

PROGNOSIS

How the Covid-19 pandemic will end in 2022 and why we still need adapted vaccines.

Adrian Tudor, Jonathan Feldman, Carolina Diamandis, Olga Ivanova

Corresponding Author

LCG Research
Dr. Olga Ivanova
16 Kifissias Avenue
115 26 Athens, Hellenic Republic
www.your-doctor.com

Abstract

There is still debate in the virological community about whether the Omicron variant of the Sars-CoV-2 virus means its end as a pandemic virus and whether the endemic phase is already beginning - or not. We venture the hypothesis that Covid-19 is already a virus which is very similar to the four endemic seasonal coronaviruses and poses a relatively low risk to fully (3x) vaccinated individuals and to individuals who have recovered from infections with other Sars-CoV-2 variants in 2019 to 2022. For this reason, it would now make sense to develop vaccines and drugs that are effective against all known endemic human coronaviruses (hCoV), which are often lamentably misleadingly referred to as "cold viruses," rather than limiting new vaccines to the Omicron variant or to any other variant. Such a bold step would be a milestone in protecting the vulnerable population that has been at the mercy of classic hCoV viruses for centuries without effective protection.

Assumptions

From our perspective as frontline physicians, we quite optimistically anticipate that Covid-19 will become endemic through the Omicron variant before the end of 2022. However, this will by no means make vaccinations and novel drugs obsolete.^{1,6} We have deliberately chosen to derive our hypothesis from general medical knowledge, as we are frontline physicians and prefer to leave the detailed laboratory research to our mainly exploratively working colleagues. Therefore, our prediction is based on the following axioms and is designed to hold up even if one of the axioms falters or has been incorrectly prioritized by us:

1. The infectivity of the Omicron variant is exceptionally high (with R_0 possibly as high as ~ 10), so that the probability of an even more infectious variant approaches zero.^{14,15,16}
2. Omicron actually appears to cause only clinically rather mild disease in vaccinated and recovered individuals.¹
3. We assume that Omicron - unlike the Delta variant - is able to induce a partial immunity against other coronaviruses, especially in those who are vaccinated or already had Covid-19.⁶
4. There is quite likely a presumed precursor pandemic ("Russian Flu", 1889-1895), which with increasing probability was caused by coronavirus OC43. It was clinically similar to Covid-19 and has been endemic as a less dangerous but still potent human coronavirus (hCoV) since 1895 - still causing severe outbreaks and providing a possible example of how a coronavirus pandemic can come to an end.^{10,11,12}
5. It is not entirely impossible that the comparatively mild course of the Omicron variant is caused by cross-immunity.³ For example, Omicron may have inherited genetic material from endemic hCoV 229E during its emergence.²
6. Herd immunity is unlikely for Sars-CoV-2⁴ (as for all the other endemic hCoVs), but a wide cross-immunity effect, resembling something similar to herd immunity, may occur.
7. The danger of endemic human coronaviruses (hCoVs) is generally underestimated.^{7,8,9}
8. Sars-CoV-2 shares typical coronavirus characteristics with other coronaviruses and is not a singularity.^{5,7,9}

Situation

Every year, thousands of mainly elderly and debilitated people become most severely ill from one of the known "traditional" endemic human coronaviruses (hCoVs), while others experience these pathogens only as causes of a flu-like infection.⁹ Despite the dangerous nature of pneumonia caused by human coronaviruses, these pathogens are unknown to the general population, unlike influenza, or are being grossly mislabeled as "cold viruses".^{7,8,9}

This perception is assumed to have developed due to the fact that vaccination is available against influenza but not against the hCoVs. Only in the context of the pandemic caused by Sars-CoV-2 interest in endemic hCoVs increased again, at least among experts. In this situation a former fringe hypothesis became a serious theory. It is about hCoV-OC43 having caused the deadly "Russian flu pandemic" (1889-1895) before becoming an endemic hCoV after the prevailing of a highly contagious but mild variant.

OC43 is still a potent and ubiquitous pathogen today, striking with life-threatening outbreaks in rare cases.^{10,11,12} In this respect, it is surprising that at the onset of the Sars-CoV-2 pandemic in 2020, knowledge about coronaviruses that had been known for decades was

not taken into account for months. As a *pars pro toto*, aerosol transmission should be mentioned: until summer of 2020, months after the outbreak of the pandemic, it was not a topic of public discussion. When aerosol transmission¹⁶ of Sars-CoV-2 had become obvious even for laymen, esteemed and highly knowledgeable experts acted in public as if Columbus had just discovered America. Other established knowledge about coronaviruses was also ignored for a long time, we believe. Rather, it seemed that the plans for containing a serious influenza epidemic had been taken out of the drawer, because the recommended behavioral rules were much better suited to an influenza outbreak than to a coronavirus pandemic.

