Reliable quantification of COVID-19 mortality worldwide

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Abstract:
A proper understanding of COVID-19 mortality is central to effective responses. We examine the trends in mortality rates and totals in China, South Korea, Italy, Spain, and New York State to provide some estimate of possible best and worst-case scenarios of COVID-19 deaths in high-income countries. We review also the challenges in tracking mortality in low-income countries, where many deaths occur at home without medical certification, and for which alternative systems to document COVID-19 mortality will be needed. We also explain the role and appropriate timing of antibody-based surveillance to understand the extent of the first wave of COVID-19 and resulting case fatality rates.

Introduction

Understanding the metrics of deaths attributable to SARS-CoV-2 is central to understanding the current first wave of the COVID-19 pandemic and to planning for possible subsequent waves.

We examine trends in mortality rates and death totals in China, South Korea, Italy, Spain, and New York State[1,2] to outline the range of possible scenarios of COVID-19 deaths in high-income countries. We also discuss challenges and approaches to tracking COVID-19 mortality in low-income countries, where many deaths occur at home without medical certification. Finally, we comment on the importance of establishing denominators of the SARS-CoV-2 infected—including symptomatic and asymptomatic cases— to establish fatality rates.

Excess deaths from COVID-19 in settings with nearly universal death certification

COVID-19 mortality is currently concentrated in the USA, Canada, Italy, Spain, the rest of Europe and China and South Korea, where nearly all deaths are captured, registered and medically certified.[3] While data from national death certification systems are not immediately available, these countries also have separate reporting systems, usually to public authorities. Daily COVID-19 death reports by these authorities provide a robust way to track the epidemic curve in particular geographic areas. COVID-19 deaths are largely unaffected by variations and biases in who is tested over time. Once deaths undergo certification, deaths can be attributed to COVID-19, for which World Health Organization (WHO) has created a new International Classification of Diseases (ICD-10) code, U07.2. In some countries (e.g., the Netherlands), only deaths of people testing positive for SARS-CoV-2 are counted as definitely due to the virus. Hence, deaths attributed to COVID-19 could be taken as a lower limit. Missing deaths are uncommon in each of the above settings,[3] but during the peak crises period, reporting will be delayed. Of course, the actual number of COVID-19 deaths is related both to the number of infections as well as success in managing severe disease.

Older people have higher COVID-19 death risks in both Italy and China [Table], and men are more likely to succumb to COVID-19 than women.[4-6] Those with compromised lung function—including current and possibly former smokers—other chronic diseases, particularly cardiovascular disease and diabetes, or compromised immune systems are at higher risk of developing severe symptoms and of dying.

Table: Proportion of deaths and estimated case-fatality rate by age in Italy and China

Age	Italy		China	
	Proportion of total deaths	CFR (deaths/cases)	Proportion of total deaths	CFR (deaths/cases)
<20 years	0.0%	0.0% (0/940)	0.1%	0.1% (1/965)
20 to 49 years	1.2%	0.5% (84/17106)	6.2%	0.3% (63/19790)
50 to 59 years	3.6%	1.7% (243/14508)	12.7%	1.3% (130/10008)
60 to 69 years	11.2%	5.7% (761/13243)	30.2%	3.6% (309/8583)
70 to 79 years	35.3%	16.9% (2403/14198)	30.5%	8.0% (312/3918)
≥80 years	48.7%	24.4% (3310/13539)	20.3%	14.8% (208/1408)

Source: Author estimates based on references[4-6]

Lombardy region was the first to report COVID-19 cases in Italy, and accounts for nearly 60% of all COVID-19 deaths in the country to date. COVID-19 killed 8,000 Lombardians between March 3 and April 3.[6] In the same region, about 9,000 people died of *all causes* during the same one-month period in 2019—approximately a doubling of current death rates. Lombardy's daily death totals have stabilized in recent days and may be falling [Figure] but it is still too early to rule out further increases. If, for argument's sake, Lombardy will suffer three months each of about 8,000 excess deaths (similar to the time course of deaths from other coronaviruses that cause SARS and MERS[7,8]), then the total excess deaths would be about 24,000 COVID-19 deaths for the first peak of cases, out of an annual total of about 100,000 deaths in the region (or about a quarter of annual mortality added on[6]).

Outside of Lombardy, the proportions of COVID-19 mortality (or rates per population) are no more than half as large in adjacent Emilia Romagna, the second-hardest hit region in Italy, and lower elsewhere. Spanish COVID-19 death rates per population and their trajectory are lower, as shown in the Figure. Of concern, the death rates and their trajectory in New York state (which accounts for just under half of all American COVID-19 deaths to date) are moderately higher than those in Lombardy. However, only 13 days with sufficient deaths are available for New York.[1]

By contrast to Italy, the proportions of excess deaths are far smaller in China and South Korea, which acted aggressively to organize testing, isolation, and treatment to curb the spread of COVID-19 cases. The global pandemic began in Hubei Province, China, which reports about 3,200 COVID-19 deaths from January 26 to March 26.[1] This represents about 5% excess deaths of the approximately 69,000 deaths over the two months that occurred in 2018. Concern about under-reported COVID-19 deaths necessitates further scrutiny, including of total death counts during the period. In South Korea, most of the 170 COVID-19 deaths from January 19 to March 23 occurred in North Gyeongsang province and

Daegu City.[9] Hence, excess COVID-19 deaths represent about 3% of the 5,600 deaths over two months that occurred in 2018.

