

COVID-19: From Epidemic to Endemic? The Evolution Remains Unpredictable. New Indicators Needed

Jose Luis Turabian

Specialist in Family and Community Medicine, Health Center Santa Maria de Benquerencia. Regional Health Service of Castilla la Mancha (SESCAM), Toledo, Spain

Corresponding author

Jose Luis Turabian, Health Center Santa Maria de Benquerencia Toledo, Spain.

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The coronavirus disease 2019 (COVID-19) pandemic is at a tipping point. It is no longer in the epidemic/pandemic phase; that period was characterized by quick action and very detailed surveillance which was crucial. Currently high levels of immunity to severe acute respiratory syndrome coronavirus (SARS-CoV-2) are beginning to limit its impact and scope [1].

In many parts of the world, including Europe and North America, COVID-19 has continued their journey towards endemic COVID-19. Thus, many countries are now transitioning to strategies for managing COVID-19 as an endemic disease [2]. Several potential definitions of the transition from the pandemic to the endemic phase are possible. Epidemiologically, COVID-19 can be defined as endemic when it exists at a predictable level that does not require special socio-sanitary interventions. While that level is desired to be zero, eliminating the disease is not feasible. Eradicating a disease means permanently eliminating all traces of the pathogen. This requires scientific criteria: epidemiologically vulnerable disease: no easy transmission, easy diagnosis, long-lasting immunity in survivors, and an effective intervention, such as a vaccine or cure for the disease and its transmission, and having elements that can demonstrate to large-scale the removal. Political criteria are also required: eradication efforts must be affordable and cost-effective: these efforts must be significantly better than simply controlling the disease in the long term [3].

Just as the risk of flu is considered normal, so too could be the risk of COVID-19. Furthermore, what is considered acceptable by society will differ between countries. A threshold of endemicity would come when fluctuations in disease burden cause only minimal changes in the economic and social behavior of individuals. This is mediated by individual risk factors (age, underlying conditions, etc.) [2]. If COVID-19 becomes endemic,

it will be present at a certain level in a population at certain times of the year or throughout the year. A disease that is not eradicated is, by definition, endemic. This does not necessarily mean that you are circulating at low levels, or is harmless [1].

Looking ahead, the outlook for most regions, including Europe and North America, remains relatively “favourable” for the coming months, with levels of severe disease at or below recent levels. While many people in the United States are becoming comfortable living alongside COVID-19, the average number of daily deaths is still two to four times the long-term average for influenza, and higher on a seasonally adjusted basis. But, a new immunity-evading variant could change this relatively rosy story at any time. For now, however, scientists view these variants simply as more transmissible than Omicron. Vaccines now in wide distribution still limit the incidence of serious disease [2].

Therefore, the possibility that COVID-19 is endemic is real. But unfortunately, in the current phase many of the community surveillance studies that track infection levels have ended. The virus has not gone away, however, and in fact may be on the rise in many countries. Currently there are no multiple data streams to rely on, and it is harder to say what is happening in the general population. It is in a situation of “darkness” about how COVID-19 will develop in the coming months [4]. It is true that the short-term efficacy of vaccines with respect to the severity of SARS-CoV-2 infection has been demonstrated [5]. But, on the other hand, there is growing scientific evidence that shows that the protection generated by vaccination decreases over time, although it is restored with the inoculation of booster doses. In addition, the decrease in immunity as a consequence of the new variants must be taken into account [6].

Thus, it is accepted that it may be normal to be infected by SARS-CoV-2 several times throughout life [7-10]. SARS-CoV-2 evolves very quickly, and new strains largely escape old vaccines. To be well protected against new strains we need new vaccines. Therefore, booster vaccination for the prevention of COVID-19

is required to overcome this loss of protection [11-13]. Despite vaccinations, boosters, and natural immunity, variants seem capable of evading any protection you may have gained against SARS-CoV-2 [14,15].

Although severe COVID-19 is rare, populations remain vulnerable to future waves of reinfection with emerging variants of SARS-CoV-2 despite high vaccination and infection rates [16]. After the incidence of the XBB.1.5 variant, also known as 'Kraken', health experts have turned their eyes to the rapid growth of a new variant: nicknamed 'Eris' (EG.5) and has already been detected in more than 50 countries, including Spain [17]. The problem is lack of data and sequencing due to less testing. So, WHO advises that the data should be interpreted with extreme caution; In fact, the reliability of variant detection could be affected by the reduction in monitoring activity worldwide: if in January 2023 there were almost 100,000 sequences deposited in the GISAID database, in July there were 8,662 [18-20].

