

Evidence check

16 March 2021

Rapid evidence checks are based on a simplified review method and may not be entirely exhaustive, but aim to provide a balanced assessment of what is already known about a specific problem or issue. This brief has not been peer-reviewed and should not be a substitute for individual clinical judgement, nor is it an endorsed position of NSW Health.

Endemicity of SARS-CoV-2

Rapid review question

What evidence is available about the likelihood that SARS-CoV-2 will become endemic?

In brief

- Endemicity refers to the extent to which a disease or infectious agent is always present within a given geographic area or population group.
- Pre-COVID-19, four endemic coronaviruses (229E, NL63, OC43, and HKU1) were responsible for a large proportion of upper and lower respiratory tract infections.
- Whether SARS-CoV-2, will also become endemic will be determined by the interplay between virus biology and immunity of the host population (see figure 1).
- A weak adaptive immune response, waning immunity and viral immune escape can result in reinfection or infection in vaccinated populations. This leads to endemicity.(1)
- A January 2021 survey of about 100 immunologists, infectious-disease researchers and virologists showed 90% thought SARS-CoV-2 will become endemic.(2)
- Endemicity can take multiple forms. Several post-pandemic scenarios have been described.
 - Yearly outbreaks of SARS-CoV-2, if the duration of immunity proves to be similar to that of the other beta-coronaviruses (~40 weeks).(1)
 - SARS-CoV-2 continues to circulate but becomes no more virulent than the common cold, with primary exposure in childhood.(3)
 - Apparent elimination of the virus followed by resurgence after a few years, if there is a longer immunity profile, coupled with a small degree of protective cross-immunity from other beta-coronaviruses.(1, 4)
- The nature of SARS-CoV-2 endemicity that emerges will require tailored and nuanced public health and policy responses in different jurisdictions.