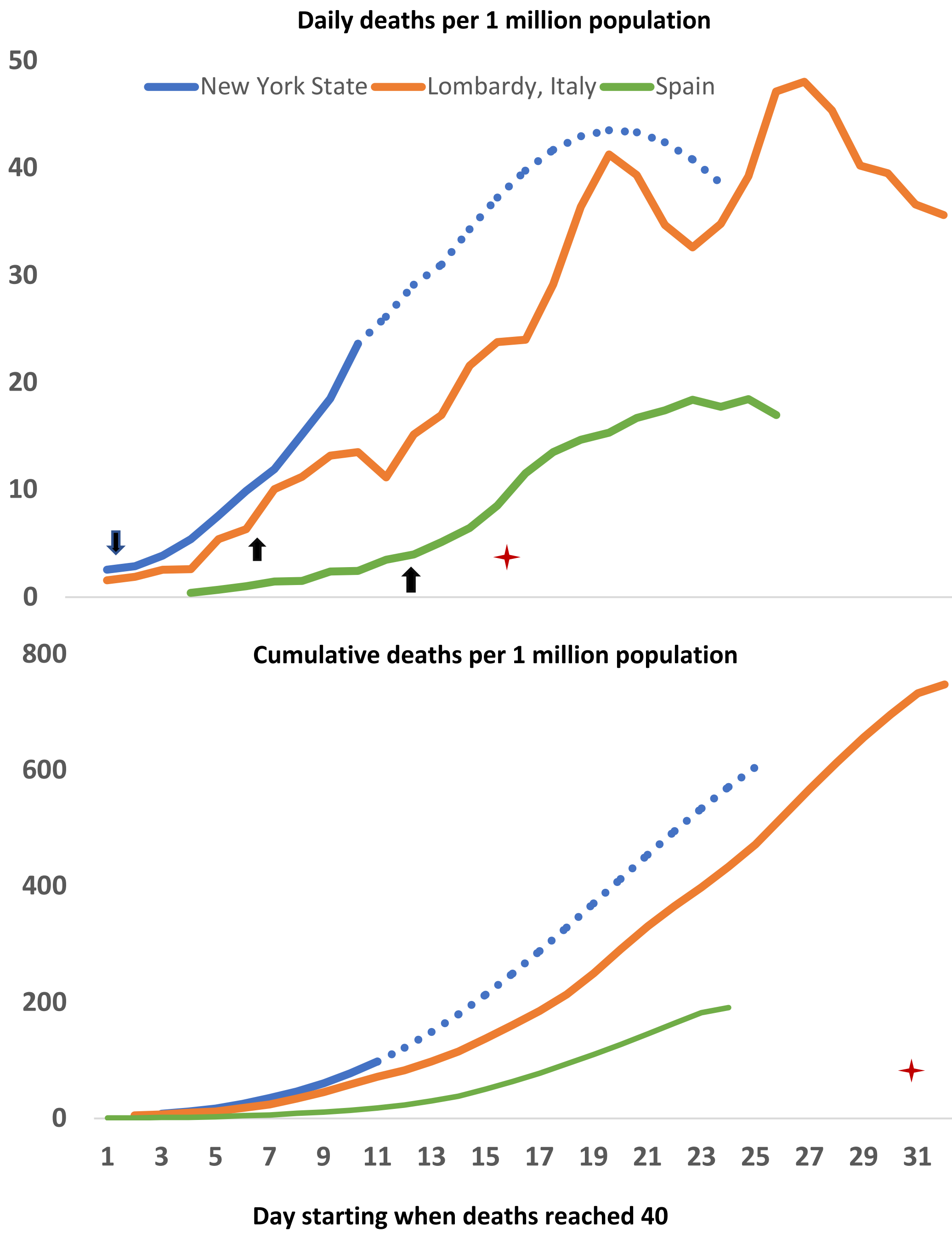

Figure: Rolling 3-day average of daily death rates (top panel), and cumulative death rates (bottom panel) per 1 million (M) population in New York State, Lombardy, Italy and Spain
Red crosses represent the peak daily death rate and cumulative death rate observed in Hubei, China. Data sources [1,2]. Black arrows represent the starting day of lockdowns in each area.
Blue solid line for New York represents actual deaths, while dotted represents the modelled projections.[11]

Initial infectious disease models have produced estimates of total COVID-19 deaths in the United States of 1 to 2.2 million (roughly 40% to 80% over and above the usual annual total of 2.8 million deaths) if no action were taken. These same projections suggested 510,000 COVID-19 deaths in the UK, roughly 90% above the usual annual total of 541,000 deaths.[10] Model-based estimates, taking into account physical distancing through May 2020, project 16,000 deaths over four months in New York, or about 30% excess (with a range of 18%-40%[11]) of total mortality in the state over that period.

