L'EVOLUZIONE DI SARS-COV-2: IMPATTO CLINICO-EPIDEMIOLOGICO, TERAPEUTICO E DI PREVENZIONE

12 Maggio 2022 – Ore 16.00-19.00

SCUOLA DI SPECIALIZZAZIONE IN MALATTIE INFETTIVE E TROPICALI

PANDORA ID - 22

TIME TO WEBINAR IN INFECTIOUS DISEASES

PROGETTO DI FORMAZIONE

SARS-CoV-2: dall'isolamento virale allo sviluppo delle varianti



Maria Rosaria Capobianchi

INTERNATIONAL UNIVERSITY OF HEALTH SCIENCES
In Lumine Tuo Videbimus Lumen
SAINT CAMILLUS

UNICAMILLUS
International Medical University in Rome

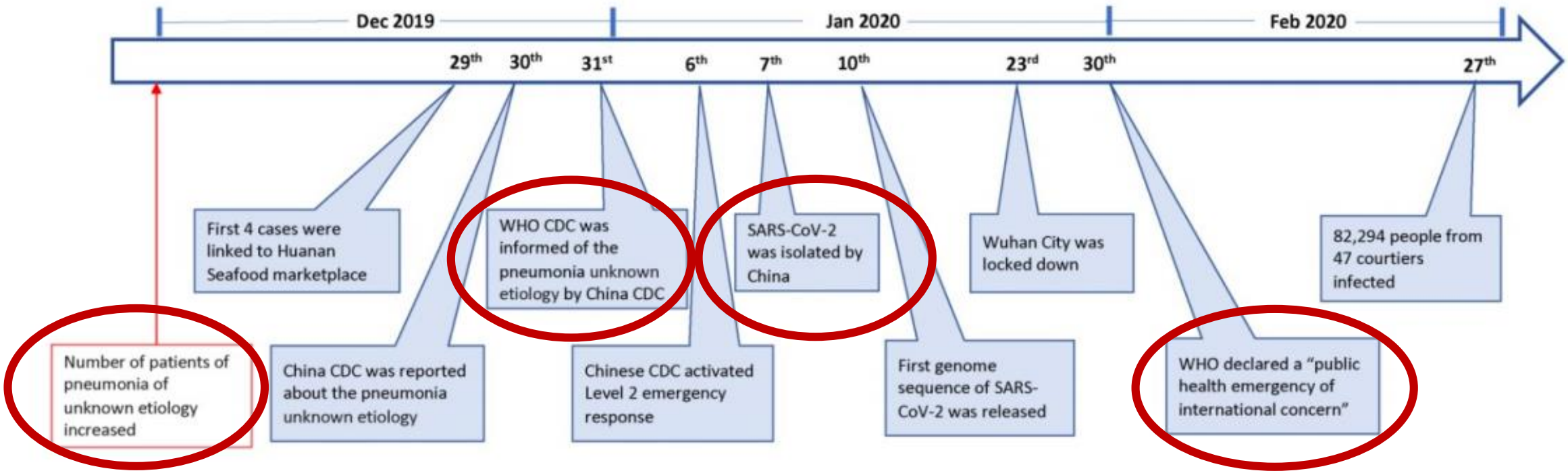
31 December 2019: China CDC informed WHO about pneumonia of unknown etiology

9 January 2020: China CDC reported that a novel coronavirus had been detected as the causative agent for pneumonia cases

10 January 2020: The first novel coronavirus genome sequence was made publicly available

Unprecedented race for virus characterization and for the exploitation of information:

- Diagnostics
- Surveillance
- Treatment
- Vaccine



Zheng J. SARS-CoV-2: an Emerging Coronavirus that Causes a Global Threat. Int. J. Biol. Sci. 2020

Coronavirus: primi due casi positivi in Italia a Roma

31/01/2020






Libero

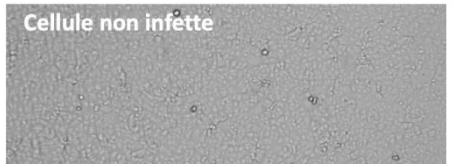
Dagli italiani una lezione al mondo

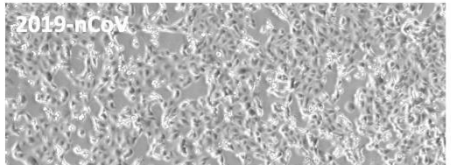
A ROMA IN 48 ORE TROVANO IL VIRUS

Medici donne dello Spallanzani (meridionali) sono riusciti a fare il miracolo Meritano applausi e gratitudine. E poi dicono che al Sud non fanno nulla...

Renzi a Conte: giù le mani dalla giustizia o ti licenzio

Il virus 2019-nCoV/Italy-INMI1 isolato in coltura





Roma, 2 febbraio 2020: conferenza stampa allo Spallanzani





il Fatto Quotidiano

Quotidiano

Consiglio Nazionale delle Ricerche

Data 25-02-2020
Pagina 1+6
Foglio 1 / 2

4. LO STORICO: PESTE, SPAGNOLA & C.

"È sempre caccia all'untore"

L'INTERVISTA

Andrea Grignolo *Il professore del San Raffaele: "La paura delle infezioni è frutto di una lunga storia, ma la lotta contro i virus è una storia di successi"*

"Lo straniero come untore: accusare gli altri è tipico"

il Fatto Quotidiano
Quotidiano
Consiglio Nazionale delle Ricerche
Data 25-02-2020
Pagina 1+6
Foglio 1 / 2

4. LO STORICO: PESTE, SPAGNOLA & C.

"È sempre caccia all'untore"

L'INTERVISTA

Andrea Grignolo *Il professore del San Raffaele: "La paura delle infezioni è frutto di una lunga storia, ma la lotta contro i virus è una storia di successi"*

"Lo straniero come untore: accusare gli altri è tipico"



20 febbraio primo caso a Codogno



21 febbraio primo decesso a Vo'



il Fatto Quotidiano
Quotidiano
Consiglio Nazionale delle Ricerche
Data 25-02-2020
Pagina 1+6
Foglio 1 / 2

4. LO STORICO: PESTE, SPAGNOLA & C.

"È sempre caccia all'untore"

L'INTERVISTA

Andrea Grignolo *Il professore del San Raffaele: "La paura delle infezioni è frutto di una lunga storia, ma la lotta contro i virus è una storia di successi"*

"Lo straniero come untore: accusare gli altri è tipico"



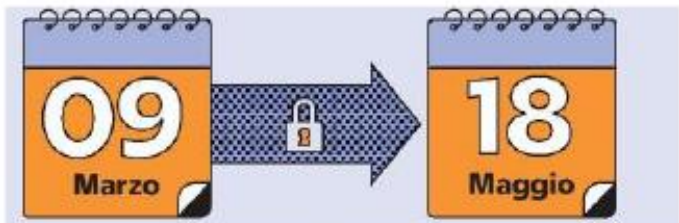


31 DICEMBRE
Le autorità cinesi segnalano all'Oms diversi casi di una misteriosa polmonite a Wuhan (città nell'Hubei). Molti lavorano al mercato del pesce e animali vivi di Huanan, in centro città

11 FEBBRAIO
L'Oms dà un nome al virus, Sars-CoV 2, e alla malattia che causa, Covid-19



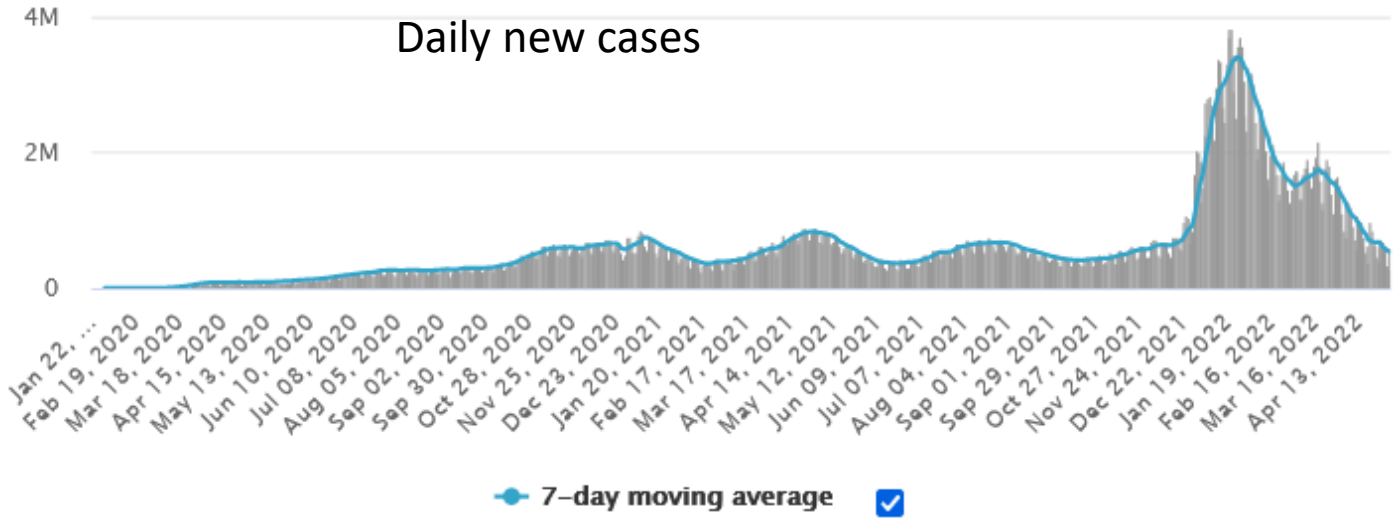
21 FEBBRAIO
La prima vittima italiana è Adriano Trevisan, un 78enne di Vo' Euganeo, in provincia di Padova. Poche ore prima era stato identificato il paziente zero, un 38enne di Codogno. Scoppiano focolai in alcune zone della Lombardia



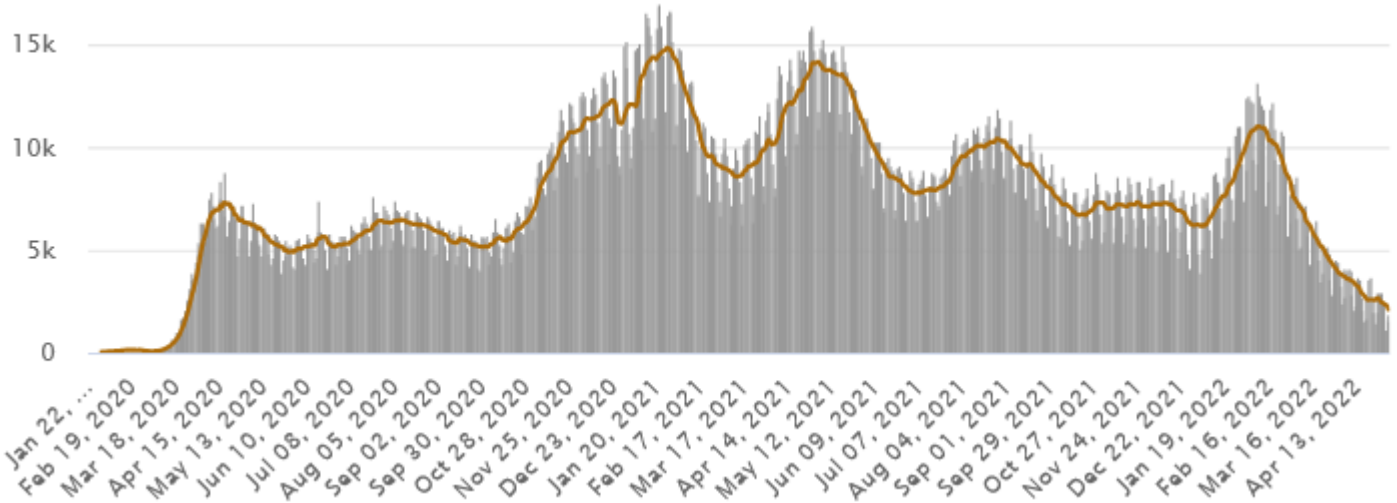
9 MARZO
Con un decreto in vigore dal giorno successivo inizia il lockdown nazionale. L'Italia è il primo Paese occidentale ad adottare misure così restrittive. Il lockdown terminerà il 18 maggio

worldometer

Daily new cases



Daily deaths



https://www.worldometers.info/coronavirus/Last updated: May 4, 2022

Coronavirus Cases:

514,763,538

view by country

Deaths:

6,266,199

Recovered:

469,501,523

In Italy:

16,586,268 cases

>1/4 (27.5% overall population)

163,889 deaths

Comparing pandemics

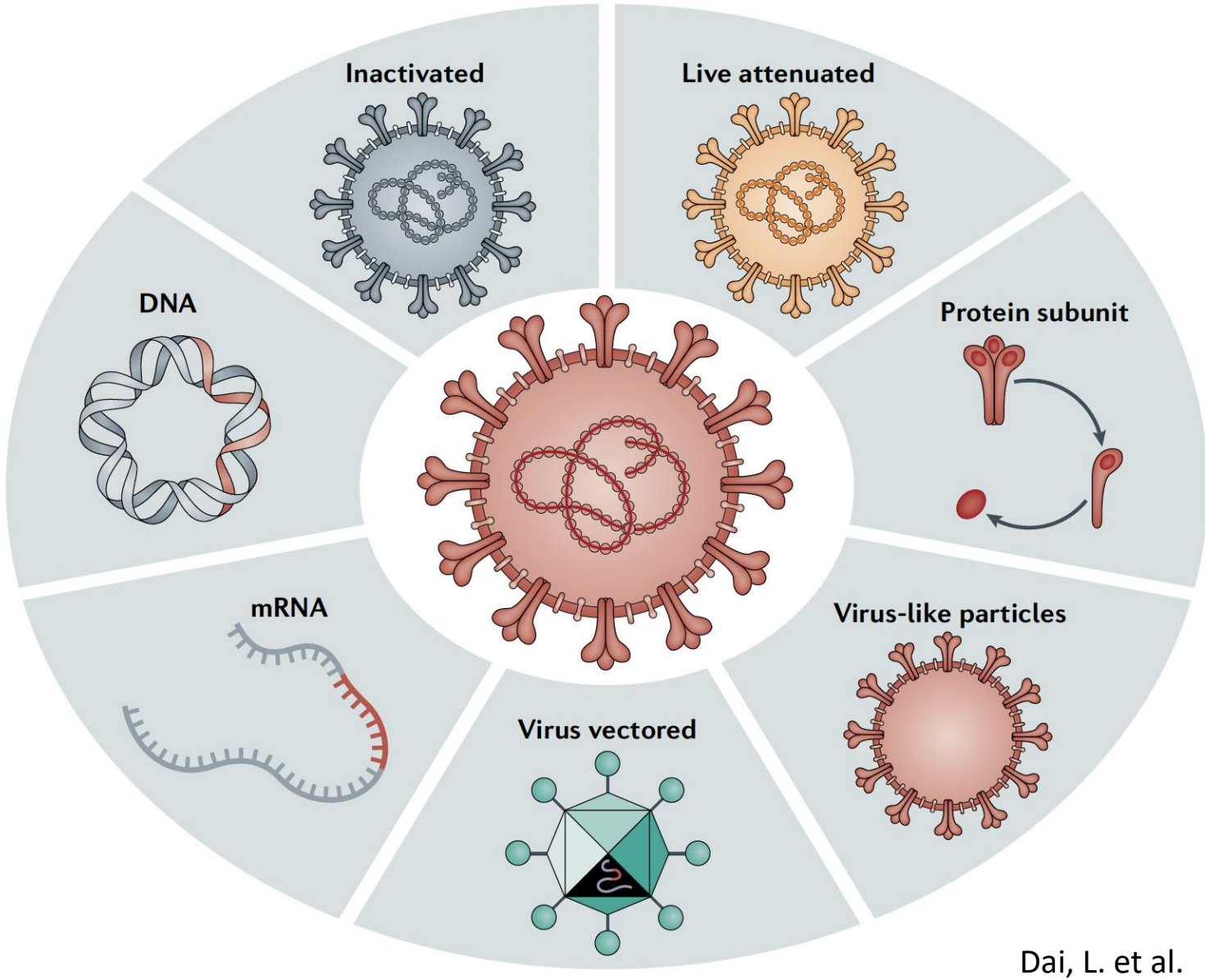
The COVID-19 pandemic is the largest since the 1918–20 H1N1 influenza pandemic when scaled to 2020 populations.
Sources: Simonsen, L. & Viboud, C. eLife 10, e71974 (2021); COVID-19 estimates: The Economist's model (to January 2022); age of death data: US CDC, UKHSA.

