

# Series COVID-19 & response strategy

SGIODA Barcelona Institute for Global Health

[This document is a one of a series of discussion notes addressing fundamental questions about the global health. Its purpose is to transfer scientific knowledge to the public conversation and decision-making process. The papers are based on the best information available and may be updated as new information comes to light.]

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Photo: Bangladesh / Maruf Rahman (Pixabay)

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We are almost two years into a pandemic that has resulted in over 300 million confirmed cases and over 5.5 million reported deaths, although **the real death toll** has been estimated at as high as 17 **million**. We now have 10 safe and effective vaccines approved by the World Health Organization (WHO), but **the number of cases is rising** in many countries around the world, even in countries where vaccine coverage is high.

It is still early to know what will happen with the **Omicron variant**, but early data indicate that Omicron has a growth advantage over Delta which is partly due to a greater ability to evade immunity acquired through vaccination or previous infection, coupled with waning vaccine immunity. In any case, the emergence and spread of Omicron is a clear example of what we may be facing in the future, as long as **the virus continues to replicate and spread**. Accordingly, the only way to reduce this risk and accelerate our way out of the pandemic is to **maintain certain <u>non-phar-</u>** <u>maceutical interventions (NPIs)<sup>1</sup></u> in place and ensure **truly global access to vaccines and treatments**.

We believe the major health threats posed by **this pandemic will end**, as has occurred with all previous pandemics. The question is **when**, **how** and **after how many deaths**. As we discuss below, the "when" will likely be at different times in different parts of the world. Regarding the "how", the pandemic will not go out with a bang, but rather as a slow transition towards an, endemic state. Getting this transition right will not be easy. It requires a smart use of available tools and interventions, and clear goals and and the criteria for meeting them •

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# The Virus Is Here to Stay

"The most likely scenario for the coming years or decades is that the virus will become endemic and we will live with it as we do with the other four human coronaviruses which cause common colds." SARS-CoV-2 will be extremely difficult to eliminate from the human population.

**Cannot be eradicated:** The virus has **animal reservoirs** and can therefore not be eradicated (i.e. eliminated from the planet). Its main reservoir is very likely the horseshoe bat, but the virus is capable of infecting other non-human species. Human to animal transmission of SARS-CoV-2 has been documented for dogs, cats, farmed mink, captive felines, and even wild animals such as <u>deer</u><sup>2</sup>. Viral transmission among these animal reservoirs can facilitate viral mutations (as documented in mink farms) and represent a potential source of reintroduction into human populations.

**Extremely difficult to eliminate:** Eliminating viral transmission in a given region requires enormous coordination efforts and has a high socioeconomic cost in the long-term. Moreover, the deployment of effective vaccines has <u>shifted efforts</u> from eliminating the virus to mitigating its impact<sup>3</sup>. SARS-CoV-2 is expected to continue circulating among the human population, at least in the foreseeable future, due to:

• Its **high transmissibility** – unlike SARS, which was eliminated from the human population despite the lack of vaccines, this virus is much more transmissible and can be transmitted before symptoms appear.

• Waning immunity against infectionalthough the vaccines currently deployed are very effective at preventing severe disease (which is what they were originally tested for), they are less effective at preventing infection, particularly by more transmissible variants. Furthermore, immunity (acquired through infection or vaccination) seems to wane over time. • Unequal vaccine coverage within and between countries, which will leave pockets of virus-susceptible populations.

• The **risk of new viral variants** that prove more transmissible than Delta or have a greater capacity to evade immunity (as seems to be the case for Omicron).

**Will probably become a seasonal endemic virus:** Hence, the most likely scenario for the coming years or decades is that the virus will become endemic and we will live with it as we do with the other four human coronaviruses which cause common colds. Recent studies suggest that COVID-19 will behave like a <u>seasonal infection</u><sup>4</sup>, much like flu, leading to epidemic peaks during cold months when people are indoors more and ventilate less •

<sup>&</sup>lt;sup>2</sup> Kuchipudi SV, Surendran-Nair M, et alt. Multiple spillovers and onward transmission of SARS-CoV-2 in free-living and captive White-tailed deer (Odocoileus virginianus). bioRxiv preprint doi: this version posted November 1, 2021.

<sup>&</sup>lt;sup>3</sup> Oliu-Barton M, Pradelski BSR, et alt. Elimination versus mitigation of SARS-CoV-2 in the presence of effective vaccines. *The Lancet Global Health*. Vol, Issue 1, E142-E147, 1 January 2022.