These models are highly uncertain for obvious reasons.[12] However, examination of mortality in particular areas provides a crude, but plausible assessment of the lower and upper end of expected COVID-19 deaths. For the USA and the UK, the lower estimate of 2-5% of mortality in China and South Korea might be unrealistic given current growth of cases and deaths. However, it is equally improbable that the whole of each country would experience the high death rates observed in Lombardy, or that the whole of the USA will mimic the mortality patterns emerging in New York City.

Possible lower death totals than expected by models should not give false comfort. First, for every death there are many more cases needing hospitalization. In the whole of Italy, per death there were about three hospitalized cases including many who needed intensive care.[6] Model-based estimates for the USA suggest that above age 55 years, ten people will need hospitalization for every COVID-19 death.[11] Second, the sick cases and deaths are clustered over time, such that they can overwhelm health systems capacity. Italy faced more pressures in one month on ventilator and critical-care bed supply that routinely handle burdens corresponding to 9,000 acute pneumonias deaths per year. Finally, if COVID-19 behaves as has MERS, or influenza, we might have seasonal recurrence. On the other hand, SARS occurred only once in 2003/4.[7,8]

Tracking COVID-19 deaths in lower-income countries

The evolution of COVID-19 epidemics in low- and middle-income countries (LMIC) outside of China is largely undocumented. Many such countries in Asia and Africa lack both adequate death registration and medical certification,[13] and also have limited public health reporting. Under the best of circumstances, most deaths occur at home without medical attention. Hence, unlike in the above settings, a large increase in COVID-19 deaths might go undetected. South Africa has a reasonable mortality surveillance system, and India, Mozambique, and Sierra Leone implement verbal autopsies among random samples of deaths.[14] However, most other LMICs have no such systems.

Emergency, albeit imperfect, solutions to gather better mortality data need to be considered. Many city authorities in LMICs record deaths. They can start daily reporting of all deaths (regardless of cause) by age and sex. This would provide a crude baseline to assess mortality from COVID-19, if indeed there is a large excess in overall mortality from COVID-19. Another feasible strategy might be to conduct SARS-CoV-2 antigen and antibody testing among a convenient sample of post-mortems that are done in various LMICs. A similar post-mortem study in South Africa was able to establish that HIV was common in the population, by showing high prevalence in adults killed in road traffic accidents or from causes unrelated to HIV.[15] Post-mortem sampling would have obvious biases, but could nonetheless give some crude estimate of COVID-19 distribution and background prevalence. Finally, the COVID-19 pandemic is a sharp reminder about the need to expand the number of LMICs that conduct nationwide cause-of-death surveys on random populations.[16]

Reliable denominators of infected populations

Case fatality rates (CFR) are defined as deaths divided by the cases, which are typically defined as those testing positive for SARS-CoV-2 on antigen testing or using the WHO case definition. CFR estimates early in infectious outbreaks tend not to be reliable, mainly because of underestimating the denominator. For example, in the influenza A H1N1 outbreak in 2009, the early CFRs from Mexico (which were instrumental in WHO's declaration of a global emergency) were at least five-fold higher than the eventual estimated CFR of about 0.2 to 0.5%.[17]

WHO's current COVID-19 CFR estimate is about 2-3%, based on early data, but has obvious limitations.[18] The one population where CFR was measured reliably was among the *Diamond Princess* cruise ship, which tested 3,063 and found 712 positives (23%) of which 10 (1.4% CFR) have died and 18% were asymptomatic.[1,19] However, these were generally older adults and deaths are too few to apply to other populations. Around the world, the reported CFR ranges from less than 1.0% in areas of China outside of Wuhan, to 13% in the Lombardy region of Italy, with many figures in between—e.g., 6% in non-Lombardy Italy and in Wuhan.[1,18] It is impossible to know how much this variation reflects real and important differences, or is a consequence of the lack of a denominator of infected individuals, many of whom never develop symptoms.

Antibodies produced in response to infection—even among people who were asymptomatic—should be detectable for some period after the infection is cleared, and would provide some indication of the likely susceptible and non-susceptible (or partially immune) population. While evidence is scant, it appears that antibodies in infected patients are mounted aggressively.[20] Antibody testing has some urgency because we don't know how long antibodies will last.

A practicable strategy would be to survey randomly-selected individuals (and some risk-selected populations such as health care workers and nursing home residents) shortly after the first wave of infection has largely abated in an area. Use of dried blood spots from finger pricks are sufficiently simple and safe to enable self-collection at home. These samples can be mailed centrally, and tested with current, and future improved antibody tests.[21]

In sum, accurately characterizing the dynamics of this pandemic requires worldwide, rapid, and systematic examination of actual COVID-19 deaths by age, sex, location, access to care, and other potential risk factors, including robust comparisons to baseline mortality in previous years. It will also require better denominators of the proportions of infected populations with strategic deployment of antibody assays.

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