		Swine	Hong Kong	Asian	Spanish
Metric	**COVID-19**	**Flu 2009 (H1N1)**	**Flu 1968 (H3N2)**	**Flu 1957–59 (H2N2)**	**Flu 1918–20 (H1N1)**
Per-capita excess mortality rate (estimate)	0.15–0.28%	0.005%	0.03%	0.04%	1%
Global excess deaths (estimate) adjusted to 2020 population	12–22 million	0.4 million	2.2 million	3.1 million	75 million
Mean age at death (years; United States and Europe only)	73–79	37	62	65	27

Adam D. Nature 2022


GAME
CHANGER

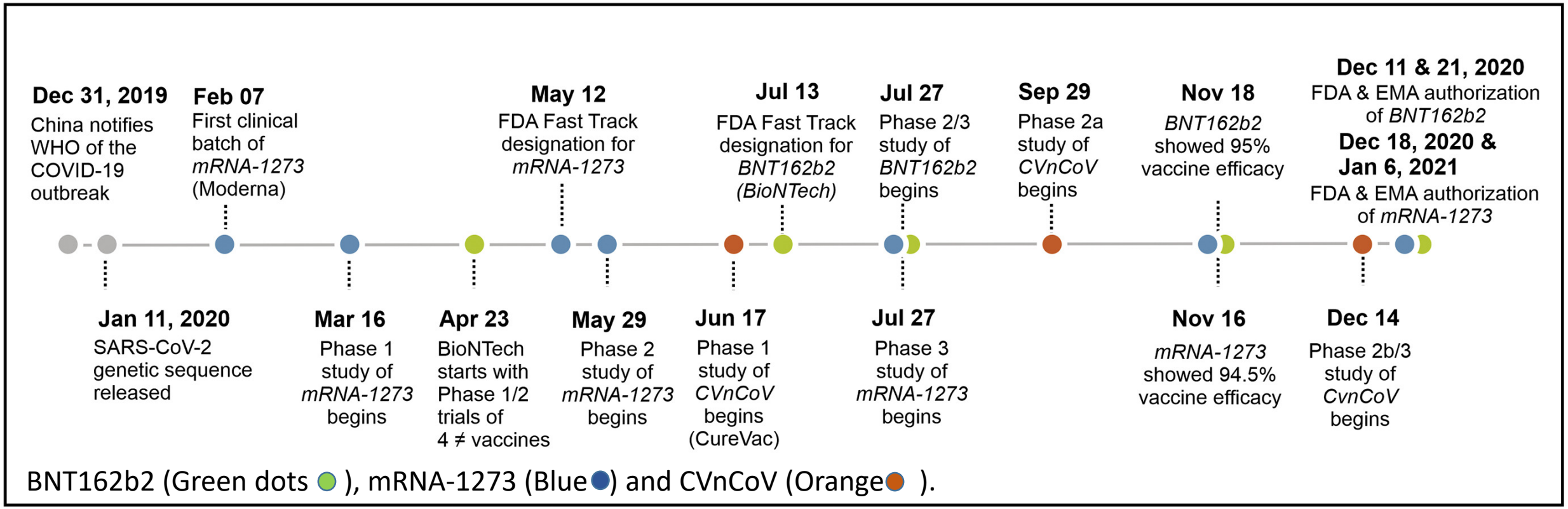
Sars-CoV-2 vaccines



Dai, L. et al. Nat Rev Immunol 2021

Few weeks after the release of the virus genome sequence the prototype mRNA vaccine production was started

One of the most spectacular progress in the fight against infectious diseases: from sequence to the design and delivery of vaccines



BNT162b2 (Green dots), mRNA-1273 (Blue) and CVnCoV (Orange).

Verbeke R.et al. J Control Release 2021

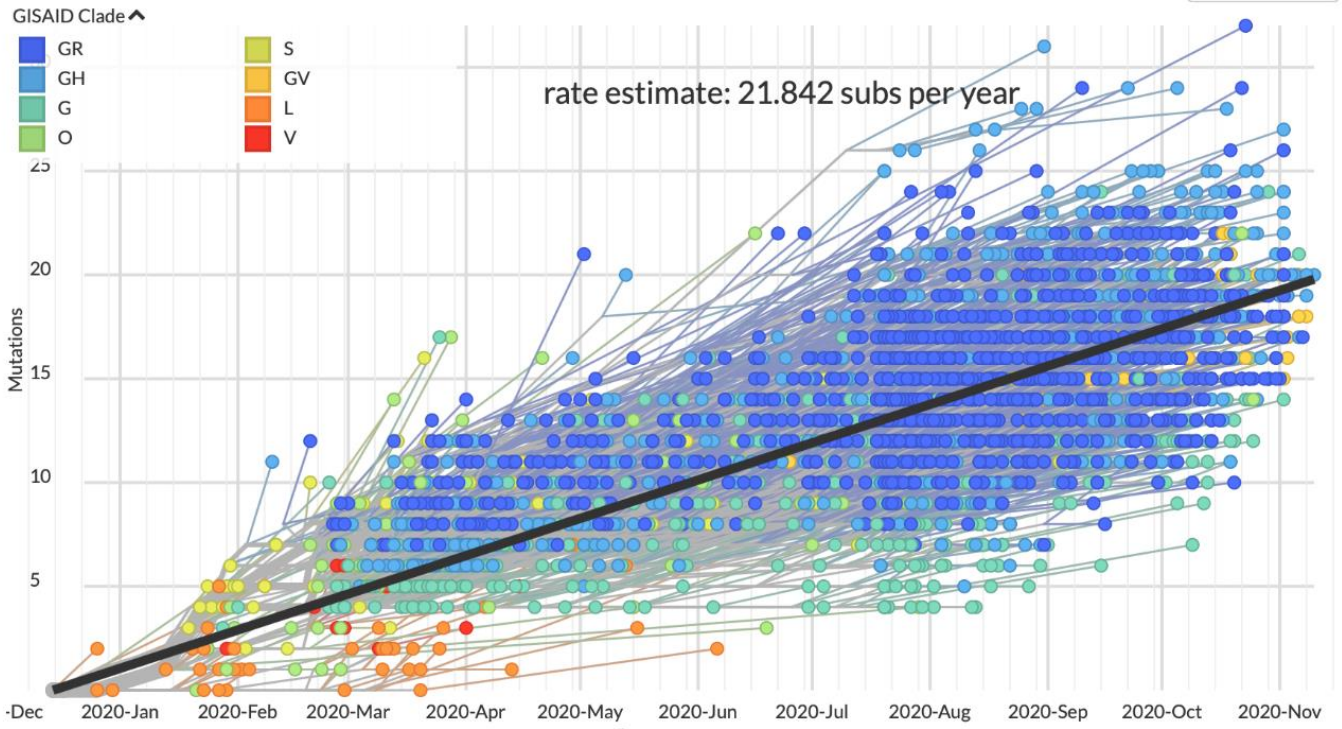
What around the corner?



Sars-CoV-2: Virus variability

SARS-CoV-2 mutation rate estimate:

- Between **1.2/10,000** and **6.6/1,000 nucleotides per year**
- Considering a genome of 30,000 nt, we expect about 2 mutations every months (average)



GISAID. https://www.gisaid.org/epiflu-applications/phylodynamics/

Nextstrain

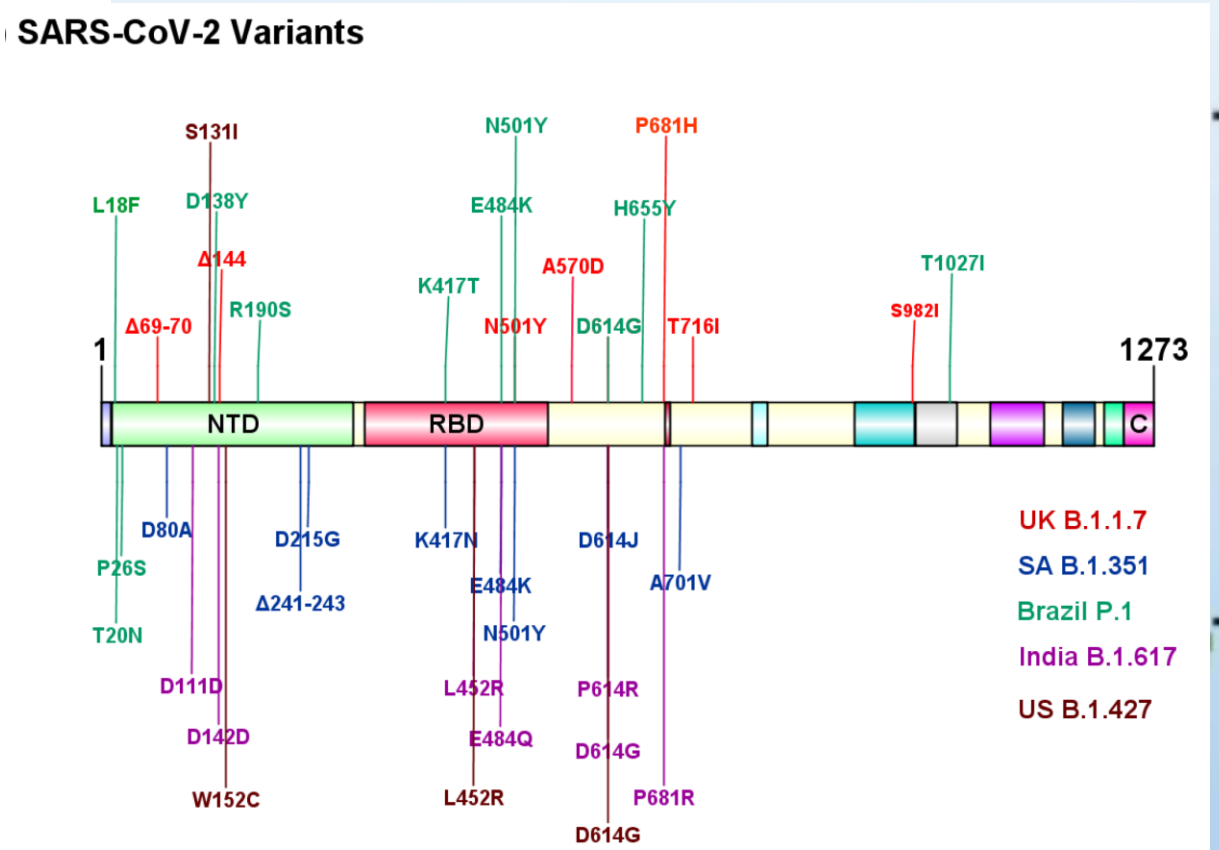
GISAID

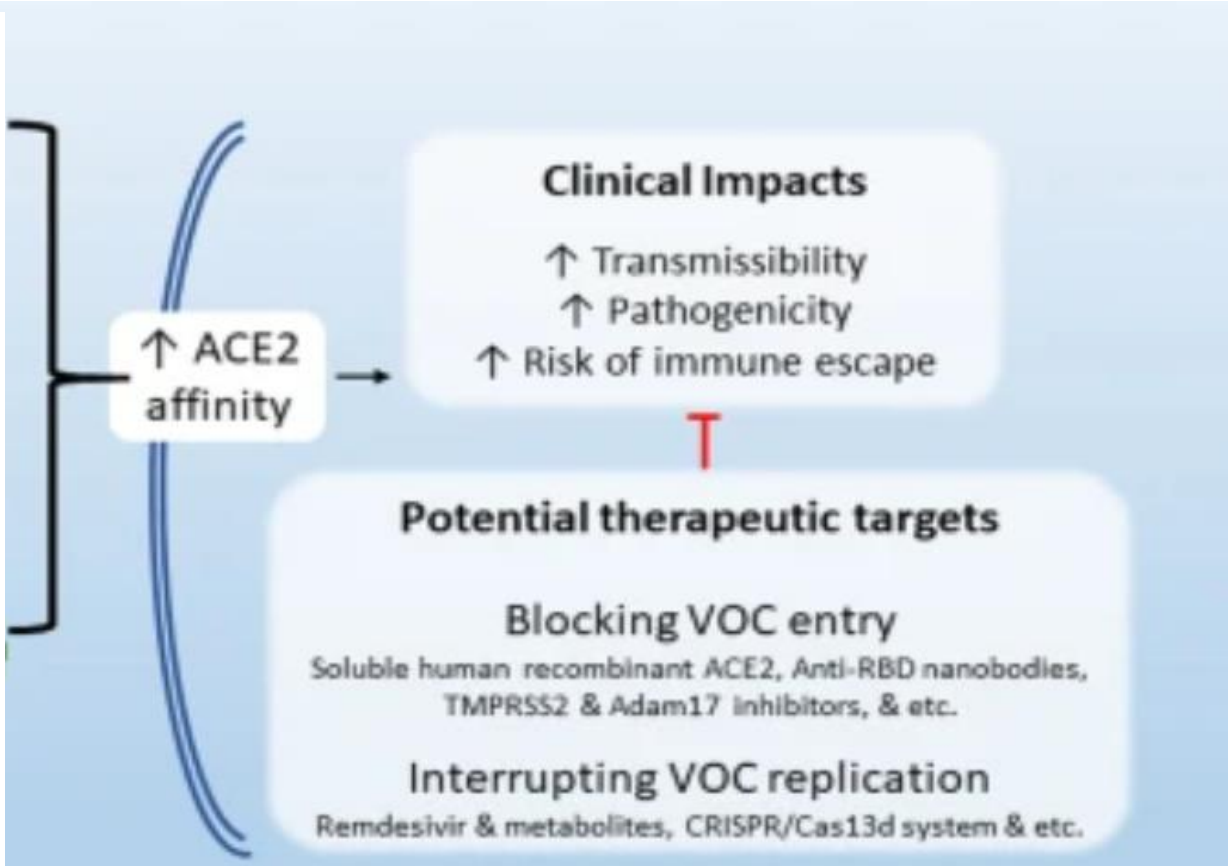


- As of December 1st, 2021, there are **10,381 distinct amino acid substitutions**, insertions, or deletions in Spike sequences from the GISAID database.
- These mutations occur in different combinations, creating **over 160,000 unique Spike** protein sequences.