The development of Sars-CoV-2 vaccines is certainly a milestone in the history of science. However, the belief that 'vaccinating out of the pandemic' with vaccines which do not produce sterile immunity was a pretty bold assumption. Similarly, the mutational propensity of coronaviruses was apparently persistently underestimated and the power of the vaccines was initially over-estimated. The reasons for this remains unclear to date. What is certain, however, is that the enormous promises of efficacy that were initially made¹³ and communicated to the general public were untenable - foreseeably untenable, if one is even rudimentarily familiar with the basic 'behavior' of coronaviruses. However, there is little room for doubt that the vaccinations very often prevent severe courses of Sars-CoV-2 type Omicron in people at risk.³

There was also irritation regarding the propagation of herd immunity as a goal, since such immunity is simply not known for coronaviruses.⁴ What is known, however, are certain variants that induce so-called cross-immunity better than other variants. Thus, logically, repeated contact with some coronaviruses and their variants (now also with vaccinations) leads to an increasingly complex cross-immunity, so that a dangerous coronavirus can become a relatively mild one, measured by symptom severity.

Another possible contributing factor is that Omicron seems to carry components of hCoV 229E², a virus with which virtually everyone has been infected in childhood or more than once in their lifetime. Partial cross-immunity can therefore at least be suspected.^{2,3} There is also no question that pandemics have always ended with a highly contagious but less dangerous variant ultimately prevailing. This now seems to be the case with Omicron. Much more important than the milder course compared to other variants of the Sars-CoV-2 virus is Omicron's infectivity.^{14,15} While it is conceivable that a more infectious variant may yet emerge, based on the brute infectious force of Sars-CoV-2 type Omicron, this possibility is more theoretical than of importance for real life.

Prognosis

Based on the aforementioned facts and additional findings as well as observations, the community-relevant aspects of the Sars-CoV-2 pandemic currently appears to be nearing its end. But the virus will remain. As Omicron or future Omicron variants it will quickly join the arsenal of endemic coronaviruses. But this is by no means the end of the issue. The four endemic coronaviruses known to date, which will soon be five, and all of them are not banal cold viruses but potent pathogens that cause hundreds of thousands of pneumonias every year, especially in winter, and which are not infrequently fatal in weakened and elderly people.⁹ It would therefore be wise for vaccine manufacturers to focus on a vaccine against the endemic coronaviruses⁷ now that viable biotechnological platforms exist.

We do not believe that a separate vaccine against Omicron is necessary.⁶ Rather, a vaccination strategy is needed that covers the known and relevant Sars-CoV-2 variants as well as the four hCoVs that have been known for some time. This would bring the Covid-19 pandemic to a favorable end, and the new technologies accelerated by the pandemic could save many lives year after year in the future. But this would require slowly lowering the alert mode for Sars-CoC-2 type Omicron now, and motivating as well as supporting vaccine manufacturers to develop broader-acting vaccines which can be administered alongside the yearly influenza vaccine. This also applies to the new drugs against coronavirus diseases. For this important step towards endemicity, a rapid alignment with reality and an end to panic mode is as important as it is desirable.

