Editorial

The Facts, Fallacies and Uncertainties about Coronavirus Disease 2019 (COVID-19)

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It is now widely recognised that the coronavirus disease 2019 (COVID-19) outbreak has become the most significant pandemic of the century, and that we are only experiencing its initial stages.[1] After weathering the first wave of COVID-19 from around the world, it is appropriate to pause at this juncture to take stock and make some sense of this new respiratory infection to better anticipate its trajectory and the prospects for effective interventions.

The unprecedented speed at which the global scientific and public health communities have collaborated, collated and published their findings—a large proportion of which had been expedited in pre-print versions—has enabled us to begin to view a clearer picture, at least of some important aspects, of this pandemic. Unfortunately, it has also resulted in publications that were of poor quality and had errors by even some of the most prestigious medical journals.[2]

Most reports of COVID-19, especially in the media, had described it as a deadly respiratory tract infection with the assumption of a high case fatality rate (CFR). This is a fallacy which might lead, in certain situations, to inappropriate reactions, decisions and actions. The CFR of any new infectious disease can only be definitively known after epidemiological investigations are completed.[3] This is not yet the case for COVID-19. However, the salient clinical and epidemiological features in confirmed COVID-19 patients had been well described and a specific diagnostic test had been widely deployed globally. Based on this case definition, most experts now estimate that the CFR of COVID-19—as it is currently defined—is about 1%.[4] This is higher than seasonal flu, which is 0.1%, but is a lot less lethal than many other infectious diseases.

An important and—for a respiratory tract infection—a rather unusual feature of COVID-19 is the very high proportion of infections that are very mild or even asymptomatic. Consequently, the true CFR of this disease can only be determined after extensive population-based serological investigations are completed.[5] Preliminary results from a few limited serological surveys in selected populations suggested that the number of infected people may be much higher than those detected using current methods. One may conclude that the CFR of COVID-19 infection itself may be well below 1%. This makes it much lower—and less deadly—than severe acute respiratory syndrome that had a CFR of 14% in Singapore or the Middle East respiratory syndrome which had a CFR of 39% based on a meta-analysis.[6]

The likelihood of dying from COVID-19 may also be appreciated by comparing the mortality rates of patients hospitalised with COVID-19 against those with community-acquired pneumonia (CAP). A nation-wide analysis of outcomes of hospitalised patients with COVID-19 from 575 hospitals in Mainland China had reported an overall mortality rate of 3.2%; the rate was 7.3% in Hubei Province, the epicentre of the pandemic, against 0.3% outside the epicentre.[7]

In Singapore, the hospital mortality rate for COVID-19 is <1% and was influenced by case severity and hospital admission thresholds. This finding contrasts sharply with that of a recent large study from the island state that found a hospital mortality rate of 13.4% for CAP,[8] which was comparable to findings on expected mortality from CAP in the literature. Thus, one may say with some degree of certainty that, in Singapore, it is much less risky to be hospitalised with COVID-19 than CAP. Indeed, there is about a 10-fold difference in the risk of dying from these 2 diseases in local hospitals. Important factors that should be taken into account for the high hospital mortality rates reported in Hubei Province, Europe, the United Kingdom and the United States included extreme

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case overload on acute care services, particularly the availability of ventilators, inadequate protective equipment and COVID-19 infections and deaths among medical staff.[9]

Additionally, there is a great deal of interest and concern about COVID-19 as a potent killer of older adults.[10] Consequently, there was a spate of public health recommendations and advisories on ways to avoid infection by the older population. Although old age is a pivotal risk factor for mortality in respiratory infections, it is not unique to COVID-19 and is true of pneumonia that is caused by all types of pathogens. Age is incorporated into the most widely used clinical severity score in CAP, the "CURB-65" (Confusion, Urea, Respiratory rate, Blood pressure and ≥65 years old).[8] The recommendation that influenza and pneumococcal vaccines should be administered to the older healthy population is also motivated by such expectations.

It is still not certain whether COVID-19 poses any special risk to the elderly compared to other chest infections; careful examination of age-specific mortality rates in COVID-19 against that of CAP did not suggest that COVID-19 is more deadly than CAP in older patients. It should, however, be noted that most bacterial CAP infections are not transmissible; thus, they may not have the wider impact of COVID-19. Still, it is prudent to advise caution in the elderly against all types of respiratory tract infections, but keeping them "safe" through strict isolation in an extended lockdown while the rest of society returns to normal life could be viewed as another version of ageism that needs to be guarded against.

With daily reports in the media on the death toll and images of rows of newly dug graves in Qom, churches packed with coffins in Lombardy and body bags inside container trucks in New York, COVID-19 has been viewed as a deadly disease. However, one not only fails to consider the total number of infected individuals in those communities, but also fails to appreciate the real denominators of so many deaths for an accurate assessment of how truly lethal COVID-19 is. Uncontrolled epidemics can grow exponentially; when they reach the steep upstroke of the exponential curve in a naïve population, the number of cases and deaths will increase and spiral.

In COVID-19, the fatalities form just the tip of an iceberg that comprises a huge number of mild cases below the surface of detection. In communities that did not roll out robust detection and testing programmes, this translates into a sudden, unexpected surge in the number of critically ill and dying patients that threaten to overwhelm an unprepared health system. This was especially true of COVID-19; recent studies of the initial outbreak in Mainland China that used more precise information based on integration of high-resolution domestic travel data and early infection data reported in provinces other than Hubei Province to infer outbreak dynamics in Wuhan City had calculated the basic reproductive number (R0) at 5.7.[11] This was much higher than previous R0 estimates of 2–3 and suggested that COVID-19 was more contagious and spread faster and wider than previously thought. This high infectivity—combined with a large asymptomatic base—accounted for the apparent paradox of a high death toll despite a relatively low CFR.

When the outbreak is at the steep upstroke phase of the exponential curve, the sheer number of individuals in the community who become very ill at the same time is likely to overwhelm any health system since there will be a sudden surge in the number of critically ill patients.[9,12–14] Consequently, the ongoing efforts in Singapore to slow down the spread of COVID-19 among her migrant workers are critical; by mounting huge infrastructural and manpower resources to provide appropriate care for infected workers, it has helped to protect the functional integrity of her acute health services.

An important reason for the high contagiousness and transmission rate of COVID-19 is the potential for spread by asymptomatic and thus, undetected cases. By using a networked, dynamic metapopulation model and Bayesian inference to model the early spread of COVID-19 in Mainland China, analysis of data from Tencent—one of the largest social media and technology companies in the world—concluded that 79% of COVID-19 cases were attributed to undocumented infections before travel restrictions were implemented in the country on 23 January 2020.[15] These novel clinical and epidemiological features of the COVID-19 outbreak pose a much greater challenge to interventional strategies than had been previously anticipated based on models that were developed from respiratory pandemics of the past. To be effective against COVID-19, these interventions must be implemented as early and as stringently as possible.

Additionally, since the epidemic is driven predominantly by asymptomatic and thus undiagnosed cases, conventional symptom-based contact tracing is

relatively ineffective. This may also account for the success in South Korea and Taiwan to control their COVID-19 outbreaks through contact tracing using social media and mobile phone technology without the need to lock down a whole community.[16,17]

To be effective in eliminating COVID-19, there is an urgent need to learn more about the critical unknowns of this new disease, particularly its molecular biology, immunology and pathophysiological mechanisms and pathways to disease, complications and death.[18,19] Meanwhile, a high degree of control and containment can still be achieved when deliberate efforts are made to apply—with insight—the valuable and costly lessons that have been learned in the first few months of this spectacular global pandemic.

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