Why should we monitor SARS-CoV-2 variants

- Because SARS-CoV-2 has infected and spread within an immunologically naïve population, it has yet to experience the sort of immune pressure that helped shape the evolution of the endemic viruses and its own capacity to evolve remains unknown
- We must continue to be diligent in tracking genetic changes in the novel coronavirus, both to follow their spread and quickly identify antigenic shifts should they occur

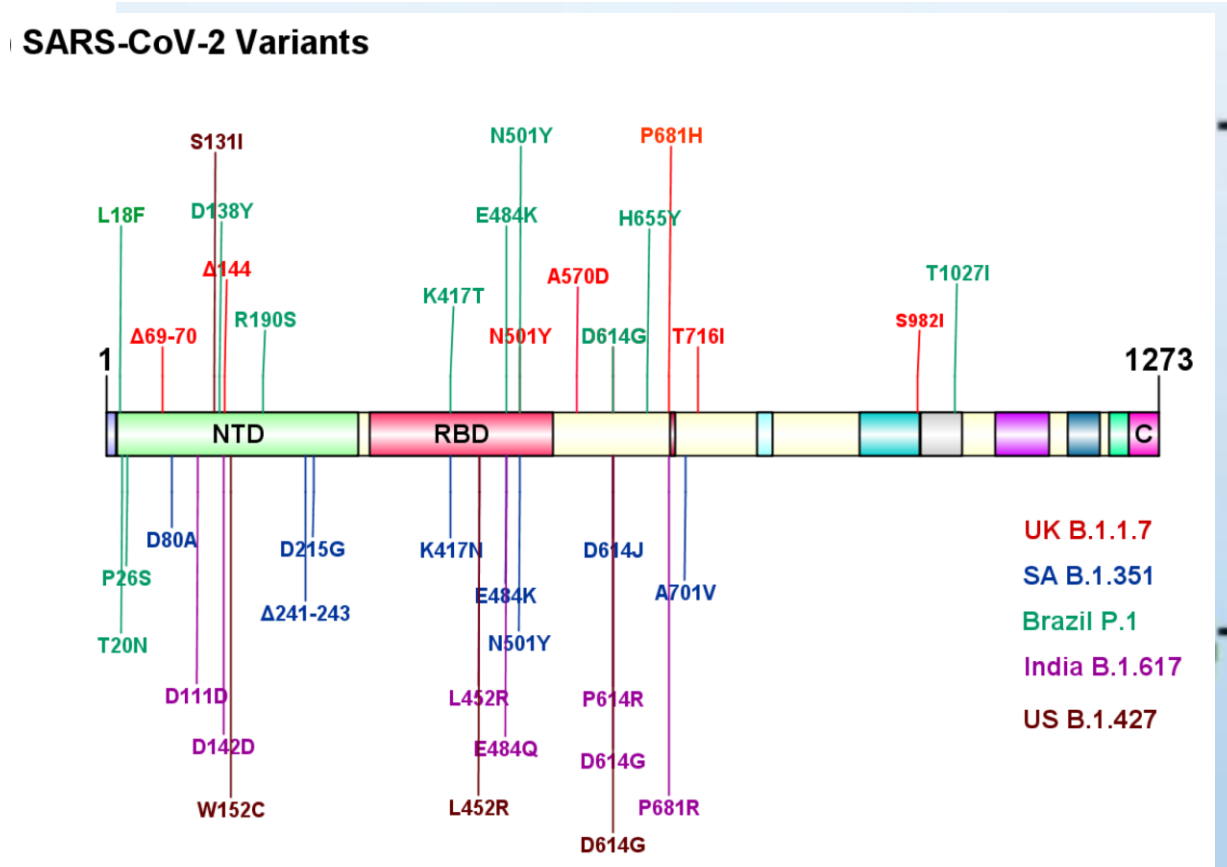


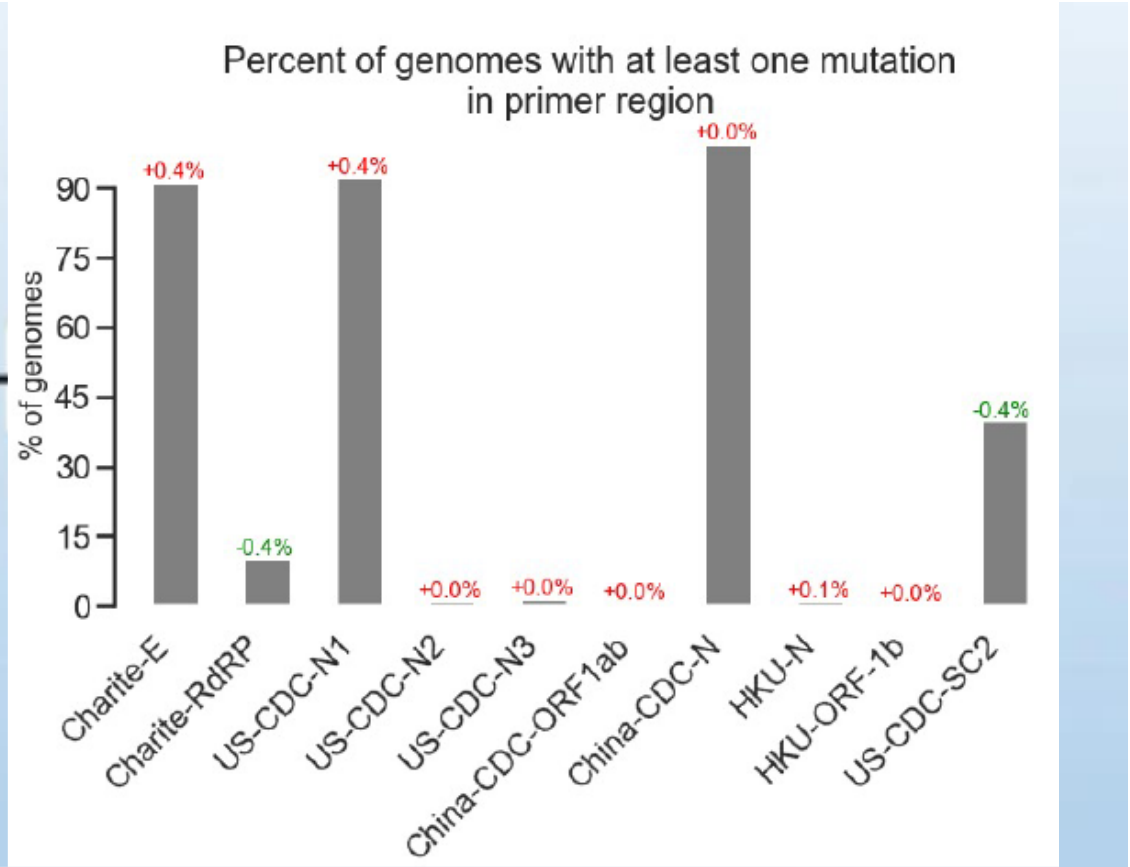


Khateeb, J. et al. Crit Care 2021
Raman R. et a. Biomolecules 2021

Why should we monitor SARS-CoV-2 variants

- Because SARS-CoV-2 has infected and spread within an immunologically naïve population, it has yet to experience the sort of immune pressure that helped shape the evolution of the endemic viruses and its own capacity to evolve remains unknown
- We must continue to be diligent in tracking genetic changes in the novel coronavirus, both to follow their spread and quickly identify antigenic shifts should they occur
- Mutations may impact diagnostic efficacy

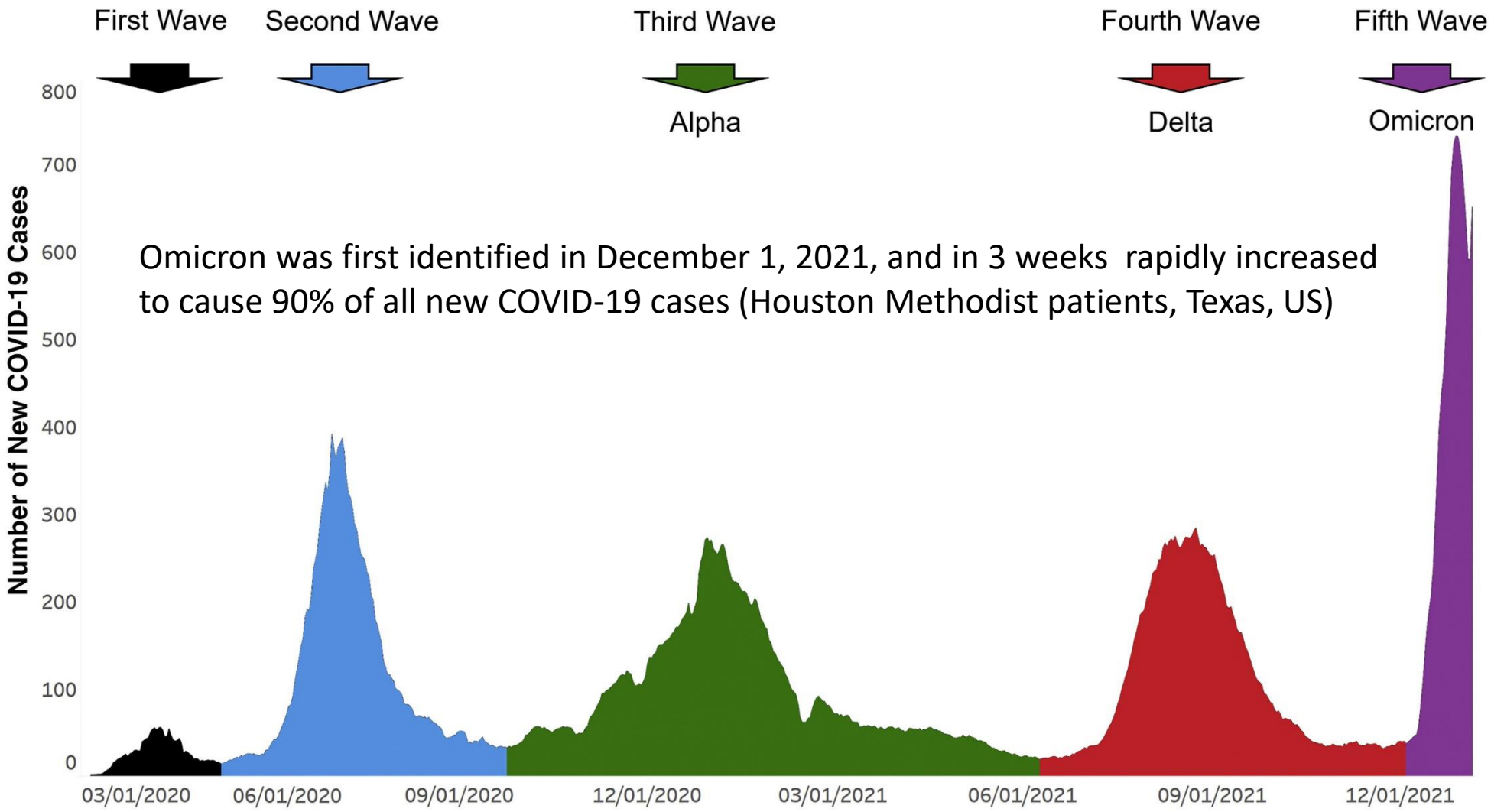




GISAID

Khateeb, J. et al. Crit Care 2021
Raman R. et a. Biomolecules 2021

The virus changes: new variants underpin the spread of the new waves



Omicron was first identified in December 1, 2021, and in 3 weeks rapidly increased to cause 90% of all new COVID-19 cases (Houston Methodist patients, Texas, US)

Christensen PA et al. Am J Pathol 2022

Timecourse of variant distribution in all submitted sequences
2022-05-03

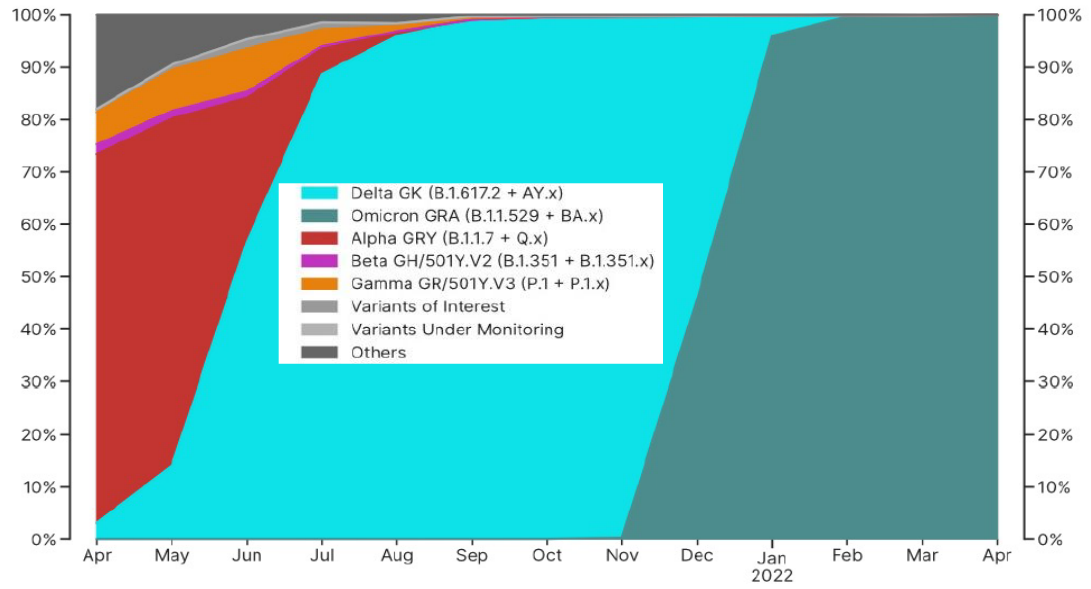


Tabella 5 – Andamento delle stime di prevalenza delle VOC di SARS-CoV-2 (24 febbraio 2020 - oggi)

