DEPARTMENT OF THE PRIME MINISTER AND CABINET
TE TARI O TE PIRIMIA ME TE KOMITI MATUA

TITLE	**Possible Long-Term Outcomes or Endings for the COVID-19 Pandemic**
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Introduction

1. The Insights and Reporting Team in DPMC's COVID-19 Group have analysed what the potential long-term outcome, or ending, of the COVID-19 pandemic may look like, by drawing on information about how pandemics of the late 19th, 20th and 21st centuries and illnesses similar to COVID-19 have progressed. It should be noted that due to changes in interconnectivity and scientific understanding, that pandemics occurring closer to the present day are likely to present more relevant data than those occurring earlier.

2. The definition of the end of the pandemic is left somewhat vague, as what constitutes the end of a pandemic is something that is open to debate. For example, the pandemic ends when the virus becomes endemic, i.e. the disease continues to circulate but overall infection rates remains roughly stable over time. Another way to define the end of the pandemic could simply be to say the point in time when public bodies decide to stop taking action to control the virus, and public sentiment moves to a state of acceptance of the virus's presence.[1] [2] This insight focuses on possible trajectories of the pandemic over the coming years.

3. This draws on work carried out by a number of thought leaders including epidemiologists on this topic. For example, the World Health Organisation produced three likely scenarios for the pandemic, including: 1) *endemic*, 2) *flu-like*, and 3) *an ongoing pandemic through new variants*.[3] Slightly modified versions of scenarios are detailed below, as well as a fourth scenario, of *suppressed and eliminated*. This fourth scenario is considered here as a survey of 119 immunologists carried out by *Nature*, a world leading multidisciplinary science journal, published in February 2021, found that 39% of respondents thought elimination was either likely or very likely at least from some regions. It should be noted that this survey was carried out before the delta and omicron outbreaks, which may have impacted opinions on the likelihood of this scenario among respondents. [4]

4. The scenarios detailed in this insight can be summarised as follows:

   - **Scenario 1 - Common Cold-like Endemic Coronavirus**: COVID-19 remains contagious but causes mild disease in most cases. Most people catch the disease in young age and develop immunity to severe infection later in life. Vaccines provide further protection to vulnerable groups. **Likely.**[1]
   - **Scenario 2 - Flu-like Seasonal Coronavirus:** COVID-19 presents as recurring epidemics when the conditions of transmission are favourable (similar to seasonal flu). COVID-19 continues to circulate as in scenario 1, but in a seasonal pattern and requires reformulation of vaccines. **Realistic Possibility.**
   - **Scenario 3 - Ongoing Pandemic through New Variants:** A new COVID-19 variant evades immunity, overloads health systems and returns the world to a situation similar to the start of 2020. **Unlikely.**
   - **Scenario 4 - Suppressed and Eliminated:** COVID-19 is initially restricted to a few locations before eventually being completely eradicated as a result of herd immunity through infection and vaccination. **Highly Unlikely.**

[1] See appendix for probability language key.

5. These scenarios and their likelihood of occurring are elaborated on below.

Scenario 1 – Common Cold-like Endemic Coronavirus

Similar Scenarios in History

6. There are currently four endemic coronaviruses circulating in the population, designated as OC43, 229E, NL63, and HKU1, that are endemic to human populations. It is thought that at least three of these viruses have been circulating in humans for hundreds of years, whilst two of them are responsible for 15% of all respiratory infections. In the case of the currently endemic coronaviruses, the virus is often caught in childhood, which in turn leads to an immune response, which although may wane and not prevent reinfection entirely, does prevent the person getting severe cases later in life from the same infection. In this scenario therefore the virus stays present, but enough people have immunity through infection or vaccination that it becomes a milder illness encountered in childhood when it is typically mild.[5]

7. A possible historic example of where this transition from epidemic coronavirus to endemic coronavirus may have occurred is the 1890 pandemic, often referred to as the 'Russian flu pandemic', although the evidence suggesting this is based on historic records rather than definitive scientific observation. Despite the name there is evidence to suggest that the pandemic was caused by the OC43 coronavirus, rather than a strain of influenza. The evidence comes from genetic analysis which suggests the OC43 virus jumped from bovines to humans at around the same time the 1890 pandemic occurred. The 1890 pandemic was characterised by symptoms similar to flu, but also included patients reporting a loss of taste and smell, similar to COVID-19, and not something observed during flu pandemics.[6] The first outbreaks of the illness occurred in 1889 in a region stretching from Northern India to Siberia, before moving westward through Europe and to the Americas before reaching Australia, Africa, and other parts of Asia by the second half of 1890.[7] Other similarities include the fact that the pandemic came in a number of waves and that some patients who recovered reported a lingering feeling of exhaustion similar to that of long-COVID.[8] It is unclear what the final death toll from the 1890 pandemic was. Also, since there are no samples of genetic material available, it is impossible to prove definitively whether the OCR43 coronavirus, which circulates today and is a cause of the common cold, was the virus behind the pandemic.[9]