<sup>&</sup>lt;sup>4</sup> Fontal A, Bouma MJ, San-José A, et al. Climatic signatures in the different COVID-19 pandemic waves across both hemispheres. Nat Comput Sci 1, 655–665 (2021).

# From Pandemic to Endemic: How to Get There, and Stay There

**"One of the most** pressing issues at the moment is how do we reach the endemic phase while minimising the health. social and economic impact of the virus. What restrictions can be lifted and what measures do we need to keep in place? And what criteria can we use to decide?"

#### The near future

Predicting what will happen next has proved extremely risky during this pandemic. This upcoming winter is threatened by a feeling of "pandemic fatigue" among the population and the poor handling of the situation by some political leaders, together with the arrival and subsequent spread of the Omicron variant, even in countries like Denmark and Spain, with high vaccine coverage.

The speed at which different countries manage to reach an endemic phase will depend on their access to, and use of, the currently available tools - vaccines, rapid tests and a range of non-pharmaceutical interventions from facemasks to improved ventilation. The imminent arrival of specific antiviral treatments that reduce hospitalizations represents a much-needed tool that will accelerate this transition, as long as they are globally accessible and affordable, and as long as early testing is feasible. However, as mentioned above, this transition may also be delayed or even reversed by waning immunity in certain groups of the population (and the need for booster doses), the worrying level of vaccine hesitancy and misinformation in many countries (regardless of whether they are high, middle, or low-income countries), and/or the emergence and spread of new viral variants of concern. Global surveillance (at the epidemiological and viral levels), as well as effective communication strategies, will be a critical element to counter these risks.

#### The distant future

In the ideal future scenario, when all those who wish to be vaccinated have been, continuous circulation of SARS-CoV-2 in the community would be expected to cause **mild disease in children**, particularly those who have not yet been vaccinated. These early infections would generate protective immunity <u>against</u> <u>severe disease</u><sup>5</sup>, which could be reinforced with vaccination. Among vaccinated individuals, immunity could be reinforced with **booster shots** or even by breakthrough infections.

Second generation vaccines that are adapted to dominant circulating viral variants or that boost sterilising immunity (i.e. intranasal vaccines) will likely play an important role in the future, as well as **prophylactic or early antivi**ral treatments that not only reduce the risk of developing acute COVID-19 but also of <u>long-COVID<sup>6</sup></u>. These antiviral treatments target the replication machinery of the virus and should therefore be more resistant to the mutations present in the circulating viral variants.

It is **still not clear** whether we will eventually manage to eliminate severe disease with highly effective vaccines and treatments, or whether COVID-19 will continue to cause significant health and economic damage, equal to or even larger than that caused by the seasonal flu.

Ultimately, a vaccine that provides broad protection against coronaviruses is a feasible but challenging endeavor that needs to be <u>urgently pursued</u><sup>7</sup>.

Therefore, one of the most pressing issues at the moment is **how do we reach the endemic phase** while minimising the health, social and economic impact of the virus. What restrictions can be lifted and what measures do we need to keep in place? And what criteria can we use to decide? •

<sup>5</sup> Abu-Raddad LJ, Chemaitelly H, Bertollini R. Severity of SARS-CoV-2 Reinfections as Compared with Primary Infections. *The New England Journal of Medicine*. 24 November 24 2021. DOI: 10.1056/NEJMc2108120

<sup>6</sup> Lopez-Leon, S., Wegman-Ostrosky, T., Perelman, C. et al. More than 50 long-term effects of COVID-19: a systematic review and meta-analysis. *Sci Rep* 11, 16144 (2021).
 <sup>7</sup> Morens DM, Taubenberger JK, Fauci AS. Universal Coronavirus Vaccines — An Urgent Need. *NEJM*. December 15, 2021. DOI: 10.1056/NEJMp2118468



"The following criteria should allow us to determine whether we have reached endemicity or not, and should be accompanied by indicators to help guide decisions on the need of adding NPIs." Reaching the endemic phase - and staying there - requires a global strategy in which the objectives and criteria are clearly established. For example, do we seek to limit viral transmission at all costs, or is our goal to reduce hospitalizations and deaths? **How many hospitalizations or deaths are acceptable?** Each community and country will probably have different risk perceptions and therefore will accept different criteria of endemicity, which is not an optimal situation.