Variante	Alpha	Beta	Gamma	Delta	Omicron	Altro
18/02/2021	54%	0,40%	4,30%	0	0	41,30%
18/03/2021	86,70%	0,10%	4,00%	0	0	9,20%
20/04/2021	91,60%	0,10%	4,50%	0%	0	3,80%
18/05/2021	88,10%	0,30%	7,30%	1,00%	0	3,30%
22/06/2021	57,80%	0%	11,80%	22,70%	0	7,70%
20/07/2021	3,20%	0	1,40%	94,80%	0	0
24/08/2021	0,30%	0	0	99,70%	0	0
06/12/2021	0	0	0	99,72%	0,32%	0
20/12/2021	0	0	0	79%	21%	0
03/01/2022	0	0	0	19,22%	80,75%	0
17/01/2022	0	0	0	4,20%	95,80%	0
31/01/2022	0	0	0	0,90%	99,10%	0

Timecourse of variant distribution in all submitted sequences 2022-05-03

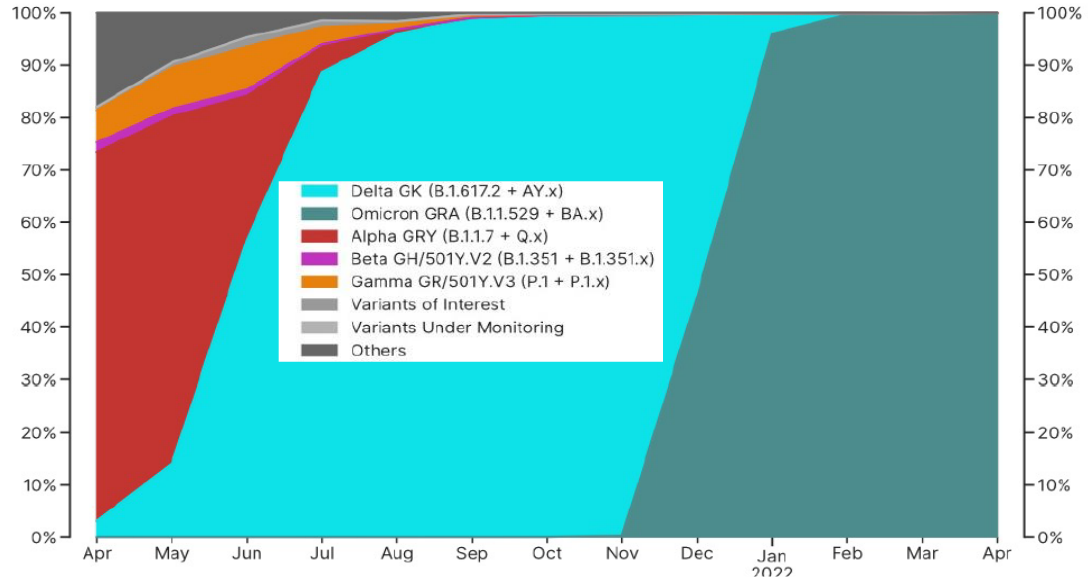
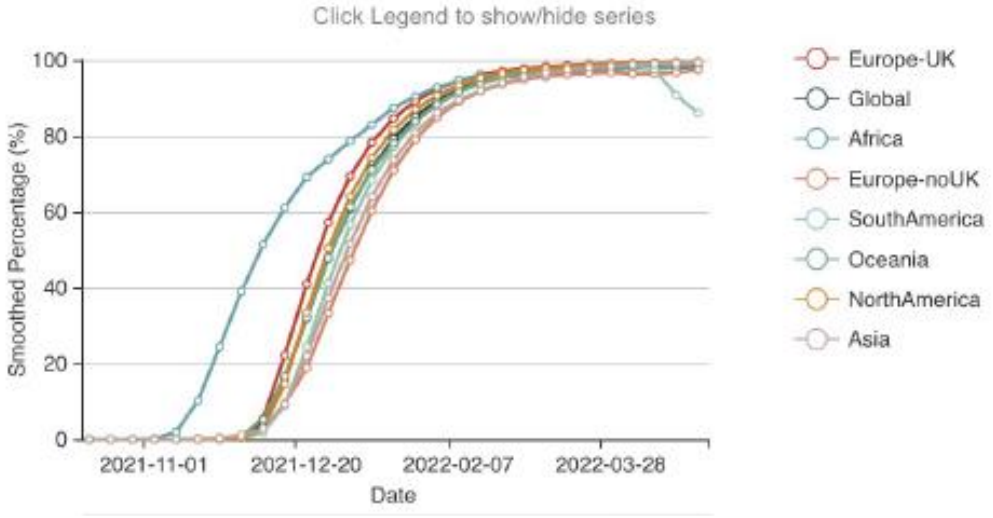


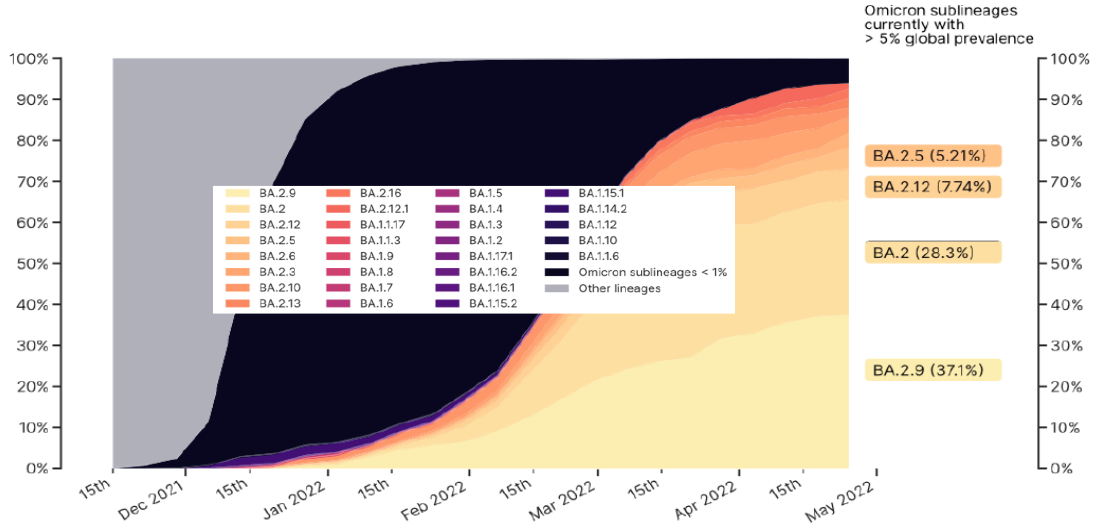
Tabella 5 – Andamento delle stime di prevalenza delle VOC di SARS-CoV-2 (24 febbraio 2020 - oggi)

Variante	Alpha	Beta	Gamma	Delta	Omicron	Altro
18/02/2021	54%	0,40%	4,30%	0	0	41,30%
18/03/2021	86,70%	0,10%	4,00%	0	0	9,20%
20/04/2021	91,60%	0,10%	4,50%	0%	0	3,80%
18/05/2021	88,10%	0,30%	7,30%	1,00%	0	3,30%
22/06/2021	57,80%	0%	11,80%	22,70%	0	7,70%
20/07/2021	3,20%	0	1,40%	94,80%	0	0
24/08/2021	0,30%	0	0	99,70%	0	0
06/12/2021	0	0	0	99,72%	0,32%	0
20/12/2021	0	0	0	79%	21%	0
03/01/2022	0	0	0	19,22%	80,75%	0
17/01/2022	0	0	0	4,20%	95,80%	0
31/01/2022	0	0	0	0,90%	99,10%	0

Relative Variant Genome Frequency per Region (exponentially smoothed alpha=0.3)



Timecourse of Omicron variant sublineage distribution 2022-05-03

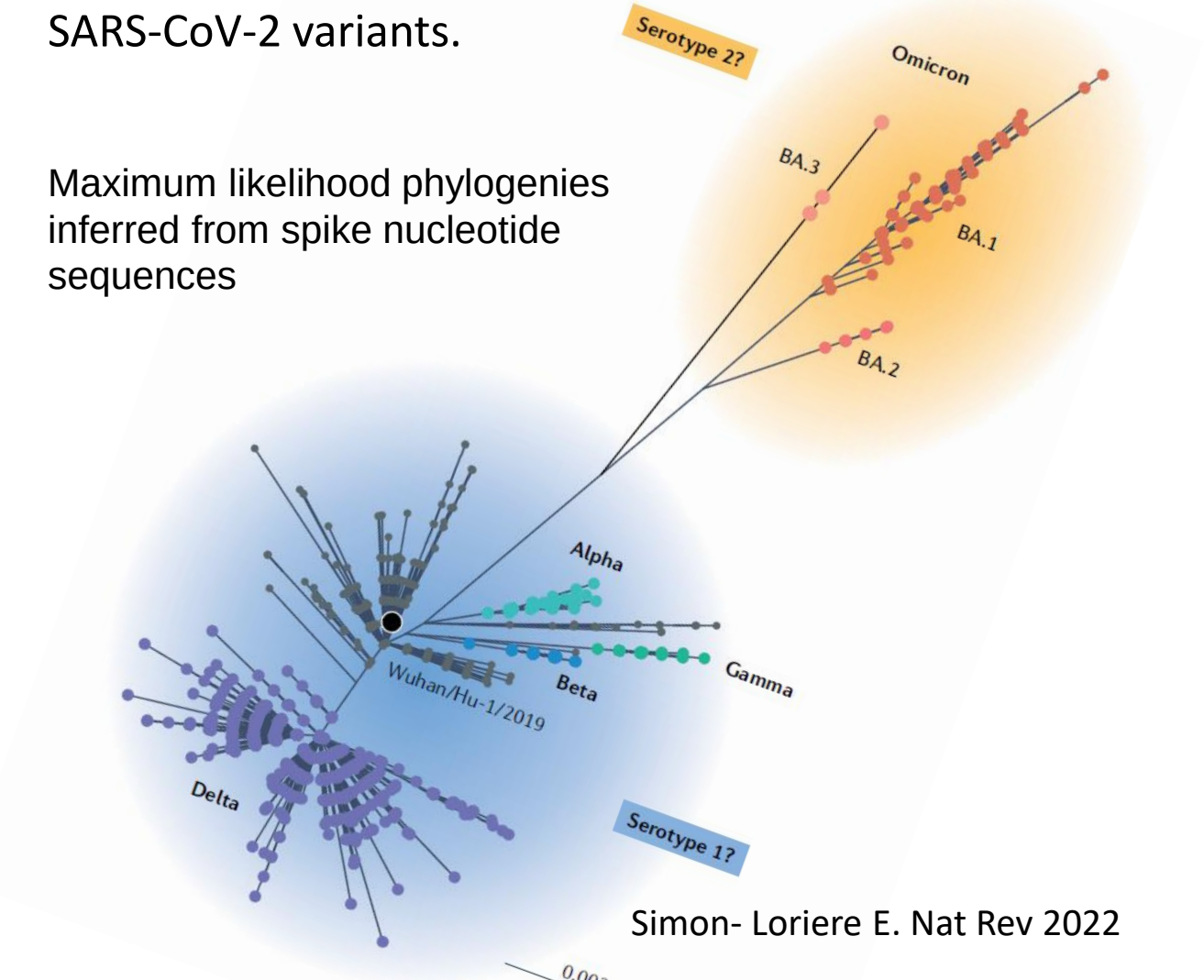


Molecular characterization

The omicron lineage does not derive from recently circulating variants, and comprises sublineages.

Omicron displays pathological, genetic, structural and antigenic features that clearly distinguish it from prior SARS-CoV-2 variants.

Maximum likelihood phylogenies inferred from spike nucleotide sequences



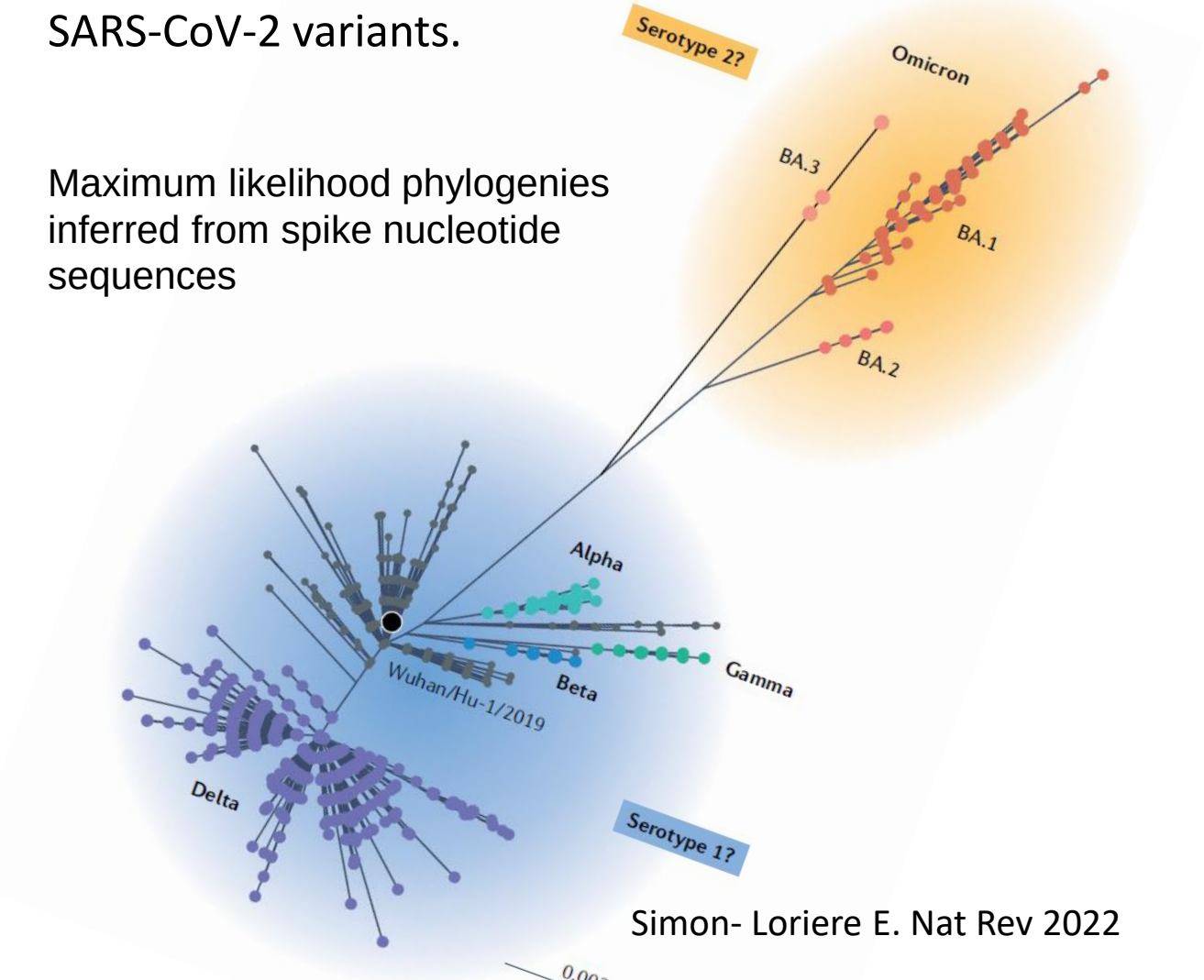
Simon- Loriere E. Nat Rev 2022

Molecular characterization

The omicron lineage does not derive from recently circulating variants, and comprises sublineages.