Likelihood

8. It is **likely** that COVID-19 will become endemic, and something encountered in childhood as a mild illness, based on the current behaviour of the four other endemic coronaviruses, but it may take a number of years to be realised. The survey of more than 100 immunologists mentioned earlier, found that 89% of respondents think that the virus will become endemic, and continue to circulate in pockets of the population. This would mean a scenario similar to either endemic or flu-like COVID-19 (scenarios 1 and 2) depending on how the virus evolves and how governments respond with public health measures.[10] It is, however, unclear whether COVID-19 will behave in the same way as the four endemic coronaviruses. It is also unclear how long the process of becoming an endemic virus would take.[11] The likelihood of COVID-19 become endemic is also strengthened by the evidence suggesting that this is the path taken by coronavirus OC43, during the 1890 pandemic. Although not conclusive, evidence suggests that OC43 caused a major pandemic before becoming endemic and now is a major cause of the common cold.[12]

Wider Impacts

9. Should COVID-19 become endemic, it is **likely** that the COVID-19 virus will have little wider impact on New Zealand society. Like other coronaviruses, COVID-19 would continue to cause illness similar to that of the common cold, with most people coming into contact with it in childhood. The most serious likely impact on society is that those that are at risk of developing serious illness as a result of COVID-19 infection, may need to continue to receive regular vaccinations or in the worst-case, be shielded from certain activities, at least for a few years after the end of the pandemic. Under this scenario however it is likely that even for those at-risk groups, COVID-19 infection will lead to a less severe illness than has

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been observed during the pandemic, due to vaccinations and previous exposures. The more stringent public health measures for the wider public such as lockdowns are unlikely to be required, beyond awareness of steps to improve hygiene and potentially the requirement for further vaccinations. The economic, and social impacts that the COVID-19 pandemic had are likely to begin to be resolved. It also important to note however that in order for this scenario to be realised globally, a significant amount of the world's population would need to either contract COVID-19 to develop immunity, or be vaccinated, which may take a number of years and would mean the pandemic is drawn out.

Scenario 2 - Flu-like Seasonal Coronavirus

Similar Scenarios in History

10. Influenza (or flu-like) pandemics, occur when populations are exposed to a new strain of influenza virus. By the time they have become seasonal, a large proportion of the population has become immune, either through vaccination or through prior infection. Seasonal outbreaks of flu are then observed in colder months for many reasons such as spending more time indoors near other people.[13] A feature of the seasonal flu is the presence of seasonal waves of the disease and distinct seasonal variants. COVID-19 may follow a similar fate achieved by a drop in infections through acquired immunity either through contracting the disease as in the 1918 flu pandemic or through vaccination as in the three subsequent flu pandemics. This may point to a possible end-road for the current pandemic. Another feature of the seasonal flu is that due to the evolution of influenza viruses, annual vaccines must be reformulated, which may also be an outcome should this scenario be realised.

1918 Flu Epidemic- (Spanish Flu) - 1918 – 1919.

11. The Spanish flu of 1918 - 1919 was the most severe influenza outbreak of the 20th century and was caused by the influenza A subtype H1N1 and is thought to have resulted in between 25 and 50 million deaths worldwide.[14] The pandemic occurred in three waves, first occurring in March 1918 during World War I. It remains unclear where the virus originated, however it quickly spread through Western Europe. This first wave was characterised by relatively mild symptoms. However, In August of 1918, a second more deadly wave of the virus developed, followed by a third wave in the winter of 1918 - 1919. The second and third waves were noted for being particularly deadly amongst 20 to 40 year-olds, a unique feature of this particular outbreak, and spread to almost every part of the inhabited world, breaking out first in ports before spreading to the wider population. [15] [16] The virus re-emerged in early 1920, although faded again by the spring of that year. As with other flu viruses its spread was faster during winter months, partly due to people spending more time indoors. Public health measures such as social distancing, mask wearing, isolating and encouraging handwashing were also put in place. In some places, public spaces such as schools and non-essential businesses were closed. [17] The pandemic is believed to have come to an end due to a combination of increased immunity after infecting around a third of the global population, and the process of attenuation whereby the virus becomes less severe. Viruses which are descendants of the Spanish virus continue to circulate today.[18]