**Shifting the focus from cases to hospitalizations:** With a Zero-COVID strategy, detecting all cases (symptomatic or not) is key to eliminating viral transmission. Accepting SARS-CoV-2 as an endemic virus, on the other hand, will require shifting our goal towards achieving low, controlled transmission, and greatly reducing severe cases and hospitalizations, as well as cases of long-COVID.

The following criteria should allow us to determine whether we have reached endemicity or not, and should be accompanied by indicators to help guide decisions on the need of adding NPIs (from facemasks to limiting the size of public events or mobility, to making travel safer).

• Stable and controlled transmission: Achieving stable transmission does not mean that COVID-19 will not cause epidemic peaks, probably in the winter, much like other seasonal respiratory viruses. Therefore, one must consider the dual threat posed by flu and COVID-19 in terms of mortality, morbidity, burden on healthcare services, and impact on productivity. *Indicator:* Accumulated incidence (number of cases per 100,000 people) over the last 7 days, with a particular focus on increases among those aged 60 and above.

• Healthcare services can continue functioning normally: This is probably the most important criterion. The imminent arrival of early antiviral treatments is expected to contribute considerably to reducing COVID-19 hospitalizations among unvaccinated people or high-risk vaccinated individuals that get infected, as long as they are used appropriately and rapid testing can be ensured. This would allow primary healthcare centers and hospitals to continue functioning normally, despite a winter-related increase in transmission. However, as stated above, the combination of COVID-19 and seasonal flu could still exert a considerable strain on primary healthcare services and hospitals. *Indicators:* **Hospital and ICU occupancy** over the last 7 days (number of COVID-19 hospitalisations and ICU beds occupied per 100,000 people).

• Reduced mortality and morbidity: Currently approved vaccines have already managed to considerably reduce deaths. Certain populations, such as the elderly and those with chronic conditions or compromised immune systems, remain more vulnerable to dying from COVID-19 in case of a breakthrough infection and will likely need booster doses more frequently. Regarding morbidity, it is believed that current vaccines reduce the risk of long-CO-VID in case of a breakthrough infection, although more data are needed. Early antiviral treatments will likely be more effective in this regard. Indicator: Mortality rate (number of deaths per 100,000 people) over the last 7 days. Establishing actionable indicators for morbidity (i.e. long-COVID rate) is currently challenging without a clear case definition.

• Limited impact on productivity: Mild and moderate cases of COVID-19 will also impact society through sickness-related absence from work due to acute infections and, in some cases, the long-COVID. For influenza, the cost of lost productivity in France and Germany alone has been estimated between 6 and 10 billion euros per year, respectively. Therefore, businesses must learn to adapt in order to deal with a second major seasonal virus. This means taking actions to limit viral transmission at work, for example by facilitating teleworking, giving paid sick leave, and ensuring proper ventilation at the workplace. Indicator: Average number of lost work days per year.

**The need for high-quality data:** The above goals and criteria will also define the type of data that need to be collected to closely monitor the situation and decide whether additional public health interventions are needed. This means a **close and constant monitoring** of cases, hospitalizations and deaths, stratified by age, sex, vaccination status and socioeconomic status among others, as well as a close genomic surveillance of the virus.

is exceeded, special measures can be taken regarding access to recreational, cultural or sporting events and facilities, and indoors can be restricted to vaccinated and recovered persons. If the rate exceeds 6, additional measures such as requiring negative tests can be requested. Above 9, the states can use more restrictive measures such as limiting mobility •

**Spanish authorities** have a series of indicators to determine the risk level, although they have not yet detailed the type of restrictions to be implemented at each level *(see Tables 1 and 2)*. **Germany**, for example, has established that if the hospitalisation rate of 3 patients per 100,000 people

Risk	Alert level	Hospital beds (%)	ICU 100.000 inhab. (7 days)	Hospitalisations 100.000 inhab. (7 days)	ICU E (%)
Very high	4	>15	>4	>50	>25
High	3	10-15	3-4	30-50	15-25
Medium	2	5-10	2-3	15-30	10-15
Low	1	2-5	1-2	5-15	5-10

### Table 1. Assistance capacity (per 100,000 people)

**Source:** The Ministry of Health designs a looser 'covid traffic light' that raises the low risk of transmission from 50 to 100 cases per 100.000 inhabitants. *El País*, 15 November 2021.

