PATHOGENS AND GLOBAL HEALTH
2021, VOL. 115, NO. 4, 211–212
https://doi.org/10.1080/20477724.2021.1894399

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Lessons from the devastating impact of the first COVID-19 wave in Italy

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ABSTRACT

Herein, we are critically examining the chain of events and discussing previously unrecognized factors that led to the 'perfect COVID-19 storm' in northern Italy during the first epidemic wave in spring 2020. SARS-CoV-2 was circulating uncontrollably at least for five weeks before the adoption of containment measures, and the role of exponential growth in the spread of the virus, conveyed by a high R_0, was likely underestimated. An understanding of this failure's causes and contexts will help us to control the strong second wave of the pandemic we are now facing in Europe, and to be better prepared for future outbreaks.

KEYWORDS

SARS-CoV-2; COVID-19; epidemic waves; basic reproduction number R_0; day zero; asymptomatic cases

Italy was among the countries with the highest death toll records during the first wave of coronavirus disease 2019 (COVID-19) pandemic [1]. Understanding the reasons why this happened could help global efforts for optimal actions to confront both current and future COVID-19 pandemic waves.

Advanced age and comorbidities are established risk factors for severe cases of COVID-19. Compared to China, where 4,746 deaths (3 per million population) were recorded as of 25 October 2020 [2] and the median population age is 38.4 years [3], Italy's population (median age = 47.3 years) is comparatively aged. However, this demographic fact alone cannot explain Italy's 620 deaths per million in the same period; the populations of most European countries, which experienced significantly fewer deaths, are similarly aged (e.g. COVID-19 deaths per million were 120, 54, and 109 in Germany, Greece, and Austria up to 25 October, with corresponding population age medians of 45.7, 45.6, and 43.5 years) [2,3]. The death toll in Japan, which has the oldest population in the world (median age = 48.4 years) with the exception of the Principality of Monaco, was substantially lower than in Italy (14 *vs.* 620 deaths per million, as of 25 October 2020) [2]. High rates of ischemic heart disease, chronic obstructive pulmonary disease, and diabetes are prevalent in Italy, where the proportion of patients with a history of smoking is also high [4]; however, similarly high rates of smoking and related comorbidities are found in Greece, for example. Differences in the host genetics of the local population are rather unlikely to explain why the north of Italy was hit so hard, while the south was largely spared. Factors pertaining to the virulence of locally circulating viruses are also unlikely explanations.

Phylogenetic analyses suggested that SARS-CoV-2 entered northern Italy, presumably on a single introduction event, between the second half of January and early February 2020, although, currently, the earliest evidence of viral detection is ~3 months before Italy's first reported COVID-19 case [5]. By applying a compartmental modeling and numerical optimization approach, we estimated that 14 January 2020 is the most likely date for the introduction of SARS-CoV-2 to northern Italy [1]. This date precedes the official identification of the first COVID-19 cases in Italy (the two Chinese tourists in Rome on 31 January), and in Lombardy (the 38-year-old Italian who was admitted to a hospital in Codogno on 21 February following repatriation from Wuhan), by at least two and five weeks respectively. In Lombardy, containment measures were initially adopted on 22 February. On the eve of their commencement, the Champions League football match was held in the San Siro stadium in Milan in front of 45,792 spectators: a third of Bergamo's population who supported Italy's Atalanta and ~2,500 Spain's Valencia fans contributed to the spread of the virus locally and internationally [6]. Movement restrictions were expanded to all of Italy on March 8.

The epidemic thus had a critical period of approximately five weeks to grow. Mildly infected Italians were allowed to self-isolate at home, further spreading the virus as movement continued even under lockdown conditions. The initial COVID-19 case definition that included mandatory epidemiological criteria of history of travel to China, resulted in the scarce testing and

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identification especially of asymptomatic cases that were not likely to seek medical assistance [1]. The direct flights connecting Italy to China, as many Chinese immigrants work in the fashion industry in northern Italy, are also implicated in the early virus introduction and propagation. We estimated that the actual cumulative number of asymptomatic cases in Lombardy before the lockdown was 10–15 times the confirmed number of cases; moreover, we found the basic reproduction number R_0 to be 4.53, a value suggestive of very fast spread [1]. This R_0 is higher than previously reported by other studies, which did not consider the asymptomatic cases that can transmit the virus [1].

R_0, the average number of secondary cases caused by a single infected individual in a susceptible population, provides a measure of the contagiousness of infectious agents and the speed by which an epidemic is growing [7]. R_0 was likely underestimated in Italy, as was the role of exponential growth in the spread of SARS-CoV-2 that was circulating uncontrollably for weeks.

The realization of the devastating effects of SARS-CoV -2 spread came when the number of cases exploded in Lombardy, asphyxiating patients and the decentralized health system. A dramatic spike in deaths followed in very shortly after patients' onset of symptoms (8 days in Lombardy *vs*. 2–8 weeks in China), possibly due to the saturation of ICUs [1], and the lack of understanding of the disease phases then. Italy had indeed transformed into a 'red zone'. Who can forget the images of the army trucks that were massively transporting coffins from Bergamo to remote cremation sites because local morgues could not cope with the coronavirus deaths? The actual COVID-19 death toll could be much higher than confirmed since it is largely affected by the criteria used for death notification [1]. Two months of widened lockdown across Italy were required to lower R_e<1 and achieve some sort of control over the epidemic, until the second wave started to build.

The crucial question now is: are we better prepared for subsequent COVID-19 waves and possibly for future pandemics? Preparedness entails the long-term goal of intensifying basic research efforts to improve our understanding of coronavirus biology, and the urgently pressing goal of strengthening healthcare systems. The Italian healthcare system suffered cuts of more than €37 billion over the past decade [8], leading to severe shortages in ICU beds, medical equipment and personnel that contributed to Italy's tragedy during the first wave. Timely government action can save lives, as can the allocation of adequate resources. A few countries, including Sweden and the Netherlands, without the degree of medical shortages seen in Italy, intentionally let the virus spread and infect at least part of the population for some time during the pandemic. Nevertheless, delays in enforcing SARS-CoV-2 containment measures, whether deliberate or unintended as in the case of Italy, can cost lives. Extensive laboratory testing and early contact tracing, as well as genomic surveillance for the detection of viral variants with potentially altered biological characteristics pertaining to transmission or pathogenicity, following the examples of South Korea, Taiwan and the United Kingdom, respectively, offer learning strategies of successful containment from the first wave to the second and beyond.

Authors' contributions

CA and AT conceived the study. CA wrote the manuscript. All authors collaborated on content development, revised the manuscript and, approved the final version of the manuscript.

Disclosure statement

The authors of this manuscript declare no conflicts of interest regarding the publication of this paper.

Funding

No specific funding was obtained for this study.

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