1957 Flu Pandemic (Asian Flu) – 1957 - 1958

12. The 1957 flu pandemic began in February 1957 with the first case reported in Singapore. The pandemic was caused by a substrain of the H2N2 influenza virus, which was a strain of the virus originating from a recombination event between avian and human influenza viruses. It is thought the virus killed between 1 and 2 million people worldwide and is the least deadly of the 20th century's three major flu pandemics.[19] [20] The virus spread throughout China during the opening months of the pandemic and reached the United States by the summer of 1957. Infections initially spread slowly in the United States; however, cases began to be reported, particularly amongst the young, elderly and pregnant women, during a second wave with a major upswing in cases in the northern hemisphere beginning in November 1957. [21] The 1957 flu pandemic came to an end with the rapid development of a vaccine. In the 1960s

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the human H2N2 strain underwent mutations resulting in more minor outbreaks, before being displaced in humans by the H3N2 virus that resulted in the 1968 flu pandemic. [22] [23]

1968 Flu Pandemic (Hong Kong Flu) – 1968 - 1970

13. The 1968 flu pandemic was a global outbreak of the H3N2 influenza virus originating in China in July 1968 and lasted until 1970 and is believed to have killed between 1 and 4 million people during this period. It is also suspected that the virus evolved from the 1957 pandemic flu virus H2N2 via a process known as antigenic shift. Because the virus maintained some of its original characteristics, some of those infected during the 1957 epidemic apparently retained some immune protection. [24] This particular strain of the influenza virus was very contagious and resulted in 500,000 cases within two weeks of its emergence in Hong Kong in July 1968. Within a matter of months, the virus was detected in the United States, carried by soldiers returning from Vietnam, and by December had spread throughout the United States and Western Europe before infecting parts of Africa, Japan, and Australia. The highest levels of mortality were observed in infants and the elderly, and whilst a vaccine was developed it was only made available after the pandemic had peaked in many countries.[25] The 1968 flu pandemic occurred in two major waves with the second causing the greatest number of deaths in most countries. The end of the pandemic came about after the arrival of vaccines, new antiviral drugs, and the accumulated immunity of populations. The H3N2 strain of influenza has not disappeared but is now a recurring winter flu, still present today, in the same way as the Asian flu of 1957.[26]

2009 Flu Pandemic (Swine Flu) – 2009 - 2010

14. Just as the Spanish flu epidemic of 1918 – 1919, the swine flu epidemic of 2009 was caused by the H1N1 strain of influenza, albeit a novel version of the strain. In comparison to the three major flu pandemics of the 20th century, its impacts were limited, resulting in the deaths of between 151,700 and 575,400 according to the US Centers for Disease Control and Prevention.[27] The first detected case of the pandemic was detected in the spring of 2009, in the United States, although it is believed that it may have originated in Mexico. After this point the pandemic spread quickly around the world. It was noted that through antibody testing that very few young people had an existing immunity to the disease whilst around 60% of those tested over 60 years old, did have existing immunity, likely due to exposure from earlier H1N1 flu viruses. This is likely the reason why 80% of swine flu related deaths were amongst those younger than 65, which compares to typical seasonal flu where between 70 – 90% of deaths occur in those aged 65 or older. It was also noted that existing vaccines for seasonal flu offered little protection to the virus.[28] As with the previous H1N1 influenza pandemic in 1918 – 1919, the swine flu epidemic came to an end after a level of herd immunity had built up amongst affected populations. Unlike the earlier H1N1 pandemic this was aided by the development and deployment of a vaccine to combat the new strain. The vaccine was made available at the end of 2010, and by November 2010 the World Health organisation had declared the pandemic over. The antiviral drug Tamiflu was also used to reduce complications of flu in those infected such as bronchitis and pneumonia, as well as reducing the spread of the virus itself, by decreasing the amount of virus people released through coughs and sneezes. There were however concerns that the overuse of Tamiflu may have led to higher risk of the flu virus mutating to become resistant to antivirals. It is believed that the end of the pandemic was also hastened by the early deployment of testing, and by introducing public health measures such as school closures; in the United States for example over 600,000 school children were sent home in May 2009, around a month after the first case was detected there. As with other influenza strains the H1N1 swine flu strain continues to circulate today as seasonal flu. [29] [30] [31] [32]