In addition, at present, reinfection episodes and associated risk factors remain unclear [21,22]. And data on cellular immune responses in people with SARS-CoV-2 infection after vaccination are limited [23]. On the other hand, the future acceptance of reinforcements is a big unknown. In the United States, only about half of those who received the initial course of COVID-19 vaccines received the first booster. It is not yet clear if public interest in boosters will continue to wane or if demand will eventually match the historical uptake of flu vaccines (about 50 percent of adults) [2]. In addition, it appears that uptake has declined recently, due to complacency about the need for vaccines, mistrust fuelled by misinformation, safety concerns, and pushback from delivery schedules [24]. Without continued immunization, population immunity to current variants will decline over time [2].

In this scenario, understanding the risk factors for reinfection is crucial to assess how infections could increase and whether the health system will be able to cope with them. Ultimately, studying reinfections will help researchers understand what the transition of SARS-CoV-2 to an endemic virus will look like [25]. Scientists say that having a good surveillance system to monitor and track emerging virus variants is very important, as infection cycles will continue to occur [26]. However, it seems that political decisions are going the other way. In many countries, such as Spain, they no longer publish their COVID-19 case counts, it is not clear how many people are infected, nor can the evolution of new waves be evaluated; Of course, it is difficult to make estimates without precise data [27]. But based on previous research, it is estimated that at least 30% of the population could be reinfected in successive waves [26].

COVID-19 testing has increasingly shifted to a home-based model. With so few home test results being reported, it is difficult to estimate the true magnitude of the current situation. Official statistics, which already tend to underestimate the number of cases, may become even less sensitive to the true dimensions of viral transmission [2]. The researchers believe that many countries will see an infection cycle every six months now that all COVID-19 restrictions have been lifted and highly infectious variants are dominant. But continuing waves of infection carry the risk of new variants emerging that can compete with current ones and are more severe [7-10,26,28].

Variant emergence patterns for COVID-19 are largely unknown and COVID-19 is not simply following seasonal patterns [4]. Every time someone is contaminated, billions of new viral particles are produced and, as a result of copying errors, the risk of random mutants is increased. In most people, the infection lasts less than two weeks and it is estimated that one or three virions establish a new one. This bottleneck significantly limits the diversification of the virus. However, in immunocompromised people, the infection can last for several months and cause serious complications. This increases the rate of evolution because mutations drive natural selection. Therefore, prevention and monitoring of immunosuppressed people is essential [29].

Policymakers, governments, and individuals need data on incidence rates, in the general population, and in people vaccinated, to assess the impact of additional doses of vaccines [24,30]. The possible indicators now when the COVID-19 data are no longer updated could be, in addition to the best-known levels of SARS-CoV-2 in wastewater and the number of hospitalizations the following: 1) Since home tests became more widely available in late 2021, consumer purchases of them reflects consumer awareness of symptomatic illness (when family members get sick, for example) and it could be an indicator of early warning of future waves of illness [2,31]. 2) Because in some countries, such as Spain, general practitioners (GP) are the gateway for all patients to the system, and each person is assigned a GP, another indicator could be the frequency of visits to the GP due to upper respiratory infection and/or to report a positive COVID-19 test at home, which can be equated to "minimum incidence" rates [32-34]. 3) And finally, another indicator can be the community risk estimate. The risk that COVID-19 represents for a community at any time is a function of the immunity of its members; Although the level of immunity of each individual cannot be measured in real time, estimates of the level of risk in the community can be based on what is known about vaccination rates and previous infections [2].

In a possible endemic phase of COVID-19, it is about conserving the gains in terms of national capacity and preparing for future events, in order to avoid a cycle of panic and carelessness; integrate COVID-19 vaccination into vaccination programs throughout the life course, and maintain measures to increase COVID-19 vaccination coverage for all people in high-priority groups (elderly and frail and immunosuppressed subjects). WHO has also recommended integrating respiratory pathogen surveillance and continued data reporting [19]. In short, in this context, COVID-19 evolution remains unpredictable.

