



World Health Organization				Analysis	Published online: 14 December 2022 Nature www.nature.co
Health Topics v	Countries v	Newsroom ~	Emergencies v	The WHO est associated wi	imates of excess mortality ith the COVID-19 pandemic
lews / 14.9 million excess de	aths associated with the COVI	ID-19 pandemic in 2020 an	ıd 2021	https://doi.org/10.1038/s41586-022-0552 Received: 19 May 2022	William Msemburi ¹¹⁵ , Ariel Karlinsky ² , Victoris Knutson ³ , Serge Aleshin-Guendel ⁴ , Somnath Chatterji ¹⁶ & Jon Wakefield ⁴⁴
14.9 million excess deaths associated with the COVID-19				Accepted: 3 November 2022	The World Health Organization has a mandate to compile and disseminate statistic on mortality, and we have been tracking the progression of the COVID-19 pandemic
				Published online: 14 December 2022	
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WHO announces simple, easy-to-say labels May 2021 for SARS-CoV-2 Variants of Interest and Concern 31 May 2021 | WHO has assigned simple, easy to say and remember labels for key variants of SARS-CoV-2, the virus that causes COVID-19, using letters of the Greek alphabet. These labels were chosen after wide consultation and a review of many potential naming systems. WHO convened an expert group of partners from around the world to do so, including experts who are part of existing naming systems, nomenclature and virus taxonomic experts, researchers and national authorities. WHO will assign labels for those variants that are designated as Variants of Interest or Variants of Concern by WHO. These will be posted on the WHO website. $\prod_{\text{pi}} \pi P_{\text{rho}} \rho \sum_{\text{sigma}} \sigma/\varsigma T_{\text{tau}} \tau V_{\text{upsilon}} \upsilon$ These labels do not replace existing scientific names (e.g. those assigned by GISAID, $\Phi \phi X \chi \Psi \psi \Omega \omega$ Nextstrain and Pango), which convey important scientific information and will continue to be used in research. While they have their advantages, these scientific names can be difficult to say and recall, and are prone to misreporting. As a result, people often resort to calling variants by the places where they are detected, which is stigmatizing and discriminatory. To avoid this and to simplify public communications, WHO encourages national authorities, media outlets and others to adopt these new labels. https://www.who.int/news/item/31-05-2021-who-announces-simple-easy-to-saylabels-for-sars-cov-2-variants-of-interest-and-concern

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Variants of interest (VOI)

Working definition

A SARS-CoV-2 variant :

- with genetic changes that are predicted or known to affect virus characteristics such as transmissibility, disease severity, immune escape, diagnostic or therapeutic escape; AND
- Identified to cause significant community transmission or multiple COVID-19 clusters, in multiple countries with increasing relative prevalence alongside increasing number of cases over time, or other apparent epidemiological impacts to suggest an emerging risk to global public health.

Epsilon, Zeta, Eta, Theta, Iota, Kappa, Lambda, Mu

NOTE:

- Nu and Xi were skipped between Mu and Omicron ("new" / Xi Jinping).
- No new Greek letters have been assigned since Omicron in late 2021.
- Now also a category "Omicron subvariants under monitoring".

Variants of concern (VOC)

Working definition:

A SARS-CoV-2 variant that meets the definition of a VOI (see below) and, through a comparative assessment, has been demonstrated to be associated with one or more of the following changes at a degree of global public health significance:

- Increase in transmissibility or detrimental change in COVID-19 epidemiology; OR
- Increase in virulence or change in clinical disease
 presentation; OR
- Decrease in effectiveness of public health and social measures or available diagnostics, vaccines, therapeutics.

Alpha, Beta, Gamma, Delta, Omicron

https://www.who.int/activities/tracking-SARS-CoV-2-variants





Viral evolution occurs at two levels

Within hosts

Intra-host evolution

- Variable "swarm" ("quasispecies") of viruses • Infection with multiple versions
 - Mutations within host after infection
- Selective pressure is on outcompeting other versions of the virus within the host.
 - Faster replication?
 - Better at entering cells?
 - Attack more tissues?
- Could lead to more damage to host (increased virulence)
- Most successful version within host most likely to be transmitted to new host
- Especially likely if persistent infection

Among hosts

Inter-host evolution

- Selective pressure is on infecting new hosts.
- Getting to new hosts
 - Higher viral load, more shedding?
 - Hanging in air longer?
- Infecting new hosts
 - Enters more easily accessible tissues? (e.g., higher in respiratory tract)
 - Better at entering host cells?

