

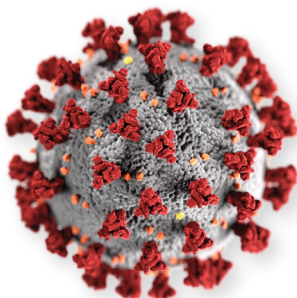
The Future of COVID-19 from a Clinical Perspective

What is the current state of COVID-19 infections and when will the pandemic end?

Dominic E. Dwyer

By 10 December 2020 there have been over 68 million cases of COVID-19 worldwide, resulting in over 1.5 million deaths

[SLD: as of 28/Jan/2021 the number is over 100 million cases and 2.1 million deaths]. As these are laboratory-confirmed cases, the true numbers are likely to be much higher as not everybody seeks medical care and testing access in many countries is limited. In Australia, there have been almost 28,000 cases and 908 deaths, with the bulk of these occurring in the second wave in Victoria in mid 2020. Australia and New Zealand are lucky in their remoteness, so that the banning of inbound travel allowed the opportunity to successfully implement physical distancing and improved infection control practices. Given there are as yet no effective antiviral drugs and licenced vaccines, these responses are remarkably similar to those undertaken during the 1918-19 influenza pandemic.



After the initial outbreak in China (starting in Wuhan, Hubei province) in early 2020, the greatest burden in cases has occurred in North and South America, and Europe. In many

countries there has been more than one wave of COVID-19 activity. The extent of outbreaks in Asia varies from country to country, but most countries have had less impact from COVID-19 than in the Americas and Europe. However, infection rates in India, Bangladesh, Pakistan, and Indonesia remain high, and these outbreaks are continuing. Activity in the Pacific has been relatively modest.

In general terms, the mortality rate has decreased in successive waves. However, this is not likely due to a reduction in virulence of SARS-CoV-2 [SLD: this is the virus that causes COVID-19; the term 'COVID-19' refers to the disease], but more likely to represent better initial diagnosis, testing and management than in the early pandemic stages. Mutations in the virus require monitoring, as there is the potential that new strains could be more (or less) virulent. Given our experience with influenza pandemics, it is likely that a number of waves will occur until a successful vaccine is rolled out.

Government public health responses around the world have varied. In Australia, the government's principles are to minimise the number of people becoming infected or sick, minimise how sick people become and reduce the mortality rate, manage the demand on healthcare systems, to assist the population to manage their own risk and the risk to their family and community, support work towards vaccine and make

sure that any future vaccines are available to Australians for free. These principles will require an enormous amount of work, and the time and infrastructure to respond to these will vary from country to country. Countries have taken different approaches to community lockdowns, international and within country travel, infection control measures (such as mask use), etc.

An important drive to public health responses is an understanding of how SARS-CoV-2 is transmitted. Respiratory viruses can be transmitted in a number of ways: droplet transmission which requires individuals to be within a metre or so of each other, aerosol transmission where virus can spread beyond one or two metres, and fomites where the virus survives on surfaces for prolonged periods of time. There is increasing evidence that aerosol transmission is important in SARS-CoV-2 transmission, which makes it somewhat different to influenza and other respiratory viruses. Certain events promote aerosolisation of viral particles – these include within hospitals (intubating patients, collecting swabs) and in the community (singing, being in enclosed spaces). During COVID-19, closed environments such as aged care facilities, cruise ships, and hospitals have been important contributors to the spread of SARS-CoV-2.

An important response to the outbreak has been aggressive and early laboratory testing. Countries with early high rates of testing (such as Australia, New Zealand, Singapore, and Taiwan) have generally fared better than countries who, although now testing large numbers of people, implemented widespread testing more slowly. There is also an issue of access of testing in different countries due to cost and reagent or kit availability. As community serostudies to detect SARS-CoV-2-specific antibodies are undertaken, it is likely that the currently reported rates of laboratory-confirmed infection are a significant underestimate of the true numbers of cases. Technology has allowed the laboratory enhancement of public health responses. For example, the ready availability of rapid whole genome sequencing of SARS-CoV-2 has allowed clearer identification of COVID-19 clusters, thus

enhancing responses to such clusters.

A major impact on the world economy has been the reduction of international travel, and even almost 12 months after the start of the pandemic, international travel is yet to return to anything like pre-pandemic levels. This obviously has a significant impact on the economies of all countries, particularly those highly dependent on tourism.

A large range of antiviral drugs and immunomodulators have been trialled in COVID-19 disease. At this stage, there is no 'standout' antiviral agent for either severe or mild disease. Successful antiviral therapy is complicated by the need to identify cases quickly, a problem given that a large proportion of patients are asymptomatic or only mildly symptomatic. Such people, of course, can still transmit the virus.

A successful vaccine against SARS-CoV-2 is the most likely way to control the pandemic and to minimise disease severity. Over 50 vaccines are in clinical trial, and another over 150 other vaccines are in pre-clinical study. Some vaccines have already reported high rates of efficacy, and others have fallen by the way side. Producing an effective vaccine is one thing, but being able to provide the world's population with two doses of the vaccine is an enormous logistics task. The vaccine studies have been rapid, and long-term safety data in all age groups is still required. It is also unknown how long immunity to SARS-CoV-2 will last, whether immunity is induced by natural infection or vaccination. It is yet to be determined if annual vaccination (like with influenza) is required. ■

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Prof. Dominic E. Dwyer is the Director, NSW Health Pathology Public Health Pathology State-wide Service; and Director, NSWHP- Institute of Clinical Pathology & Medical Research, Westmead, NSW, Australia. Prof. Dwyer was also on a select team under the auspices of the World Health Organization to investigate the origins of SARS-CoV-2.

Email: Dominic.Dwyer@health.nsw.gov.au