References

1. Mayor SJ, Welte T. From Pandemic to Endemic: How Do Influenza and SARS-CoV-2 Compare? *Medscape CME & EDUCATION*. <http://www.medscape.org/viewarticle/990634>. 2023.
2. Charumilind S, Craven M, Lamb J, Sabow A, Singhal S, et al. When will the COVID-19 pandemic end? *McKinsey & Company*. <https://www.mckinsey.com/industries/healthcare/our-insights/when-will-the-COVID-19-pandemic-end>. 2022.
3. Senthilingam M. *Outbreaks and Epidemics: Battling infection from measles to coronavirus*. London: Icon Books. <https://iconbooks.com/ib-title/outbreaks-and-epidemics/> 2020

4. Davis N. UK almost ‘flying blind’ on COVID this autumn, experts say. As cases rise, scientists say country is mostly in the dark about how infections could play out in coming months: *The Guardian*; Sat 5 Aug. <https://www.theguardian.com/world/2023/aug/05/uk-almost-flying-blind-on-COVID-this-autumn-experts-say>. 2023.
5. Hall V, Foulkes S, Insalata F, Kirwan P, Saei A, et al. Protection against SARS-CoV-2 after COVID-19 Vaccination and Previous Infection. *N Engl J Med*. 2022. 386: 1207-1220.
6. Crist C. Unvaccinated People Likely to Catch COVID Repeatedly. *Medscape* https://www.medscape.com/e/961487?spon=34&uac=327178AR&impID=3752444&sso=true&faf=1&src=WNL_mdpls_211029_mscepedit_fmed. 2021.
7. Kojima N, Klausner JD. Protective immunity after recovery from infection. *Lancet Infect Dis*. 2021. 22: 12-14.
8. Goldberg Y, Mandel M, Bar-On YM, Bodenheimer O, Freedman LS, et al. Protection and Waning of Natural and Hybrid Immunity to SARS-CoV-2. *N Engl J Med*. 2022. 386: 2201-2212.
9. Williams S. Cold-Causing Coronaviruses Don’t Seem to Confer Lasting Immunity. *The Scientist* <https://www.the-scientist.com/news-opinion/cold-causing-coronaviruses-dont-seem-to-confer-lasting-immunity-67832>. 2020.
10. Johnston C, Hughes H, Lingard S, Hailey S, Healy B. Immunity and infectivity in COVID-19. *BMJ*. 2022. 378: e061402.
11. Grant R, Sacks JA, Abraham P, Chunsuttiwat S, Cohen C, et al. When to update COVID-19 vaccine composition. *Nat Med*. 2023. 29: 776-780.
12. Callaway E. COVID ‘variant soup’ is making winter surges hard to predict. Descendants of Omicron are proliferating worldwide and the same mutations are coming up again and again. *Nature*. 2022. 611: 213-214.
13. Khoury DS, Docken SS, Subbarao K, Kent SJ, Davenport MP, et al. Predicting the efficacy of variant-modified COVID-19 vaccine boosters. *Nat Med*. 2023. 29: 574-578.
14. Thompson D. COVID reinfections are now common. Will getting a booster even help? *Medical Xpress* <https://medicalxpress.com/news/2022-07-COVID-reinfections-common-booster.html>. 2022.
15. Karmakar S. COVID-19 Reinfection Risk Is Real: Pulmonologist Explains Importance of Booster Doses. *India Dot* <https://www.thehealthsite.com/diseases-conditions/covid-19-reinfection-risk-is-real-pulmonologist-explains-importance-of-booster-doses-904334/> 2022.
16. Tan CY, Chiew CJ, Pang D, Lee VJ, Ong B, et al. Protective immunity of SARS-CoV-2 infection and vaccines against medically attended symptomatic omicron BA.4, BA.5, and XBB reinfections in Singapore: a national cohort study. *Lancet Infect Dis*. 2023. 23: 799-805.
17. OPS. COVID-19 is now an established and persistent health problem. <https://www.paho.org/es/noticias/8-5-2023-COVID-19-es-ahora-problema-salud-establecido-persistente>. 2023.