Figure 1. Endemicity flowchart

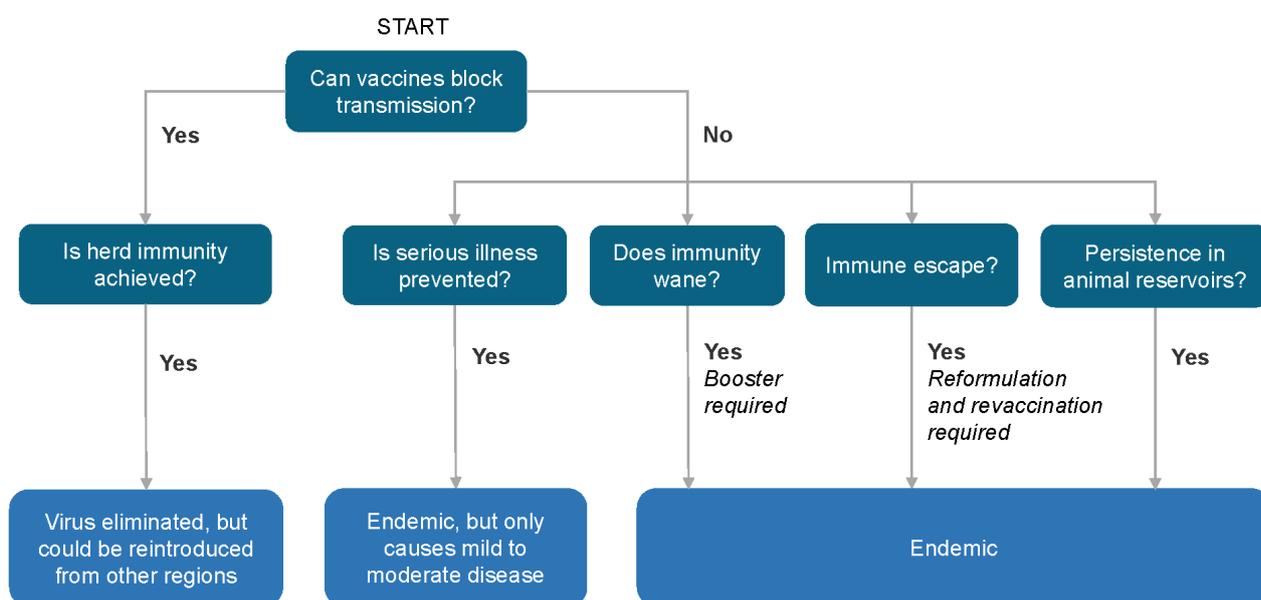


Table 1. Endemicity

Term	Definition	Evidence
Endemic	The constant presence of a disease or infectious agent within a given geographic area or population group.	Endemicity of SARS-CoV-2 cannot yet be determined. A survey of scientists (n=100) published in Nature in February 2021 found 89% said it likely or very likely that SARS-CoV-2 will become an endemic virus.
Herd immunity	A form of indirect protection from infectious disease that can occur when a sufficient percentage of a population is immune, either through vaccination or previous infection. If achieved, it reduces the likelihood of disease spread.	The percentage of people who need to be immune in order to achieve herd immunity varies with each disease, e.g. for measles, it is about 95% of a population while for polio, it is about 80%. According to the World Health Organization the proportion of the population that must be vaccinated against COVID-19 to induce herd immunity is not known. It is not yet clear what vaccine efficacies are necessary to prevent or stop the epidemic. Simulation experiments have shown that with vaccine efficacy against all infection (symptomatic and asymptomatic) of 60%, a vaccination coverage of 100% is required for

Term	Definition	Evidence
		herd immunity. There are no data available on the coverage required for symptomatic COVID-19 only.
Vaccine coverage	The percentage of a population that has received a recommended vaccine.	<p>Coverage data for COVID-19 vaccines are dynamic as the vaccine rollout continues.</p> <p>A January 2021 report by the Economist Intelligence Unit projected that the most of the adult population of advanced economies would be vaccinated by mid 2022. The timeline extends to early 2023 for many middle-income countries and 2024 for some low-income countries.</p>
Seroprevalence	The percentage of a population that has antibodies to a pathogen, such as SARS-CoV-2.	<p>The World Health Organization in December 2020 noted more than 200 peer-reviewed publications, pre-prints, manuscripts and government reports of SARS-CoV-2 seroprevalence. They vary in design, populations, serologic tests used, timing of sample collection, and quality. Overall, the population-based seroprevalence reported across available studies remains low, at below 10%.</p> <p>A systematic review of papers up to 14 August found seroprevalence of antibodies to SARS-COV-2 was around 3%. Ranging on a regional level from 1.45% in South America to 5.27% in Northern Europe.</p>
Waning immunity	When an initial adaptive immune response is robust and protective but dissipates over time, leaving the host vulnerable to reinfection.	The time scales of waning immunity and immune escape differ by pathogen and have yet to be defined for SARS-CoV-2.
Immune escape	Viral immune escape (or immune evasion) occurs when the immune system is unable to respond to an infectious agent.	<p>A number of variants of concern have been described for SARS-CoV-2.</p> <p>An early study by Public Health England, indicated that antibodies provide 83% protection against COVID-19 reinfections over a five month period. Out of 6614 participants, 44 had possible or probable reinfections.</p> <p>On 12 February 2021, a World Health Organization press briefing noted that recovered COVID-19 patients may have been reinfected with new virus strains.</p>

Term	Definition	Evidence
Animal reservoirs	The reservoir of an infectious agent is the habitat in which the agent normally lives, grows, and multiplies. Animals are one type of reservoir. Diseases are often transmitted from animal to animal, with humans as incidental hosts.	World Health Organization has formed an investigative team to explore the potential sources of infection among the first cases of COVID-19 in Wuhan, China.

Limitations

Evidence on this topic is emerging and researchers are drawing on knowledge about other coronaviruses. Given the paucity of empirical evidence, this evidence check includes commentary and opinion pieces.

Methods (Appendix 1)

PubMed and Google were searched on 27 February 2021.



Results

Table 2. Peer reviewed literature

Source	Advice
Peer reviewed sources	
<p>Immunological characteristics govern the transition of COVID-19 to endemicity</p> <p>Lavine, et al. 2021 (3)</p>	<ul style="list-style-type: none"> • Immunity may provide protection in three ways: <ul style="list-style-type: none"> ○ prevent replication ○ attenuate pathology due to reinfection ○ reduce transmissibility or infectiousness. • Immunological and epidemiological data on endemic human coronaviruses shows that infection-blocking immunity wanes rapidly but that disease-reducing immunity is long-lived. • This modelling study suggests that once the endemic phase is reached and primary exposure is in childhood, SARS-CoV-2 may be no more virulent than the common cold. • Results reinforce the importance of behavioural containment during pandemic vaccine rollout, while prompting evaluation of various options for continuing vaccination in the endemic phase
<p>Will SARS-CoV-2 become endemic?</p> <p>Shaman and Galanti 2020 (1)</p>	<ul style="list-style-type: none"> • A perspective article • Typically, following an initial infection, the human adaptive immune system develops a suite of defences, including memory B lymphocytes capable of producing neutralizing antibodies targeted to bind to that particular pathogen, and memory T lymphocytes that help regulate immune responses and induce death of infected cells. These adaptive immune components, particularly B cells, can produce sterilising immunity in which the pathogen, if reintroduced to the host, is prevented from replicating within the body. • However, for many viruses, a number of processes, particularly insufficient adaptive immune response, waning immunity, and immune escape, can undermine or circumvent the sterilising character of immunity and allow subsequent reinfection • Should reinfection prove commonplace, and barring a highly effective vaccine delivered to most of the world's population, SARS-CoV-2 will likely become endemic. The typical time scale at which individuals experience reinfection and seasonal differences in transmissibility will determine the pattern of endemicity. • Several post-pandemic scenarios for SARS-CoV-2 have been modelled.(5) A duration of immunity similar to that of the other beta-