<u>Likelihood</u>

15. It is **possible** that COVID-19 will eventually become a seasonal illness like influenza, (although the similarities to influenza would be only in COVID-19's epidemiological dynamics not in its severity), with outbreaks occurring at particular times of the year, for example during winter months when people spend more time indoors. The COVID-19 pandemic has so far followed a pattern similar to that of the

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influenza epidemics of the 20th and 21st centuries, with numerous waves of disease. Like those previous pandemics, immunity amongst populations was gained either by infection or, as in the case of pandemics since the 1957 flu pandemic, the introduction of a vaccine.[33] [34] Like influenza, mutations in COVID-19 have already been shown to lower the effectiveness of vaccines. In response, vaccine manufacturers have been exploring ways to redesign vaccines.[35] The major difference between COVID-19 and historic influenza pandemics is the type of virus that causes them. It's believed that the influenza virus evolves at a faster rate than the COVID-19 virus, and as such is able to more readily evade immune responses and may make reformulation of vaccines less of an issue for COVID-19. It should be noted that influenza behaves differently to COVID-19 in other ways in addition to the rate of mutation, such as incubation period, which impact the likelihood of this scenario.[36] In addition to vaccines it is realistically possible under this scenario that the use of antiviral drugs will also be used to combat COVID-19, particularly in cases where the patient is elderly or immunocompromised.[37]

Wider Impacts

16. The wider impacts of flu-like COVID-19 are **likely** to be similar to that of endemic COVID-19 (scenario 1). There would be two significant differences to the common cold-like endemic scenario (scenario 1); firstly, the need to regularly reformulate vaccines in order to maintain immunity and limit onward transmission and the need for a regular vaccination, similar to the seasonal flu vaccinations. The second major difference would be that COVID-19 would add to the stress already place on health services in winter by other seasonal factors such as influenza itself. There is also the added risk in this scenario, that vaccine hesitancy grows, particularly if the COVID-19 threat appears to have subsided, which may lead to an added burden on health services.

Scenario 3 - Ongoing Pandemic through New Variants

Similar Scenarios in History

17. Although there are examples of vaccines showing variable efficacy such as the BCG Tuberculosis vaccine[38], there are no recent examples where a new variant of a disease has entirely evaded vaccines, after first being brought under control through vaccination. Some similarities can be drawn with the HIV epidemic, for which there is no vaccine and the disease is only controlled though use of therapeutics, and public health measures. The HIV/AIDs pandemic remains arguably the deadliest pandemic in living memory, with around 79 million infections and 36 million deaths. There remains no available vaccine for the HIV virus and it is estimated that around 10 million people with HIV have yet to receive treatment, and around 1.5 million new cases of HIV were reported in 2020. There are also fears that variants of the HIV virus could lead to faster rates of spread and onset of symptoms.[39] Despite the lack of a vaccine, a number of initiatives have been implemented globally in a bid to control and potentially end the HIV/AIDS epidemic, including education supporting intervention to prevent infection, and the availability of antiretroviral treatments (ARTs). ARTs can suppress the viral load of patients and can prevent transmission of the disease.[40] Drawing conclusions on COVID-19 by comparison to HIV are however limited by the fact that the viruses behave differently and are transmitted differently. However, the HIV pandemic does provide an example of a pandemic that continues to be present in human populations and has yet to have been brought under control through the use of a vaccine or through immunity by infection.

Likelihood

18. It is **unlikely** that COVID-19 will be an ongoing pandemic through new variants. As mentioned above there are no recent examples as evidence for the likelihood of a scenario whereby new variants arise that entirely evade vaccines, where there is already an existing vaccine.[41] The complexity of the immune system makes it unlikely the virus could evolve far enough to avoid it completely. It's more likely immunity to COVID-19 infection would wane over time, but that protection against severe infection will be retained, through the immune systems B and T cells, as would be observed if COVID-19 became

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endemic.[42] The recent history of COVID-19 suggests that variants of concern (VOC) could continue to arise and continue to cause problems. This view is echoed by a number of leading scientists in the United Kingdom, who recently reported concerns that future variants may not necessarily be less lethal than the current Omicron strain.[43] There is also the possibility that new variants of concern could arise with higher transmissibility or virulence, or with dangerous resistance to immunity.[44] This scenario is made more likely by the fact that significant parts of the world remain at low vaccination rates. For example, at the time of writing on 12% of people in low-income countries have received their first dose of the vaccine.[45] While it should be noted, that this scenario does not appear to have been how pandemics observed in recent history, played out, this pandemic is taking place in a time of much higher international interconnectivity, meaning that the spread of new variants between historically less connected regions is more likely.