Escaping host immunity

- Can avoid detection or destruction by host immune system
- Ability to re-infect / infect vaccinated hosts
- Especially likely if unmitigated transmission























What could happen with this variant cloud?

1) One variant eventually becomes dominant everywhere.

2) One variant becomes dominant in one place, another variant becomes dominant elsewhere (then maybe they swap).

3) The same subset of variants in the cloud becomes dominant everywhere (and no single dominant variant takes over by itself).

4) Different subsets of variants become dominant in different places (then maybe they swap).

5) Turnover in variants within the soup as new ones evolve and older ones disappear, with high numbers of infections but no one variant or subset of variants ever reaches a very high frequency.







Could a major new variant (Pi or Rho) still evolve?

Yes.

At least four ways this could happen:

1) A lot of change in an Omicron lineage in a different evolutionary direction.

2) Within-host evolution of an older variant in host with persistent infection.

3) Recombination among variant lineages (e.g., "Deltacron" or worse).

4) Ping-pong zoonosis.









What about China?

- "Zero COVID" approach has kept the virus under control for 3 years. Now strict control measures are being relaxed.
- 1.4 billion previously unexposed potential hosts. 850 million live in cities.
- Limited vaccine protection (less effective, low booster rates).
- Evolutionary landscape for the virus will be very different in a new and denselypopulated host population.
 - Less about immune escape, more about transmission.
 - Lots of available hosts nearby means less selection against virulence.
- Variants that evolve in this new host population may not be able to outcompete other variants globally – but then there's the possibility of recombination.

FORTUNE Well, LIFE HEALTH MIND FAMILY MORE~

Scientists have their eyes on several 'Deltacrons' new COVID variants with the potential to attack the lungs like Delta and spread as easily as Omicron

BY ERIN PRATER November 1, 2022 at 5:00 AM EDT



















































6	chasewnelson	1 🖋 Nov '21
	Mutagenic antivirals: the evolutionary risk of	of low doses
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)ne dra nissed nucosa ntivira eachin Sadler	awback of self-administered oral medications is the risk of I doses, incomplete courses, or low initial drug penetrance al membranes in the nasal passages or lungs). Critically, i als like molnupiravir , low drug concentrations might incre- ing the level required for error catastrophe, instead inducing r et al. 2010). This could accelerate within-host evolution of	f low drug concentrations due to e at the site of action (e.g., n the case of mutagenic ase the mutation rate without g only sublethal mutagenesis of the virus, potentiating new





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Functional and genetic analysis of viral receptor ACE2 orthologs reveals a broad potential host range of SARS-CoV-2

Yinghui Liu^{a,1}, Gaowei Hu^{b,1}, Yuyan Wang^{b,1}, Wenlin Ren^{a,1}, Xiaomin Zhao^{a,1}, Fansen Ji^a, Yunkai Zhu^b, Fei Feng^b, Mingli Gong^a, Xiaohui Ju^a, Yuanfei Zhu^b, Xia Cai^b, Jun Lan^c, Jianying Guo^a, Min Xie^a, Lin Dong^a, Zihui Zhu^a, Jie Na^a, Jianping Wu^{d,e}, Xun Lan^a, Youhua Xie^b, Xinquan Wang^{c,f}, Zhenghong Yuan^{b,2}, Rong Zhang^{b,2}, and Qiang Ding^{a,f,2}

Significance

COVID-19, caused by SARS-CoV-2, is a major global health threat. The host range of SARS-CoV-2 and intermediate hosts that facilitate its transmission to humans remain unknown. We found that SARS-CoV-2 has the potential to infect a broad range of mammalian hosts, including domestic animals, pets, livestock, and animals commonly found in zoos and aquaria. Those species may be at risk for human-to-animal or animal-toanimal transmissions of SARS-CoV-2. Our study highlights the importance of banning illegal wildlife trade and consumption, and enforcing the importance of surveilling animals in close contact with humans as potential zoonotic reservoirs to prevent outbreaks in the future.



NATURE REVIEWS | MICROBIOLOGY

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Antigenic evolution will lead to new SARS-CoV-2 variants with unpredictable severity

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The comparatively milder infections with the Omicron variant and higher levels of population immunity have raised hopes for a weakening of the pandemic. We argue that the lower severity of Omicron is a coincidence and that ongoing rapid antigenic evolution is likely to produce new variants that may escape immunity and be more severe.