Source	Advice
Peer reviewed sources	
	<p>coronaviruses (~40 weeks) could lead to yearly outbreaks of SARS-CoV-2, whereas a longer immunity profile, coupled with a small degree of protective cross-immunity from other beta-coronaviruses, could lead to the apparent elimination of the virus followed by resurgence after a few years.</p>
<p>Endemic SARS-CoV-2 will maintain post-pandemic immunity</p> <p>Veldhoen and Simas 2021 (4)</p>	<ul style="list-style-type: none"> • Coronavirus vaccines have been used extensively to control infections in domestic animals. Inactivated or intramuscular parenteral vaccines induce high systemic levels of neutralising antibodies and confer effective protection against disease. However, they have lower efficacy against mucosal coronavirus infections and do not prevent viral shedding. • SARS-CoV-2 is likely to remain present in the population. • The geographical emergence of SARS-CoV-2 antigenic escape variants needs consideration in vaccine design and use, but it should not significantly influence achieving protective population immunity. <p>With sufficient cross-reactive immunity, boosted by regular natural infections that particularly increase mucosal immunity, it is unlikely that annual SARS-CoV-2 vaccination programs will be required after the initial years.</p>
<p>The coronavirus is here to stay – here’s what that means</p> <p>Phillips 2021 (2)</p>	<ul style="list-style-type: none"> • In January 2021, <i>Nature</i> surveyed more than 100 immunologists, infectious-disease researchers and virologists working on SARS-CoV-2 about whether it could be eradicated. Almost 90% of respondents think that the virus will become endemic. • About 39% of respondents thought it would be possible to eliminate SARS-CoV-2 from some regions while it continued to circulate in others. • More than 70% thought immune escape; and more than 50% thought waning immunity will be main drivers of the virus becoming endemic.

Table 3. Grey literature

(does not include news items that discuss the peer reviewed papers)

Source	Advice
Grey literature	
<p>Q&A: Will COVID-19 become endemic?</p> <p>Healio website January 4, 2021</p>	<ul style="list-style-type: none"> • Many public health experts believe that SARS-CoV-2 will become endemic. • It is not sure how the epidemiology of the virus might change. There may be some type of herd immunity effect that will mean transmission is decreased in the entire population, but this cannot yet be predicted because the length and quality of protection against infection after natural infection and after vaccination is unknown, and as the virus mutates, epidemiological characteristics may change. • All respiratory infections have a greater possibility to spread during the winter months when people are closer together indoors in poorly ventilated spaces this includes the four endemic human coronaviruses. • If vaccines are effective in preventing infection, not only modifying disease in those infected, the epidemiology will be different in different parts of the world based on vaccine coverage.
<p>The endemic endgame is nigh</p> <p>The Weekend Australian, 27 February 2021</p>	<ul style="list-style-type: none"> • Governments need to start planning for COVID-19 as an endemic disease. • In Australia, Scott Morrison has formed a taskforce to examine how the COVID-19 risk matrix has changed in light of new strains and vaccine rollout, and to develop plans to manage quarantine, borders and social distancing measures in an endemic future.

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Appendix

PubMed search terms

PubMed 27 February 2021: (covid-19) AND (endemic[Title/Abstract] OR endemicity[Title/Abstract]) 442 results

Google and Twitter search terms

Google 27 February 2021: endemicity and COVID-19

Inclusion and exclusion criteria

Inclusion	Exclusion
<ul style="list-style-type: none"> Publications on the likelihood that SARS-CoV-2 will become endemic 	<ul style="list-style-type: none"> Where no abstract or full text was accessible

References

1. Shaman J, Galanti M. Will SARS-CoV-2 become endemic? Science (New York, NY). 2020;370(6516):527-9.
2. Phillips N. The coronavirus is here to stay - here's what that means. Nature. 2021;590(7846):382-4.
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4. Veldhoen M, Simas JP. Endemic SARS-CoV-2 will maintain post-pandemic immunity. Nature reviews Immunology. 2021:1-2.
5. Kissler SM, Tedijanto C, Goldstein E, Grad YH, Lipsitch M. Projecting the transmission dynamics of SARS-CoV-2 through the postpandemic period. Science (New York, NY). 2020;368(6493):860-8.

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