likely that the prevalence of infection was several times higher in the absence of effective public health intervention. For example, it is likely that the health care system was overwhelmed in Bergamo owing to massive viral transmission during the Champions League match on February 19, 2020 (Atalanta vs Valencia), where a third of the population of Bergamo attended and continued celebrations overnight. Italian life is famous for its socialization and frequent congregations and clustering. It is possible also that in early stages, there was not much adoption of standard hygienic measures, and instructions to stay at home proved difficult to accept, with many complaints registered with the police.[4] Accordingly, a higher level of preparedness should be considered for areas where mass gatherings have occurred or where there is extensive social intermingling.

A third set of factors pertains to the standard capacity of the health care system and decisions made during hospital management of the presenting cases. Italy has a highly competent state-run health care system, but it has only a modest number of ICU beds and very few subintensive care beds. Overall, 5090 ICU beds (8.4 per 100 000 population) are available in Italy, and 2601 beds in coronary care units (4.3 per 100 000 population),[5] as opposed to much higher numbers (36 ICU beds per 100 000 population) in the United States.

Given the little experience in dealing with the new virus, it is unavoidable that some strategic mistakes were made about which patients should be hospitalized. In the winter, hospitals tend to run close to full capacity, with 87% average occupancy in Italy during the flu season. Apparently, many patients with relatively modest symptoms were admitted; by the time more patients with severe cases started to arrive, there were limited reserves.

Hospital overcrowding may also explain the high infection rate of medical personnel. As of March 30, 2020, 8920 medical personnel had been found to be infected in Italy,[6] leading to further loss of capacity for hospitals to respond. Moreover, early infection of medical personnel led to the spread of the infection to other patients within hospitals. In Lombardy, SARS-CoV-2 became largely a nosocomial infection. Nine percent of infections in Italy occurred among health care personnel.[6] Characteristically, the first patient with COVID-19 visited the emergency department twice, thus exposing all of the personnel and patients in that area before the infection was recognized.

Italy is a decentralized country; thus, preparedness and containment may have been hampered. There was a delay from the first case detection (February 21, 2020) to the first containment decree from the government that closed the relevant villages 3 days later. The lessons relevant to other countries are the need to (1) avoid bringing patients with suspected SARS-CoV-2 infection to the hospital, except

environment; and (3) act swiftly in case of exposures of medical personnel to avoid loss of personnel capacity.

Stochastic factors should also be considered. Not all of Italy, but a few cities among hundreds of cities and towns have carried most of the burden of the epidemic and have seen their hospitals crash. The Lombardy, Emilia-Romagna, and Veneto regions carry the highest numbers of infected individuals and account for 46%, 13%, and 9% of all Italian cases, respectively. The most affected provinces are Bergamo, Brescia, Milan, and Cremona, which together account for 33% of all Italian cases.[6] There is heavy seasonality of deaths (even more so in countries with high proportions of the elderly and people who smoke, like Italy), with 25% more deaths in winter as compared with summer.[7] Many of the excessive deaths are related to respiratory infections and are an annual occurrence. Although the infections are typically related to influenza, in 2020, SARS-CoV-2 is also a key contributor. In fact, in the 3 months prior to the outbreak, there were fewer deaths than is typical for the winter months in North Italian cities, thus leaving a larger pool of susceptible, elderly individuals.[8] The seasonal peak of deaths varies across hospitals, and it may be difficult to predict which hospital will have the maximal burden. The corollary is that some reserves of resources, such as ventilators, should be in a stand-by allocation with the ability to assign them rapidly to hospitals that saturate their capacity.

In the absence of prevalence and incidence data, including the results of serology testing, it is difficult to predict the effects of specific major public health decisions, such as lockdowns, on the course of the COVID-19 pandemic. For example, it is not known whether implementing a lockdown at a time when many people can infect others could lead people to spend more time in close quarters with the elderly and those who are susceptible. Similarly, it is not known whether a new epidemic wave may emerge when lockdown measures are removed. There are also unanswered questions about whether the stress and panic of a public crisis leading to major disruption and lockdown may have increased the susceptibility of elderly and frail individuals to a respiratory virus. Countries with aggressive early contact tracing and extensive laboratory testing (eg, Taiwan[9] and South Korea) seem to offer examples of successful containment. By comparison, in Italy both contact tracing and laboratory testing were more limited, and lockdown had to be used as a last, blind measure of desperation. It is important to study the effects of the policies that are adopted first on the expected wave of patients with severe illness who will need hospitalization.

