The many estimates of the COVID-19 case fatality rate

Since the outbreak of coronavirus disease 2019 (COVID-19) began in December, a question at the forefront of many people's minds has been its mortality rate. Is the mortality rate of COVID-19 higher than that of influenza, but lower than that of severe acute respiratory syndrome (SARS)?

The trend in mortality reporting for COVID-19 has been typical for emerging infectious diseases. The case fatality rate (CFR) was reported to be 15% (six of 41 patients) in the initial period,[1] but this estimate was calculated from a small cohort of hospitalised patients. Subsequently, with more data emerging, the CFR decreased to between 4·3% and 11·0%,[2,3] and later to 3·4%.[4] The rate reported outside China in February was even lower (0·4%; two of 464).[5]

This pattern of decreasing CFRs is not surprising during the initial phase of an outbreak. Hard outcomes such as the CFR have a crucial part in forming strategies at national and international levels from a public health perspective. It is imperative that health-care leaders and policy makers are guided by estimates of mortality and case fatality.

However, several factors can restrict obtaining an accurate estimate of the CFR. The virus and its clinical course are new, and we still have little information about them. Health care capacity and capability factors, including the availability of health-care workers, resources, facilities, and preparedness, also affect outcomes. For example, some countries are able to invest resources into contact tracing and containing the spread through quarantine and isolation of infected or suspected cases. In Singapore, where these measures have been implemented, the CFR of 631 cases (as of March 25, 2020) is 0·3%. In other places, testing might not be widely available, and proactive contact tracing and containment might not be employed, resulting in a smaller denominator and skewing to a higher CFR. The CFR can increase in some places if there is a surge of infected patients, which adds to the strain on the health-care system and can overwhelm its medical resources.

A major challenge with accurate calculation of the CFR is the denominator: the number of people who are infected with the virus. Asymptomatic cases of COVID-19, patients with mild symptoms, or individuals who are misdiagnosed could be left out of the denominator, leading to its underestimation and overestimation of the CFR.

A unique situation has arisen for quite an accurate estimate of the CFR of COVID-19. Among individuals onboard the Diamond Princess cruise ship, data on the denominator are fairly robust. The outbreak of COVID-19 led passengers to be quarantined between Jan 20, and Feb 29, 2020. This scenario provided a population living in a defined territory without most other confounders, such as imported cases, defaulters of screening, or lack of testing capability. 3711 passengers and crew were onboard, of whom 705 became sick and tested positive for COVID-19 and seven died,[6] giving a CFR of 0·99%. If the passengers onboard were generally of an older age, the CFR in a healthy, younger population could be lower.[7]

Although highly transmissible, the CFR of COVID-19 appears to be lower than that of SARS (9·5%) and Middle East respiratory syndrome (34·4%),[8] but higher than that of influenza (0·1%).[9,10]

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