Wider Impacts

19. If COVID-19 became an ongoing pandemic through new variants, then major outbreaks of COVID-19 would continue to occur and would require public health measures similar to that observed during the pandemic. In essence the pandemic would not end, like the HIV pandemic. Also, like the HIV pandemic, health authorities would rely on antiviral drugs, some of which have already been developed, to help control the illness, alongside public health measures. This is also likely to lead to inequality in health outcomes, with those in lower socio-economic groups less able to access antiviral treatments, a phenomenon observed in the treatment of HIV.[46]

Scenario 4 - Suppressed and Eliminated Disease

Similar Scenarios in History

Severe Acute Respiratory Syndrome (SARS) – 2002 – 2003

20. SARS was the first severe and readily transmissible new disease of the 21st century. It was caused by a coronavirus similar to the virus causing the current pandemic and led to the deaths of 774 people, out of 8,098 confirmed cases.[47] [48] The virus was detected at the end of February 2003 in China before spreading international over the next months, reaching North and South America, Europe, and Asia. This particular strain of coronavirus is thought to have had a case fatality rate of 3% with patients being identified as previously health adults between the ages of 25 – 70 years old.[49] [50] [51] After the first cases identified in late February 2003, SARS was declared a disease threat by the WHO in March 2003, and by the end of May most of the cases and deaths that were reported as a result of SARS had already happened. In response, a number of countries in Asia began taking public health measures with some schools and public buildings shutting down, and the introduction of contact tracing in some countries. Travel to, and from, affected countries was prohibited and hospitals were quarantined if a person inside was found to be infected. The combination of these actions led to the disease being controlled, and by June 2003 restrictions were eased.[52] [53]

Smallpox

21. Smallpox is thought to have been present in human populations for at least 3,000 years. After the creation of the first vaccine for any disease in 1796, and a plan to eradicate the disease by the UN in 1967 through widespread immunisation and surveillance, smallpox was eradicated. Smallpox remains the only disease to have been eradicated and as such demonstrates the difficulty in removing pathogens completely from circulation. This therefore also demonstrates the unlikeliness that COVID-19 will be supressed completely.[54]

Likelihood

22. It is **highly unlikely** that the COVID-19 pandemic will be ended through suppression and elimination. The only other example of a disease being eradicated is smallpox, an event that was announced more than 200 years after the first vaccine was introduced to combat it. The first SARS outbreak at the start of the

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21st century was effectively suppressed. However, due to the much greater spread and transmissibility of COVID-19, and with countries now looking to reduce restrictions and rely on immunity through vaccination, a similar outcome for COVID-19 looks highly unlikely. Public health measures employed both in New Zealand and abroad during the pandemic did serve to suppress the virus's transmission, but their effects have limits based on their relative stringency. The COVID-19 virus is also present in a other animals, referred to as natural reservoirs, such as the white-tailed deer, meaning that even if COVID-19 were eradicated in humans it would like come back through contact with animals carrying the virus.[55] It should, however, be noted that in the *Nature* survey mentioned earlier, 25% of the immunologist surveyed thought it is very likely or likely that COVID-19 could be eliminated from some regions.[56]

Wider Impacts

23. Should COVID-19 be supressed and eliminated, the long-term outlook for New Zealand would be similar to that of endemic and flu-like COVID-19 (scenarios 1 and 2), but without the requirement for even the minimal public health measures required in those scenarios. In this scenario the government would be able to focus solely on policies aimed at repairing the damage caused by the pandemic.

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Probability Language Key

Qualitative Statement	Associated Probability Range
Remote/Highly Unlikely	<10%
Improbable/Unlikely	15-20%
Realistic Possibility	25-50%
Probable/Likely	55-70%
Highly Likely/Very Probable	75-85%
Almost Certain	>90%

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