18. O’Mary L. US Has New Dominant COVID Variant Called EG.5. *Medscape*. https://www.medscape.com/s/viewarticle/995247?ecd=WNL_trdalrt_pos1_ous_230809_etid5730343&uac=327178AR&impID=5730343. 2023.
19. Pérez B. The new eris variant, more contagious, already alerts doctors to the rebound in COVID. *El Periódico*; Barcelona 10 de agosto. <https://www.elperiodico.com/es/sanidad/20230810/variante-eris-alerta-cataluna-aumento-casos-COVID-coronavirus-90846869#:~:text=Los%20epidemi%C3%B3logos%20dan%20por%20hecho,los%20ingresos%20en%20los%20hospitales>. 2023.
20. Santarpia V. COVID, no isolation for those who are positive: the decision expected on Monday. *Corriere della Sera*; 5 agosto. https://www.corriere.it/cronache/23_agosto_05/COVID-nessun-isolamento-chi-positivo-decisione-attesa-lunedì-55f00286-3390-11ee-a263-c6cae56880c3.shtml. 2023.
21. Slezak J, Bruxvoort K, Fischer H, Broder B, Ackerson B, et al. Rate and severity of suspected SARS-CoV-2 reinfection in a cohort of PCR-positive COVID-19 patients. *Clin Microbiol Infect*. 2021. 27: E7-E10.
22. Peghin M, Bouza E, Fabris M, De Martino M, Palese A, et al. Low risk of reinfections and relation with serological response after recovery from the first wave of COVID-19. *Eur J Clin Microbiol Infect Dis*. 2021. 40: 2597-2604.
23. Huapaya JA, Higgins J, Kanth S, Demirkale CY, Gairhe S, et al. Vaccination Ameliorates Cellular Inflammatory Responses in SARS-CoV-2 Breakthrough Infections. *J Infect Dis*. 2023. 228: 46-58.
24. Opinion. Why older adults can continue to benefit from COVID-19 boosters. *BMJ*. 2023. 382: 1662.
25. Mallapaty S. COVID reinfections surge during Omicron onslaught. Immunity acquired through previous infection is less effective against Omicron than against other variants, but the risk of severe COVID-19 remains low. *Nature*. 2022.
26. Ye Y. China’s rolling COVID waves could hit every six months infecting millions. The latest surge is unlikely to crash the country’s health-care system, but scientists fear hundreds of millions of infections. *Nature*. 2023. 618: 442-443.
27. Turabian JL. An ostrich strategy for COVID-19 is too risky. *BMJ*. 2022. 377: o1112.
28. El-Sadr WM, Vasan A, El-Mohandes A. Facing the New COVID-19 Reality. *N Engl J Med*. 2023. 388: 385-387.
29. Koppe M. The evolution of the COVID-19 virus remains unpredictable. *CNRS News*. <https://news.cnrs.fr/articles/the-evolution-of-the-COVID-19-virus-remains-unpredictable>. 2022.
30. Cohen C, Pulliam J. COVID-19 infection, reinfection, and the transition to endemicity. *Lancet*. 2023. 401: 798-800.
31. Grant K, McNamara D. It May Be Time to Pay Attention to COVID Again, *Medscape*. https://www.medscape.com/s/viewarticle/it-may-be-time-pay-attention-COVID-again-2023a1000ipk?ecd=WNL_trdalrt_pos1_ous_230815_etid5750386&uac=327178AR&impID=5750386. 2023.
32. Turabian JL. [Notebooks of Family and Community Medicine. An introduction to the principles of Family Medicine]. Madrid: Díaz de Santos. <http://www.amazon.co.uk/Cuadernos-medicina-familia-y-comunitaria/dp/8479781920>. 1995.

33. Turabian JL. Incidence Rate of Acute Respiratory Infections in General Medicine as a Tool to Correcting Official Data of COVID-19 in Places where the Tests of Polymerase Chain Reaction are not Accessible. *Epidemol Int J*. 2020 4: 000S1-005.
34. Turabian JL. [Notebooks of Family and Community Medicine. An introduction to the principles of Family Medicine]. Madrid: Díaz de Santos. <http://www.amazon.co.uk/Cuadernos-medicina-familia-y-comunitaria/dp/8479781920>. 1995.