Omicron displays pathological, genetic, structural and antigenic features that clearly distinguish it from prior SARS-CoV-2 variants.

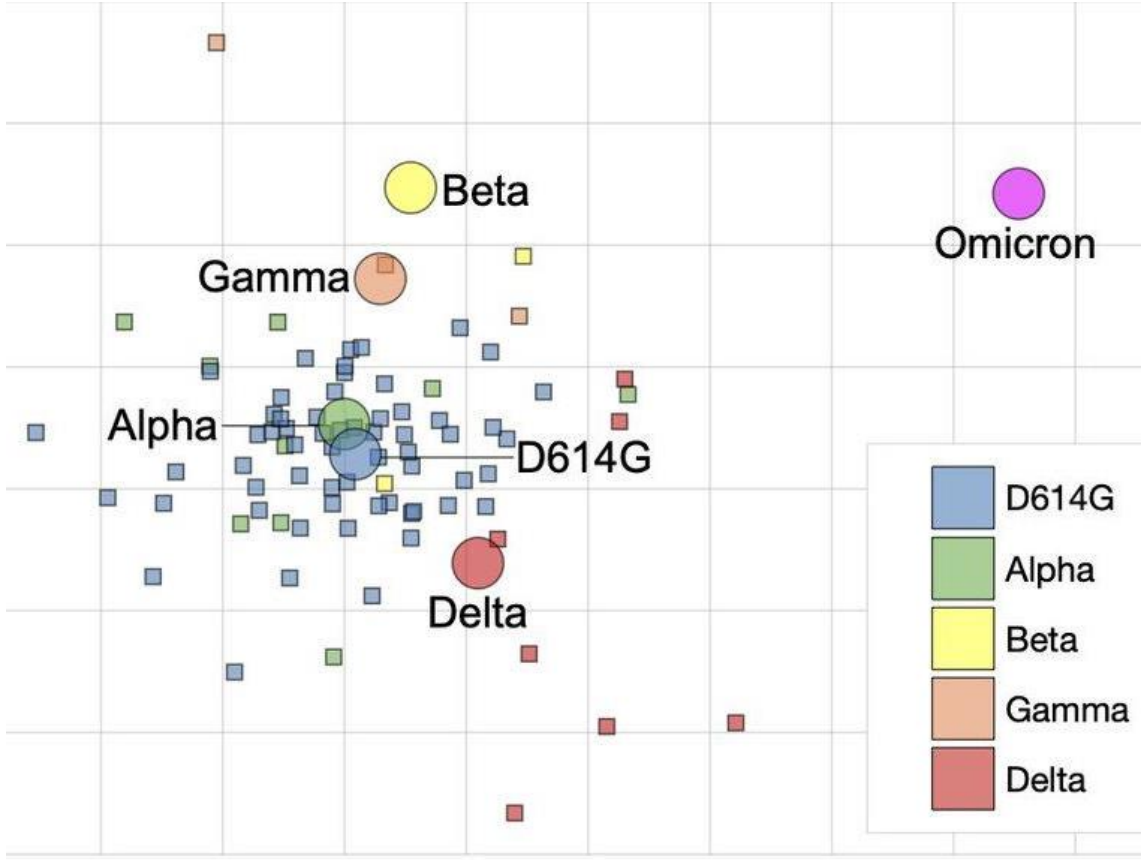
Maximum likelihood phylogenies inferred from spike nucleotide sequences



Simon- Loriere E. Nat Rev 2022

Serological characterization

Antigenic map of SARS-CoV-2 VOCs based on post-SARS-CoV-2 infection sera. SARS-CoV-2 VOCs are shown as circles and sera are indicated as squares.



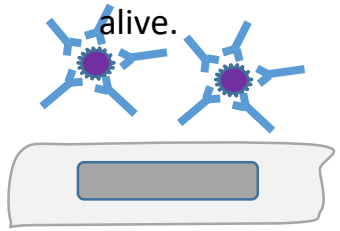
van der Straten K, et al. medRxiv 2022

Antibody neutralization assay

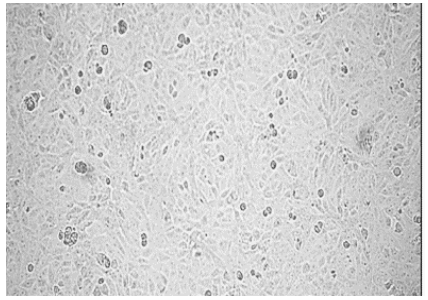
Neutralizing Ab



Neutralizing Ab coat the virions and block their ability to infect the cells that remain alive.



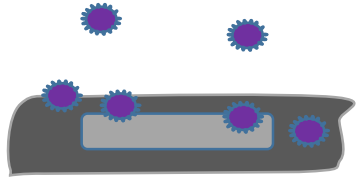
live cells



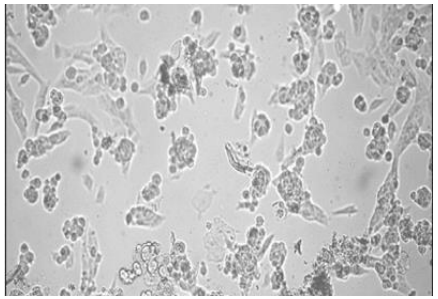
No neutralizing Ab



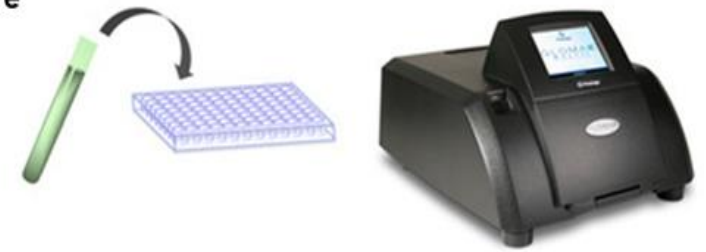
Virions are free to infect and kill target cells