Finally, a major question that should be answered is the causal contribution of SARS-CoV-2 infection to related deaths. It is difficult to differentiate between *deaths with SARS-CoV-2 infection* and *deaths caused by SARS-CoV-2 infection* because the vast majority of patients who have died had 1 or more other major pathologies (98.8% with at least 1 comorbidity, and 48.6% having 3 or more diseases) that contributed to their death.[10] Also, the lost quality-adjusted life-years of patients who died and any long-term consequences for patients who survive should be formally studied. Through this research, the relative burden of disease from COVID-19 can be better understood, and resources in overburdened health care systems during periods of crises can be better allocated.

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Back to top

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Published Online: April 7, 2020. doi:10.1001/jamainternmed.2020.1447

Conflict of Interest Disclosures: None reported.

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April 8, 2020

collateral damage

Carol Vassar, MD | retired community faculty UVM

We could learn from the experience in Italy a possible effect that such a disruption has on other patients. What was the effect on mortality for patients (and the population) that did not have COVID 19. How did that compare to other years. Knowing how this effected the rest of the population could influence the cooperation of the public. It would also be important for planning.

CONFLICT OF INTEREST: None Reported

April 9, 2020

Mortality comparison

Lovel Giunio |

Decisions have to be made on insufficient data. It is vital to question and reevaluate decisions as soon as new data and new ideas arrive. Contrarians are as important as data gatherers, and should be treated with civility, and arguments exchanged in honest discussion until a level of knowledge is reached that is necessary to make the next set of decisions. In many instances, it should be appreciated that there are not enough data, and many different explanations are valid, even if some less likely to be true.

On the other hand, contrarians should be ready to return the ...

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Italy's regional data comparisons will allow for a better understanding of the epidemic dynamics

Caterina Zanetti, MD, PhD | University Hospital of Padua

Authors state that it is difficult to predict the effects of specific major public health decisions, such as lockdowns, on the course of the COVID-19 pandemic.
Italy is a decentralized country. The national lockdown occurred at a time (March 10, 2020) when cases were unevenly distributed across the country: many thousands of cases and many hundreds of fatalities were already registered in Lombardy, Emilia, and Veneto, as opposed to few cases and fatalities registered among other regions.
So, comparing Italy's regional data, we will be able to analyze the effect of an early lockdown, as opposed to a late lockdown, ...

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April 9, 2020

Air Pollution and COVID19.

Enrique Barros, M.D. | Universidade de Caxias do Sul

Ioannidis et al, help clarify the state of scientific uncertainties arising from the COVID19 related high death toll in Italy. One other puzzle piece to investigate is the role of ambient air pollution, as some cutting edge research findings point to ambient PM2.5 levels as a significant contributor to COVID19 death toll in New York City.
(https://www.medrxiv.org/content/10.1101/2020.04.05.20054502v1.article-metrics).

CONFLICT OF INTEREST: Received a refund from the WONCA Air Health Train-the-Trainer Program

April 13, 2020

Use of convalescent plasma during the epidemic

Anthony Smithyman, BSc, PhD | Research Laboratory

As an immunologist I would be interested to learn from the Italian experience whether convalescent plasma/serum (from the 34,000 recoverees) has either already been used, or is projected to be used to treat COVID-19 patients during this crisis. If so this information would be extremely valuable for other regions/countries just entering the exponential infectivity phase.

If not, what were the reasons for not using this form of treatment? Scarcity of plasma, regulatory issues, lack of data, insufficient proof, or blood bank system simply overwhelmed? Italy has a highly sophisticated medical structure and it would be surprising if this ...

April 21, 2020

Italy's experience underscores the need for effective chronic disease management in the global response to COVID-19

TONY KUO, MD, MSHS | University of California, Los Angeles (UCLA)

We read with great interest Boccia et al.'s recent article on what other countries can learn from Italy's experience during the COVID-19 pandemic [1]. With 110,574 documented cases and 13,155 documented deaths as of April 1, 2020, the authors rightfully cautioned against rushed interpretation of death rates and immutable (e.g., age structure) as well as modifiable factors that may have contributed to this health crisis. The authors made an important distinction between deaths with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection versus deaths caused by the virus, pointing out that 98.8% of patients who had died had at ...

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