0-1

0-5

Risk	Alert level	AI* 14 days	Al 7 days	AI 14 days (cases with 65 and more years old)	AI 7 days (cases with 65 and more years old)	Positivity (%)
Very high	4	>500	>250	>250	>125	>15
High	3	300-500	150-250	150-250	75-125	10-15
Medium	2	100-300	20-150	50-150	25-75	7-10
Low	1	50-100	25-50	25-50	10-25	4-7
Controlled transmission	0	0-50	0-25	0-25	0-10	0-4

#### Table 2. Transmission indicators (per 100,000 people)

0-2

**Source:** The Ministry of Health designs a looser 'covid traffic light' that raises the low risk of transmission from 50 to 100 cases per 100.000 inhabitants. *El País*, 15 November 2021.

\*AI Accumulated Incidence

Controlled

transmission

0

eds

0-5

#### Table 3. Estimations of the impact of seasonal influenza in Spain

Seasons	2013-2014	2017-2018	2018-2019	2019-2020
Lost work days (February)	3,112	-	-	-
Primary healthcare cases	-	700,000	490,000	619,000
Hospitalisations	-	52,000	35,300	27,700
ICU admissions	-	3,000	2,500	1,800
Deaths	-	15,000	6,300	3,900

**Source:** <u>Seasonal flu disease burden and impact of the flu vaccine</u>. Instituto de Salud Carlos III. Infographics 2017-2018 to 2019-220. For the number of lost work days per year: Ligero Lopez E, Vico Garcerán B (2015). <u>Seasonal influenza as the cause of labour disability in health workers</u>. *Revista de la Asociación Española de Especialistas en Medicina del Trabajo*, 24(1), 9-16.



"Each country or region will likely transition to an endemic phase at a different moment and in a different manner, but the pandemic is not endemic until all countries have reached that phase." • Each country or region will likely transition to an endemic phase at a different moment and in a different manner, but the pandemic is not endemic until **all countries** have reached that phase.

• Access to- and combined use of - available pharmaceutical (vaccines, antiviral treatments, rapid tests) and non-pharmaceutical interventions (e.g. facemasks, ventilation) will be key. **Vaccines alone will not suffice** to end the pandemic.

• Each country will likely have its own "acceptable endemic level" but it is urgent that there is a **coordinated global strategy** based on common targets and criteria regarding transmission, hospitalizations and deaths.

• Near elimination of severe disease may become a feasible goal if effective COVID-19 vaccines and early antiviral treatments and diagnostics are **widely available around the world**. In this context, the focus should be on hospitalizations rather than cases.

• Ongoing collection of high-quality epidemiological and virologic data is key to monitoring established indicators and adopting additional public health measures if necessary.

• COVID-19 may still cause **epidemic peaks during winter** and, together with seasonal influenza, may impact healthcare services and productivity.

• Authorities and businesses need to establish a **sustainable long-term plan to mitigate the health and socioeconomic impact** of respiratory viruses (such as reinforcing influenza and COVID-19 vaccination, encouraging teleworking particularly during winter, ensuring paid sick leave, and improving ventilation and air filtration in buildings).

Regardless of when and how this pandemic ends, the world cannot afford to ignore the lessons drawn from this crisis. Intersectoral actions must be taken at the national and international level to better prepare for future infectious disease outbreaks. The global consensus reached in the last World Health Assembly<sup>8</sup> to establish an international treaty on pandemic prevention and preparedness is a step in the good direction •

<sup>8</sup> WHO. World Health Assembly agrees to launch process to develop historic global accord on pandemic prevention, preparedness and response. 1 December 2021.

# **TO LEARN MORE**

• Oliu-Barton M, Pradelski BS, Algan Y, *et al.* <u>Elimination versus mitigation of</u> <u>SARS-CoV-2 in the presence of effective vaccines</u>. *The Lancet Global Health*. 1 January 2022.

• Gottlieb, S. <u>A Second Major Seasonal Virus Won't Leave Us Any Choice</u>. *The Atlantic*. 12 September 2021.

• The Lancet COVID-19 Commission Publications.

• <u>Robertson D, Doshi P. The end of the pandemic will not be televised</u>. *BMJ* 2021; 375 :e068094 doi:10.1136/bmj-2021-068094

- BMJ's Coronavirus (covid-19) Hub.
- Our World in Data.
- WHO main page on covid.

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https://www.isglobal.org/en/-/covid-19-cuando-y-como-acabara-la-pandemia-