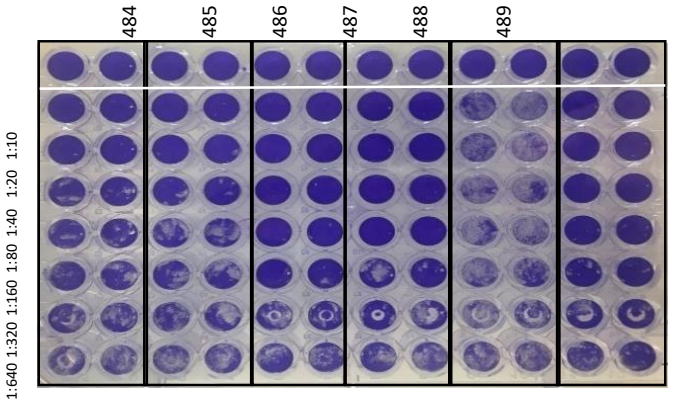


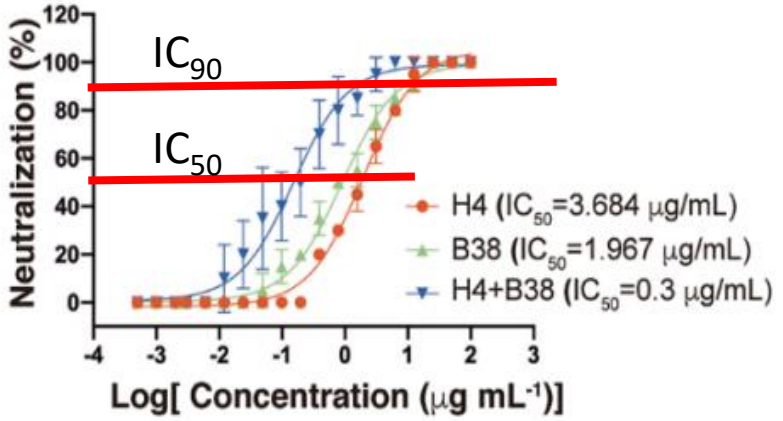
Dead cells



Day 3 stain plates with Crystal Violet and read by photometre

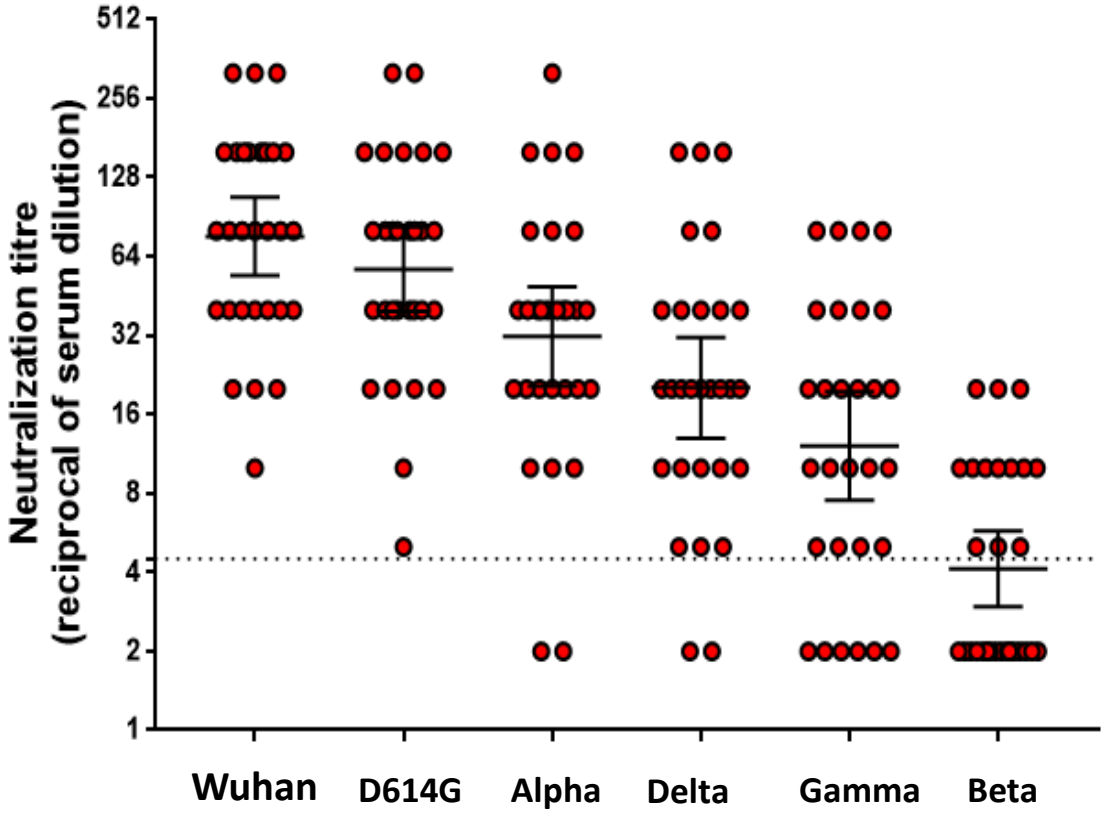




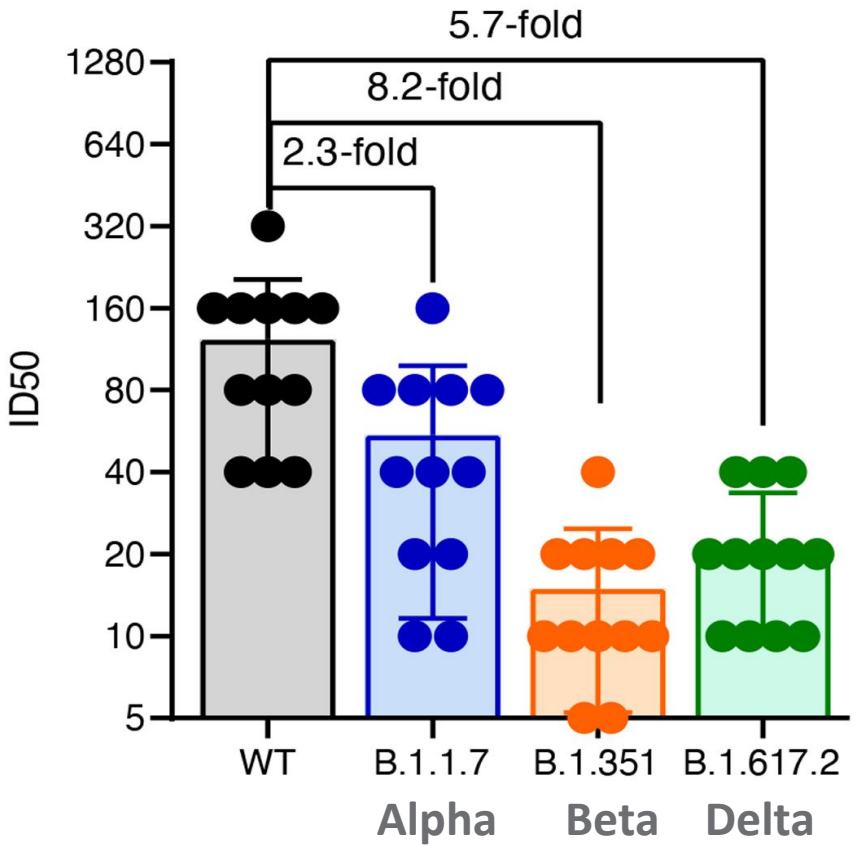


Viral variants and neutralizing antibodies

BNT162b2 vaccinees



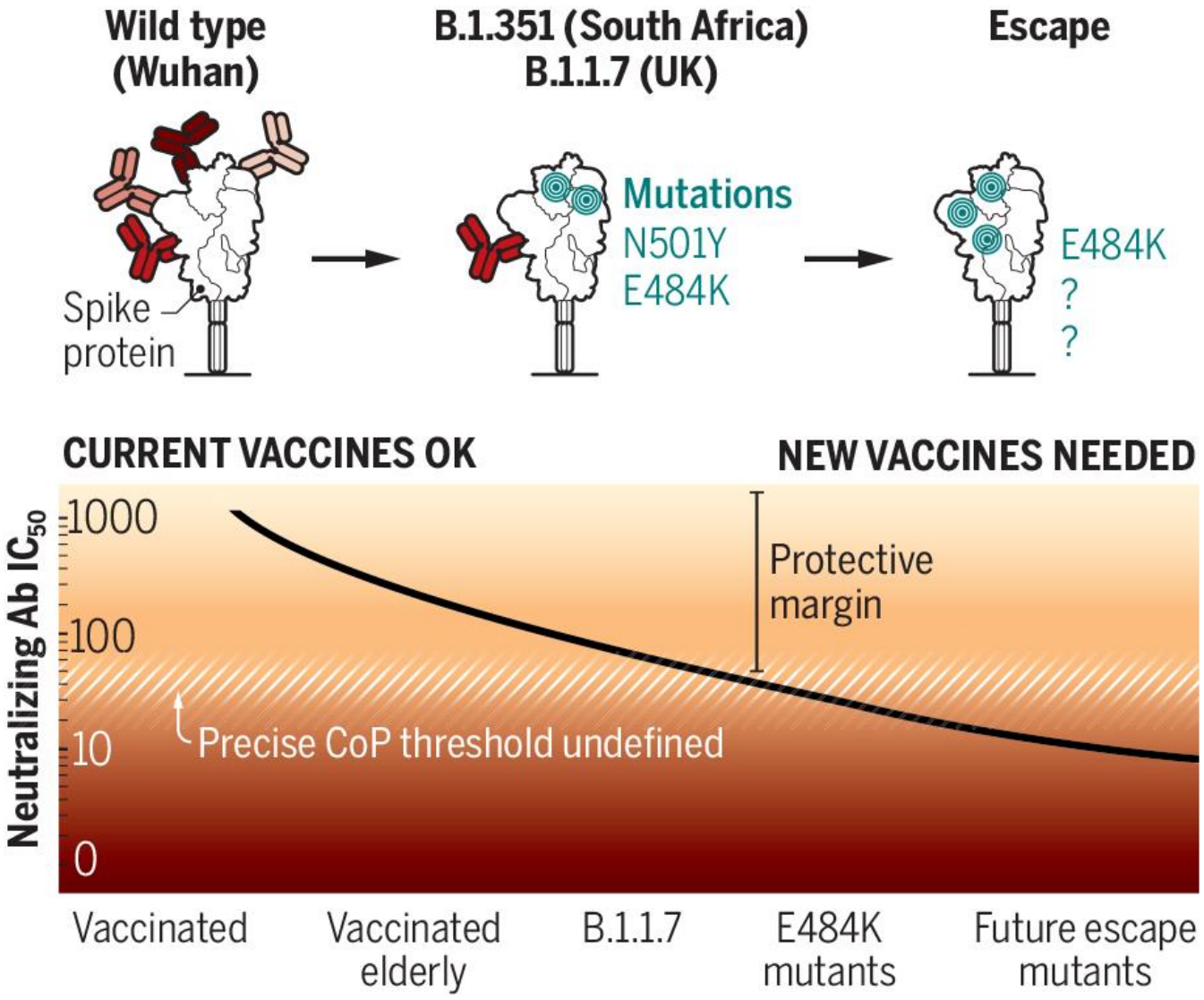
Convalescent patients (mid-2020)



Mlcochova P. et. Nature, 2021 https://doi.org/10.1038/s41586-021-03944-y

INMI unpublished data

Viral variants and immune escape



- Loss of neutralizing epitopes in S could reduce protection induced by S-based vaccines
- Most vaccinatd people develop NAb with titers sufficiently high (protective margin) although precise correlates of protection are unknown
- Extensive loss of Nab sensitivity will prompt the need for vaccine adaptation

Altmann DM. et al., Science 12 Mar 2021. https://www.doi.org/10.1126/science.abg7404

How predictable is evolution?



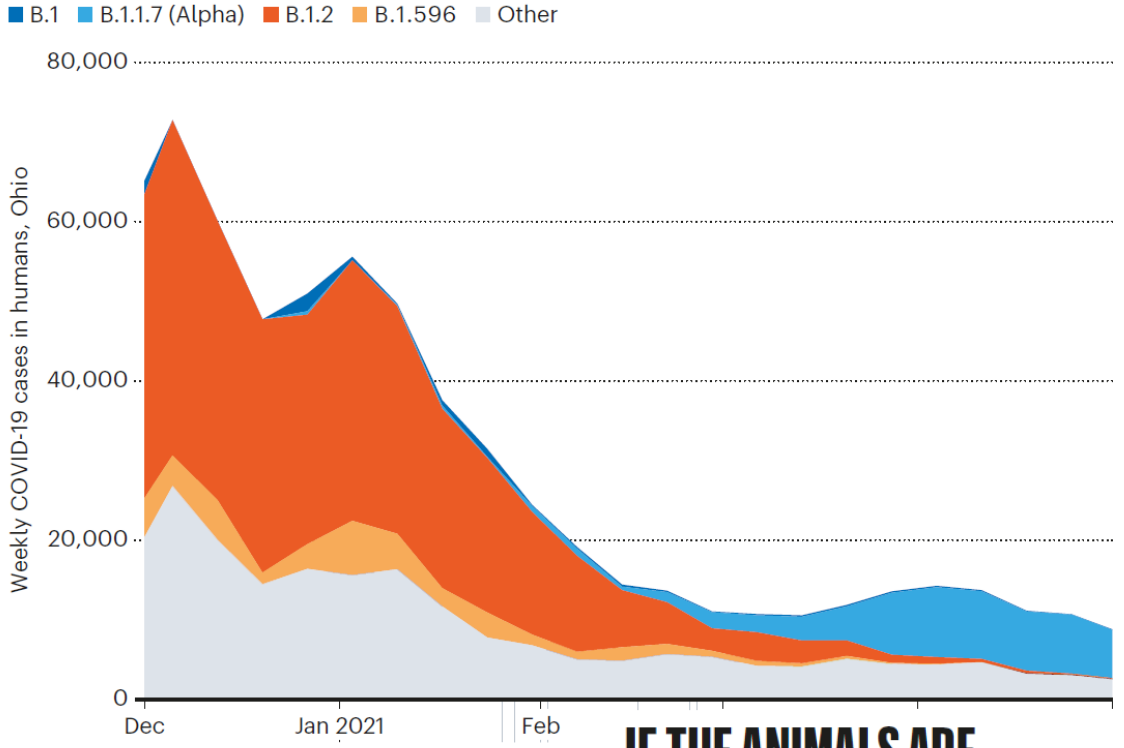


Researchers prepare to swab a white-tailed deer in College Station, Texas, to check for SARS-CoV-2.

COULD DEER BECOME A NATURAL COVID RESERVOIR?

Hundreds of white-tailed deer in North America have tested positive for SARS-CoV-2. Here's why scientists aren't panicking, yet. **By Smriti Mallapaty**

- The variants circulating in deer typically mirror those spreading in humans
- Increasing concern about the animals becoming a viral reservoir, serving as a recalcitrant source of outbreaks and potentially breeding new variants.



NO ONE'S DETECTED IT IN EUROPEAN DEER SO FAR, DESPITE A LOT OF LOOKING."

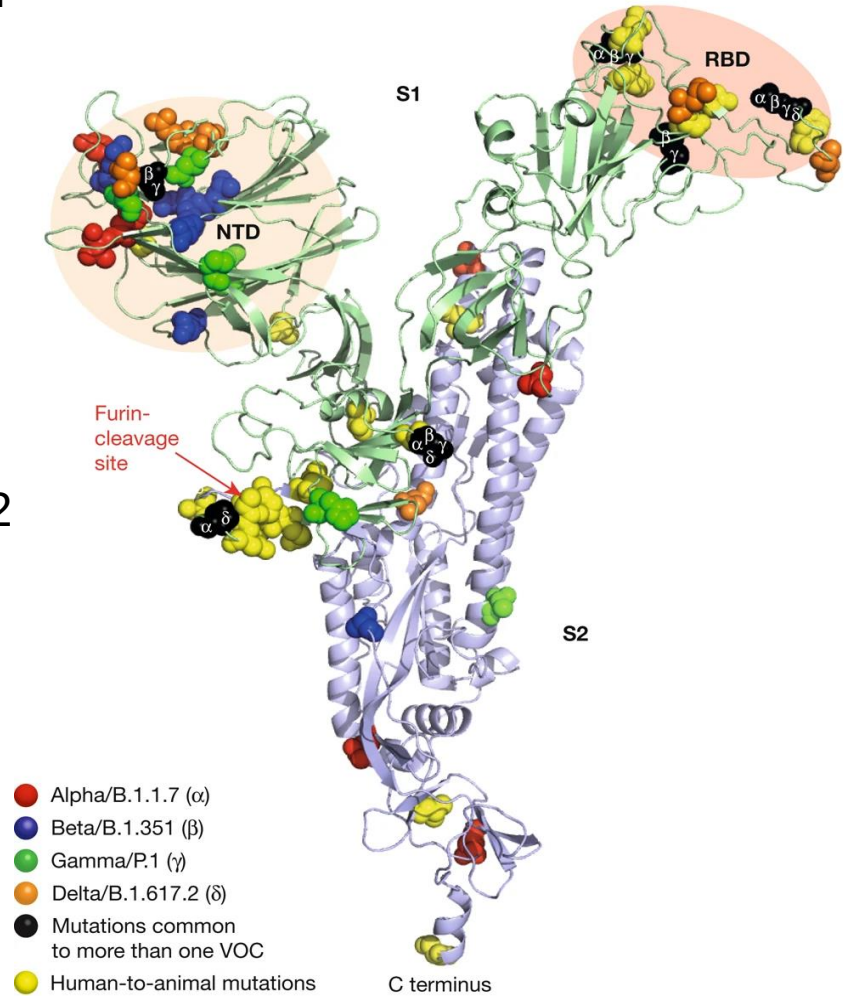
IF THE ANIMALS ARE ABLE TO BE REINFECTED, JUST LIKE PEOPLE, THEN THE VIRUS WILL NOT FADE OUT."

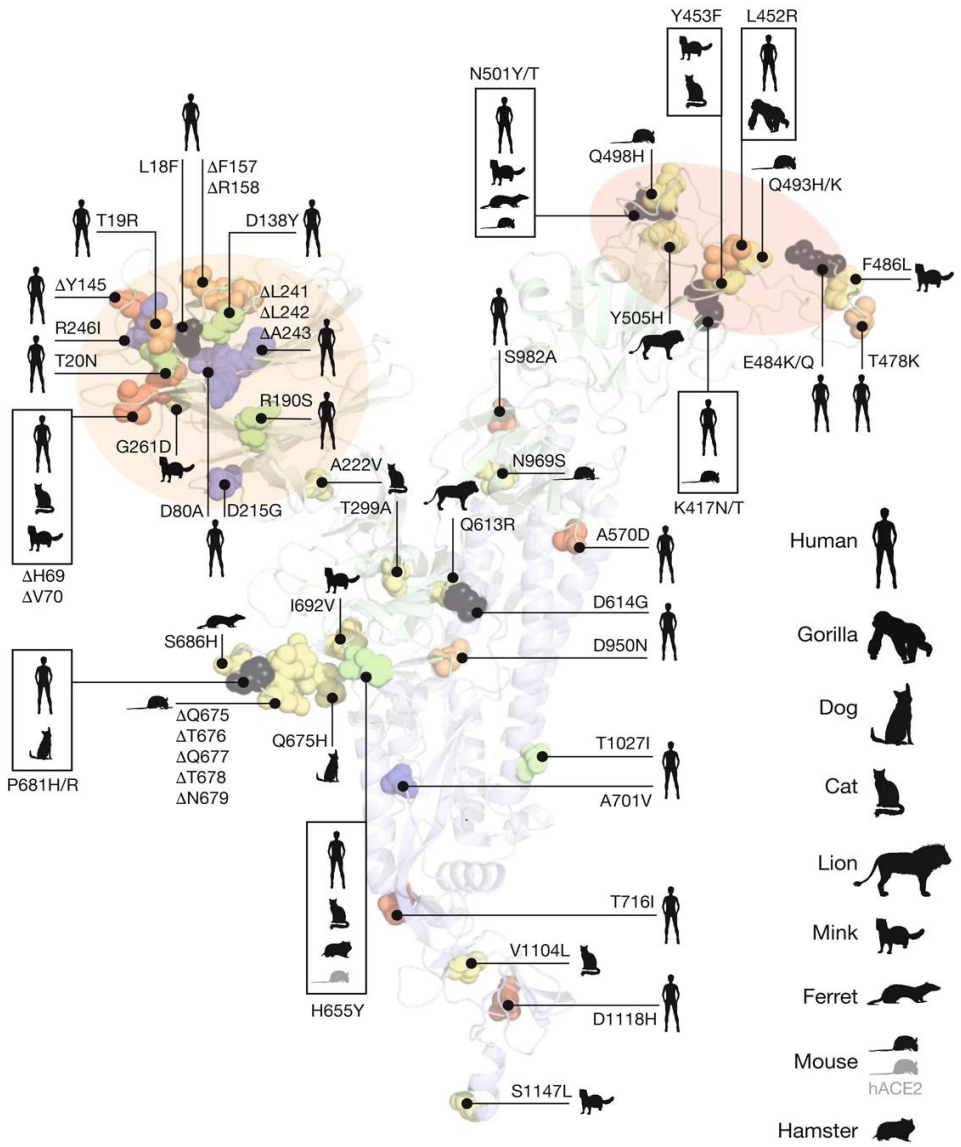
Animal are possible incubators of new SARS-CoV-variants, shuttling back to humans

SARS-CoV-2 infections have been established in a range of animal species

Virus evolution can occur in animal hosts, generating a suite of genomic changes in addition to those seen during human-to-human transfer

Establishment of SARS-CoV-2 in other species could provide a refuge for the virus to re-emerge in human populations in an evolutionarily distinct form





Telenti A. et al. Nature 2021

la Repubblica 20 febbraio 2220

Virus nei pipistrelli, trovati ceppi quasi uguali a Sars-Cov2

di Elena Dusi



La scoperta su Nature. I ricercatori francesi hanno esplorato le grotte del Laos e hanno individuato molti altri coronavirus in questi animali, tre dei quali con un genoma identico al 96% rispetto a Sars-Cov2 e capaci di infettare l'uomo