Conflicts of interest

none

References

1. Burki TK. Omicron variant and booster COVID-19 vaccines. *Lancet Respir Med*. 2021 Dec 17:S2213-2600(21)00559-2. doi: 10.1016/S2213-2600(21)00559-2. Epub ahead of print. PMID: 34929158; PMCID: PMC8683118.
2. Venkatakrisnan, A., Anand, P., Lenehan, P., Suratekar, R., Raghunathan, B., Niesen, M. J., & Soundararajan, V. (2021, December 3). Omicron variant of SARS-CoV-2 harbors a unique insertion mutation of putative viral or human genomic origin. <https://doi.org/10.31219/osf.io/f7txy>
3. Khan K, Karim F, Cele S, San JE, Lustig G, Tegally H, Bernstein M, Ganga Y, Jule Z, Reedoy K, Ngcobo N, Mazibuko M, Mthabela N, Mhlane Z, Mbatha N, Giandhari J, Ramphal Y, Naidoo T, Manickchand N, Magula N, Abdool Karim SS, Gray G, Hanekom W, von Gottberg A; COMMIT-KZN Team, Gosnell BI, Lessells RJ, Moore PL, de Oliveira T, Moosa MS, Sigal A. Omicron infection enhances neutralizing immunity against the Delta variant. *medRxiv [Preprint]*. 2021 Dec 27:2021.12.27.21268439. doi: 10.1101/2021.12.27.21268439. PMID: 34981076; PMCID: PMC8722619.
4. Christie Aschwanden (2021) Five reasons why COVID herd immunity is probably impossible. *Nature* 591, 520-522 doi: <https://doi.org/10.1038/d41586-021-00728-2>
5. Fung TS, Liu DX. Similarities and Dissimilarities of COVID-19 and Other Coronavirus Diseases. *Annu Rev Microbiol*. 2021 Oct 8;75:19-47. doi: 10.1146/annurev-micro-110520-023212. Epub 2021 Jan 25. PMID: 33492978.
6. Henning G et al. (2021) Preprint, mRNA booster immunization elicits potent neutralizing serum activity against the SARS-CoV-2 Omicron variant. doi: <https://doi.org/10.1101/2021.12.14.21267769>
7. Yin Y, Wunderink RG. MERS, SARS and other coronaviruses as causes of pneumonia. *Respirology*. 2018 Feb;23(2):130-137. doi: 10.1111/resp.13196. Epub 2017 Oct 20. PMID: 29052924; PMCID: PMC7169239.
8. Patrick DM, Petric M, Skowronski DM, Guasparini R, Booth TF, Krajden M, McGeer P, Bastien N, Gustafson L, Dubord J, Macdonald D, David ST, Srouf LF, Parker R, Andonov A, Isaac-Renton J, Loewen N, McNabb G, McNabb A, Goh SH, Henwick S, Astell C, Guo JP, Drebot M, Tellier R, Plummer F, Brunham RC. An Outbreak of Human Coronavirus OC43 Infection and Serological Cross-reactivity with SARS Coronavirus. *Can J Infect Dis*

- Med Microbiol. 2006 Nov;17(6):330-6. doi: 10.1155/2006/152612. PMID: 18382647; PMCID: PMC2095096.
9. Choi, WI., Kim, I.B., Park, S.J. et al. Comparison of the clinical characteristics and mortality of adults infected with human coronaviruses 229E and OC43. Sci Rep 11, 4499 (2021). <https://doi.org/10.1038/s41598-021-83987-3>
 10. Eskild Petersen, Marion Koopmans, Mad Unyeong, Davidson H. Hamer, Nicola Petrosillo, Francesco Castelli, Merete Storgaard, Sulien Al Khalili, Lone Simonsen (2020) Comparing SARS-CoV-2 with SARS-CoV and influenza pandemics. In: The Lancet Infectious Diseases. Vol 20.
 11. Leen Vijgen, Els Keyaerts, Elien Moës, Inge Thoelen, Elke Wollants, Philippe Lemey, Anne-Mieke Vandamme, and Marc Van Ranst (2005) Complete Genomic Sequence of Human Coronavirus OC43: Molecular Clock Analysis Suggests a Relatively Recent Zoonotic Coronavirus Transmission Event. American Society for Microbiology. Journal of Virology Volume 79, Issue 3, 1 February 2005, Pages 1595-1604. doi.org/10.1128/JVI.79.3.1595-1604.2005
 12. Brüssow H, Brüssow L. Clinical evidence that the pandemic from 1889 to 1891 commonly called the Russian flu might have been an earlier coronavirus pandemic. Microb Biotechnol. 2021 Sep;14(5):1860-1870. doi: 10.1111/1751-7915.13889. Epub 2021 Jul 13. PMID: 34254725; PMCID: PMC8441924.
 13. Gruber MF on behalf of the Food and Drug Administration, FDA, 2021, Pfizer-BioNTech COVID-19 Vaccine Emergency Use Authorization Review Memorandum. <https://www.fda.gov/media/144416/download>
 14. Torjesen I. Covid-19: Omicron may be more transmissible than other variants and partly resistant to existing vaccines, scientists fear. BMJ. 2021 Nov 29;375:n2943. doi: 10.1136/bmj.n2943. PMID: 34845008.
 15. Khan Burki T (2021) Omicron variant and booster COVID-19 vaccines. Lancet Respir. doi.org/10.1016/S2213-2600(21)00559-2
 16. Tang S, Mao Y, Jones RM, Tan Q, Ji JS, Li N, Shen J, Lv Y, Pan L, Ding P, Wang X, Wang Y, MacIntyre CR, Shi X. Aerosol transmission of SARS-CoV-2? Evidence, prevention and control. Environ Int. 2020 Nov;144:106039. doi: 10.1016/j.envint.2020.106039. Epub 2020 Aug 7. PMID: 32822927; PMCID: PMC7413047

Science. Proudly made in Greece.