RBDs of these viruses

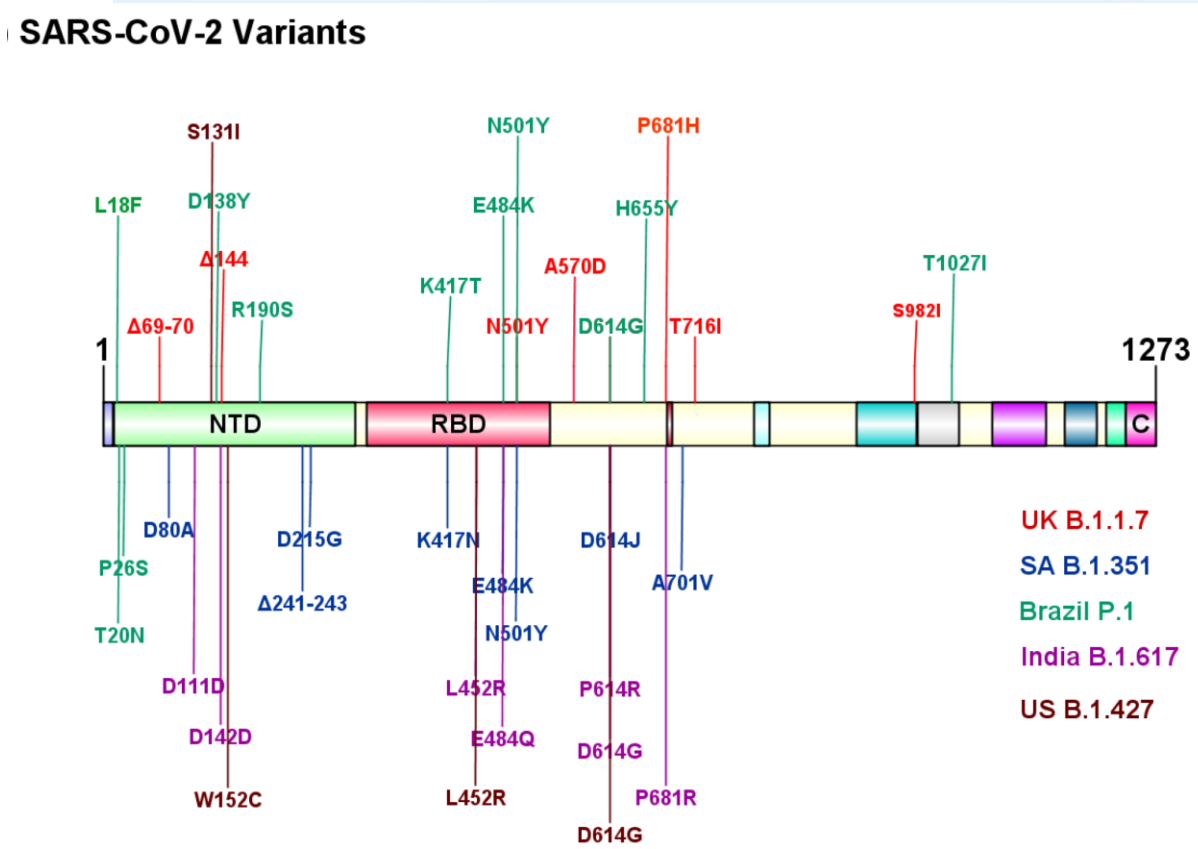
- differ from that of SARS-CoV-2 by only one or two residues at the interface with ACE2
- bind more efficiently to the hACE2 protein than the SARS-CoV-2 Wuhan strain isolated in early human cases
- mediate hACE2-dependent entry and replication in human cells
- is inhibited by antibodies neutralizing SARS-CoV-2

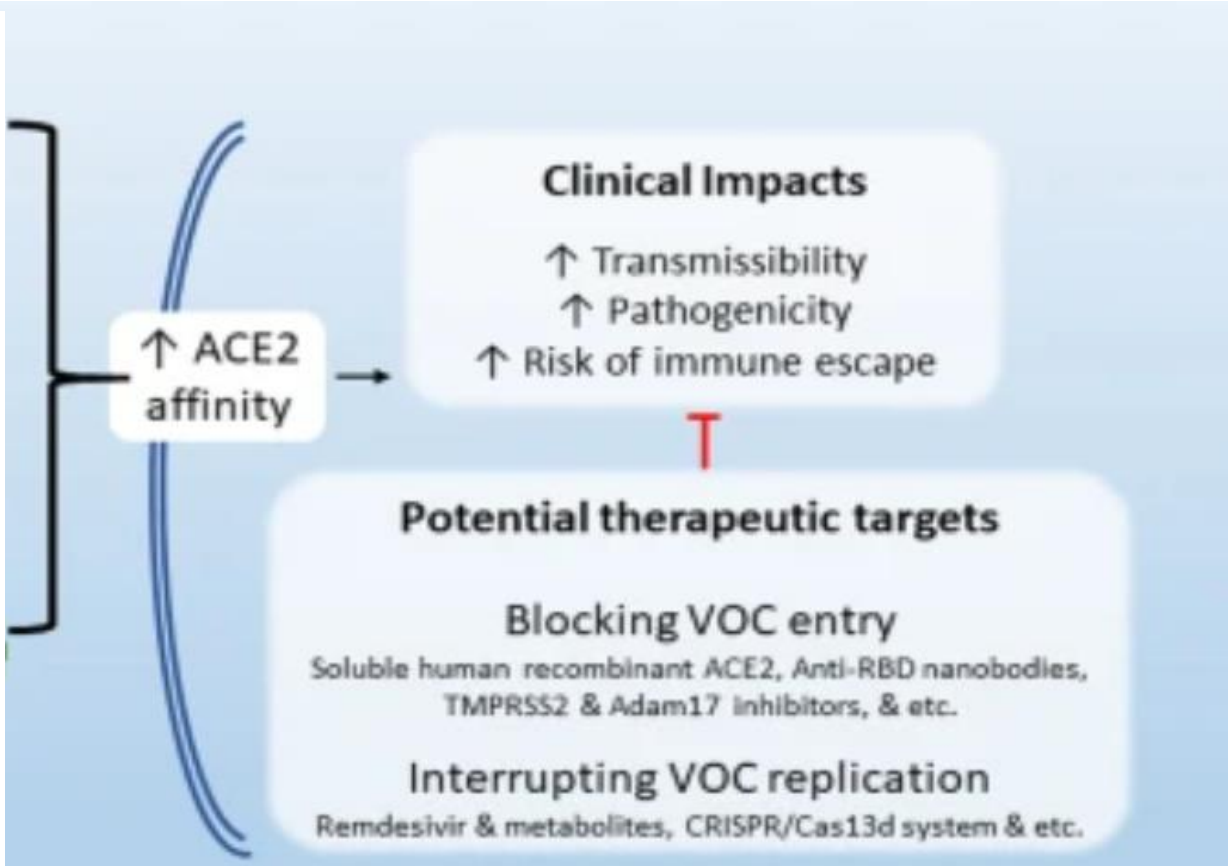
These viruses may have contributed to SARS-CoV-2's origin and may intrinsically pose a future risk of direct transmission to humans

Temmam S et al. Nature 2022

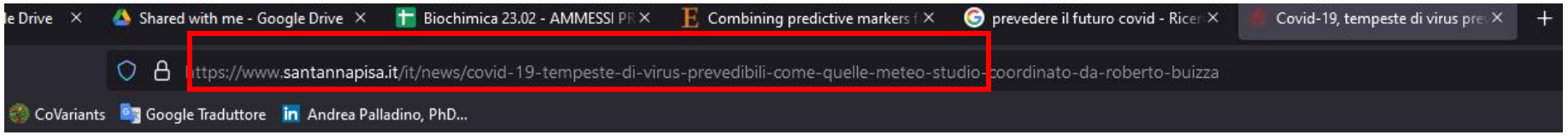
Why should we monitor SARS-CoV-2 variants

- Predicting future successful mutations would **extend the time available to develop proactive responses** at earlier stages of spread

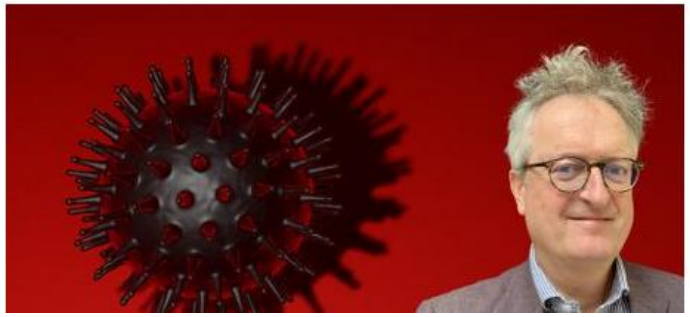




Khateeb, J. et al. Crit Care 2021
Raman R. et a. Biomolecules 2021



COVID-19, TEMPESTE DI VIRUS PREVEDIBILI COME QUELLE METEO: IN STUDIO COORDINATO DA ROBERTO BUIZZA, FISICO DELL'ISTITUTO DI SCIENZE DELLA VITA DEL SANT'ANNA, PUBBLICATO SUL JOURNAL OF TRANSLATIONAL MEDICINE, LA PROPOSTA DI UN CENTRO PER PREVEDERE EPIDEMIE



Prevedere le "tempeste di virus" come avviene da qualche decennio con nubifragi e tornado, al punto da istituire un Centro internazionale per le previsioni sulla salute che permetta di capire quando una nuova epidemia sta per emergere e l'impatto che potrà avere. E' la proposta lanciata sul **Journal of Translational Medicine** dal fisico **Roberto Buizza**, docente dell'**Istituto di Scienze della Vita** della Scuola Superiore Sant'Anna, con lo statistico **Enrico Capobianco** dell'Università di Miami, il fisico **Pier Francesco Moretti** del Consiglio Nazionale delle Ricerche (Cnr) e l'epidemiologo ambientale **Paolo Vineis** dell'Imperial College di Londra.

Buizza *et al. J Transl Med* (2021) 19:102
https://doi.org/10.1186/s12967-021-02771-z

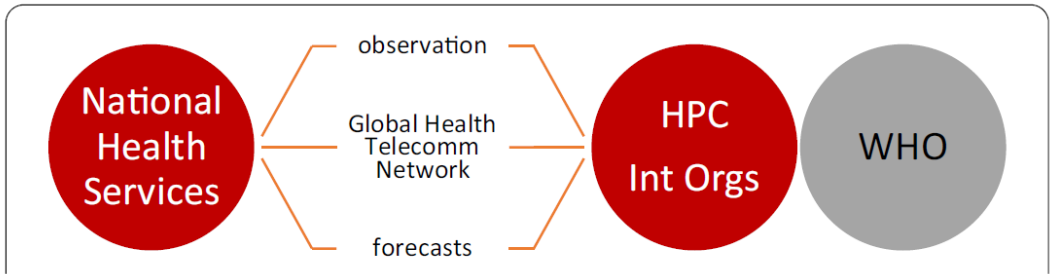
Journal of Translational Medicine

LETTER TO THE EDITOR Open Access

How can we weather a virus storm? Health prediction inspired by meteorology could be the answer

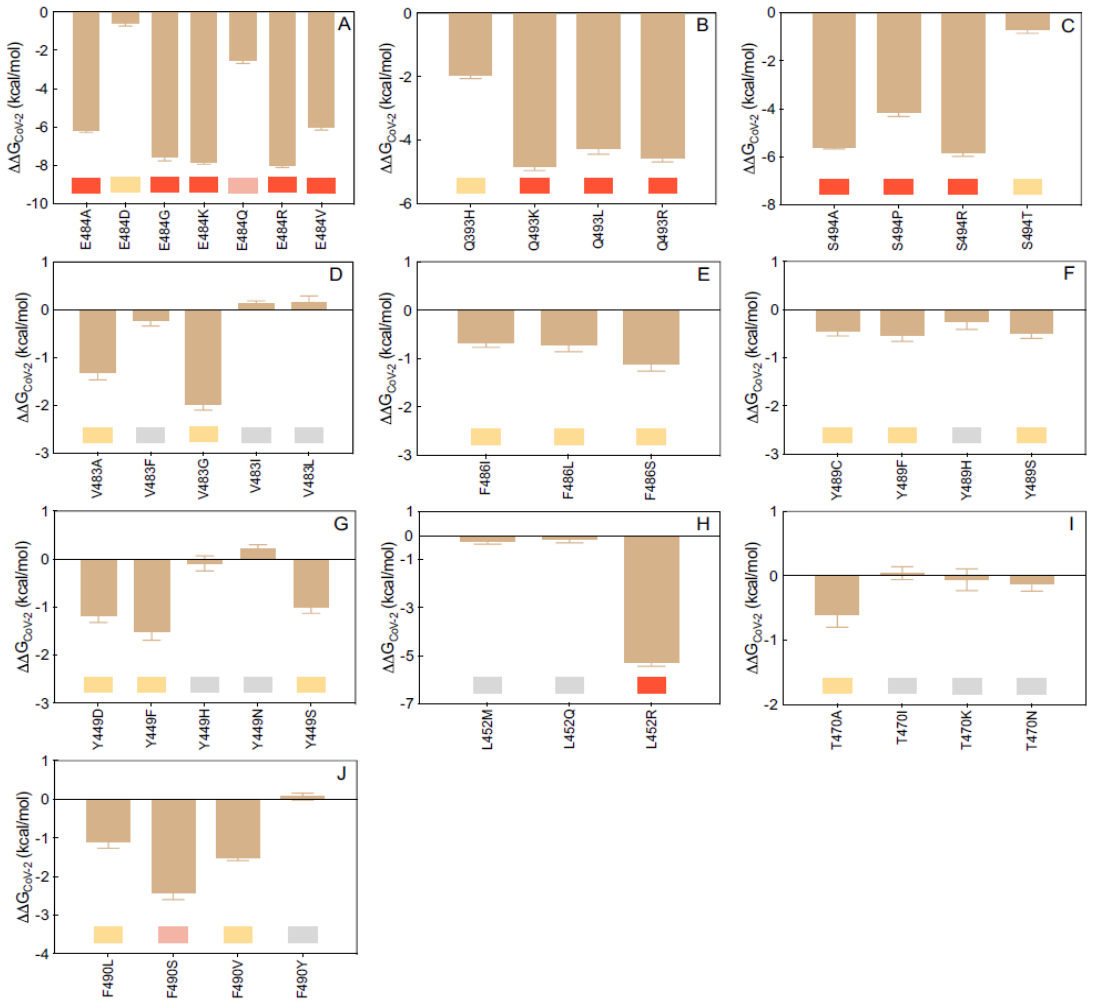
Roberto Buizza[1*], Enrico Capobianco[2], Pier Francesco Moretti[3] and Paolo Vineis[4]

Interactions between the National Health Services (NHSs), the proposed Health Prediction Center (HCP) and other international organizations, and the WHO.

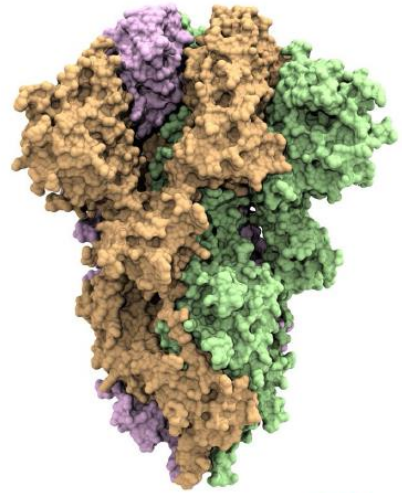


Computational mutagenesis: tool for identifying and prioritizing all present and newly reported circulating spike SARS-CoV-2 variants with respect to antibody neutralization, and **yield substantial structural information for the development of next-generation vaccines and monoclonal antibodies more resilient to viral evolution**

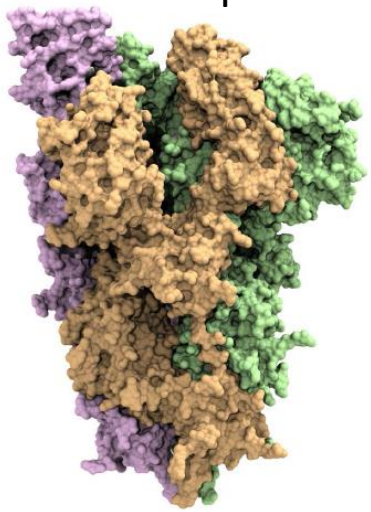
Change in binding free energy predicted for residues E484 (A), Q493 (B), S494P (C), V483 (D), F486 (E), Y489 (F), Y449 (G), L452 (H), T470 (I), and F490 (J) RBD/LY-CoV555 (bamlamivimab) mAb complexes.



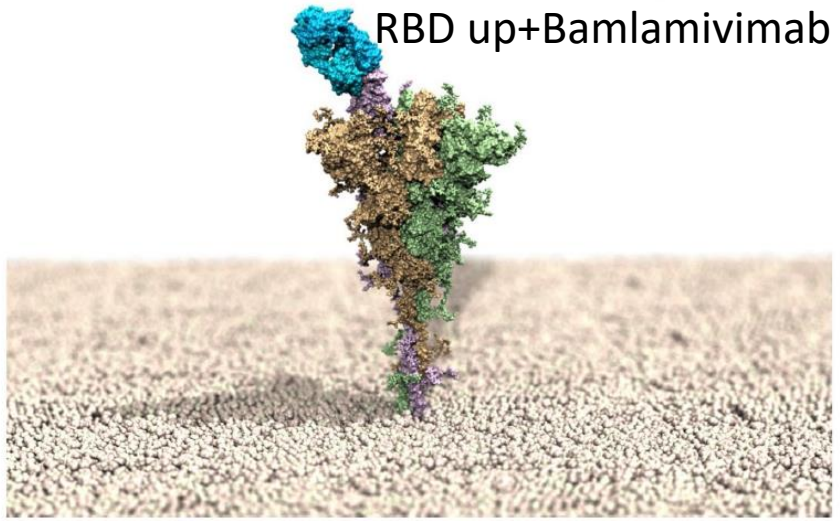
RBD down



RBD up



RBD up+Bamlamivimab



Laurini E. Sci Reps 2021

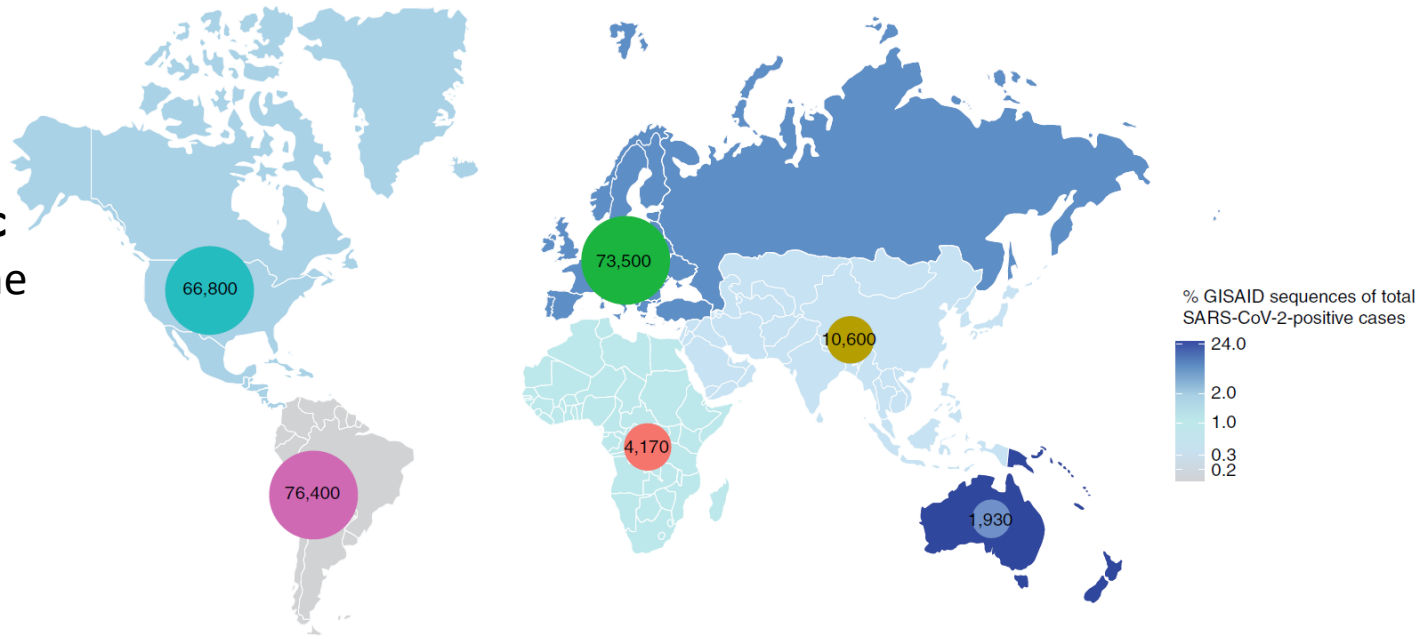
The next phase of SARS-CoV-2 surveillance: real-time molecular epidemiology

Bas B. Oude Munnink, Nathalie Worp, David F. Nieuwenhuijse, Reina S. Sikkema, Bart Haagmans, Ron A. M. Fouchier and Marion Koopmans ✉

To prepare for the next phase of the pandemic, a systematic approach is needed to **link global genomic surveillance and timely assessment of the phenotypic characteristics of novel variants,** which will support the development and updating of diagnostics, vaccines, therapeutics and nonpharmaceutical interventions.

Genomic analysis networks need to include reference centers for virus characterization.

- Epidemiological observations combined with experimental data are needed to assess virus properties.
- Experiments have to be performed using live virus and standardized for use in rapid risk assessment.
- It will be necessary to work toward a suite of standardized assays, reagents, strain collections and serum samples.



Percentage of whole-genome sequences shared on GISAID compared to the total number of COVID-19 cases per continent as of 5 July 2021.
Number in each circle indicates SARS-CoV-2 infections per 1 million people.

Munnink et al. Nature Med 2021

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

CORONAVIRUS

Predicting the mutational drivers of future SARS-CoV-2 variants of concern

M. Cyrus Maher[1]*, Istvan Bartha[1], Steven Weaver[2], Julia di Iulio[1], Elena Ferri[1], Leah Soriaga[1], Florian A. Lempp[1], Brian L. Hie[3,4], Bryan Bryson[4,5], Bonnie Berger[3,6], David L. Robertson[7], Gyorgy Snell[1], Davide Corti[1], Herbert W. Virgin[1,8,9], Sergei L. Kosakovsky Pond[2], Amalio Telenti[1]*

To predict which existing amino acid mutations in SARS-CoV-2 might contribute to future variants of concern, we tested the predictive value of features comprising epidemiology, evolution, immunology, and neural network–based protein sequence modeling and identified primary biological drivers of SARS-CoV-2 evolution.

The most predictive variable in this feature category was "**Epi Score**," the exponentially weighted mean ranking across the other epidemiological variables, calculated from GISAID.

- This score captures both lineage expansion and recurrent mutations that occurs in multiple variant lineages by convergent evolution
- It is possible to forecast the driver mutations that could appear in emerging SARS-CoV-2 variants of concern.
- **Of 50 defining mutations the median time between when a mutation was forecast to spread and when it reached 1% frequency was 5 months**

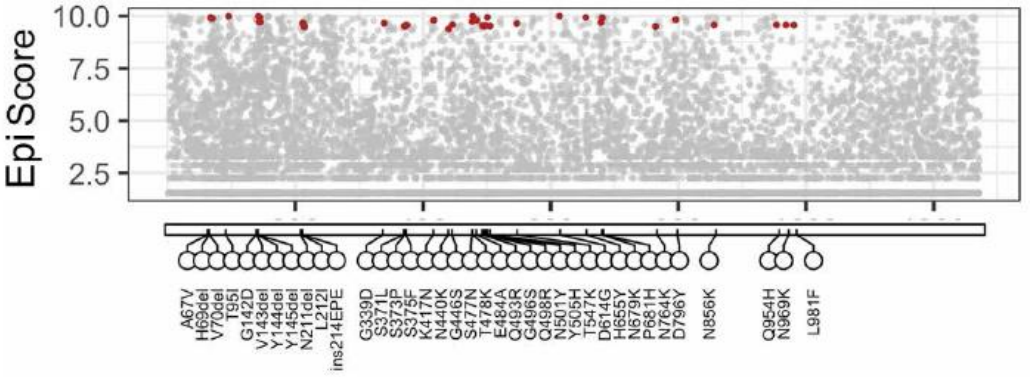
Maher et al., Sci. Transl. Med. 14, 23 February 2022

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

CORONAVIRUS

Predicting the mutational drivers of future SARS-CoV-2 variants of concern

M. Cyrus Maher[1]*, Istvan Bartha[1], Steven Weaver[2], Julia di Iulio[1], Elena Ferri[1], Leah Soriaga[1], Florian A. Lempp[1], Brian L. Hie[3,4], Bryan Bryson[4,5], Bonnie Berger[3,6], David L. Robertson[7], Gyorgy Snell[1], Davide Corti[1], Herbert W. Virgin[1,8,9], Sergei L. Kosakovsky Pond[2], Amalio Telenti[1]*



To predict which existing amino acid mutations in SARS-CoV-2 might contribute to future variants of concern, we tested the predictive value of features comprising epidemiology, evolution, immunology, and neural network–based protein sequence modeling and identified primary biological drivers of SARS-CoV-2 evolution.

The most predictive variable in this feature category was "**Epi Score**," the exponentially weighted mean ranking across the other epidemiological variables, calculated from GISAID.

Application of the analysis to Omicron

The Epi Scores of 37 Omicron-defining mutations are shown as of December 8, 2021

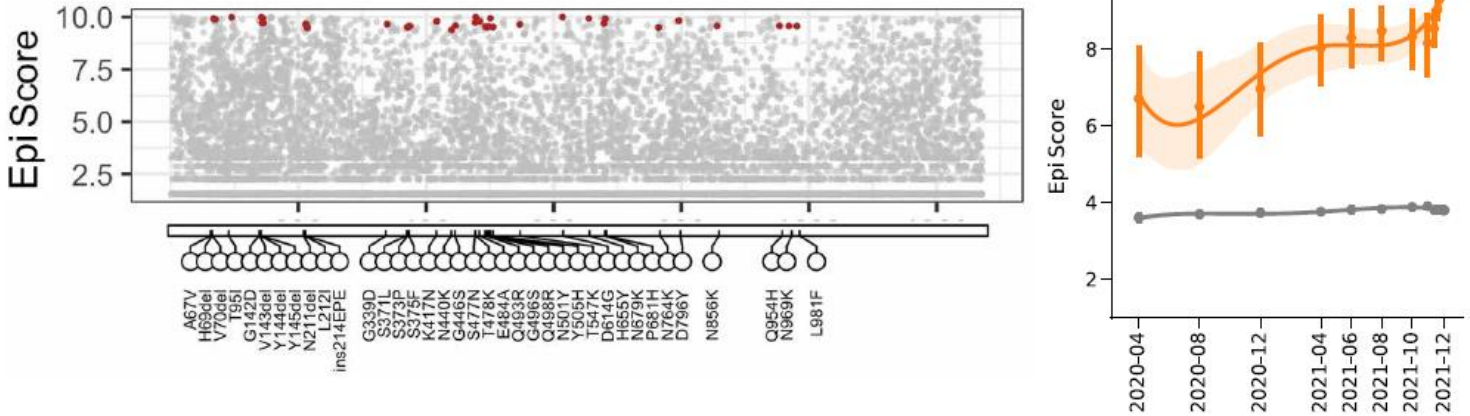
Maher et al., Sci. Transl. Med. 14, 23 February 2022

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

CORONAVIRUS

Predicting the mutational drivers of future SARS-CoV-2 variants of concern

M. Cyrus Maher[1]*, Istvan Bartha[1], Steven Weaver[2], Julia di Iulio[1], Elena Ferri[1], Leah Soriaga[1], Florian A. Lempp[1], Brian L. Hie[3,4], Bryan Bryson[4,5], Bonnie Berger[3,6], David L. Robertson[7], Gyorgy Snell[1], Davide Corti[1], Herbert W. Virgin[1,8,9], Sergei L. Kosakovsky Pond[2], Amalio Telenti[1]*



To predict which existing amino acid mutations in SARS-CoV-2 might contribute to future variants of concern, we tested the predictive value of features comprising epidemiology, evolution, immunology, and neural network–based protein sequence modeling and identified primary biological drivers of SARS-CoV-2 evolution.

The most predictive variable in this feature category was "**Epi Score**," the exponentially weighted mean ranking across the other epidemiological variables, calculated from GISAID.

Application of the analysis to Omicron

The Epi Scores of 37 Omicron-defining mutations are shown as of December 8, 2021

Emergent mutations were distinguished by the progressively increasing Epi Score between April 2020 and August 2021, long **preceding the acceleration that characterized the emergence of Omicron in November 2021**

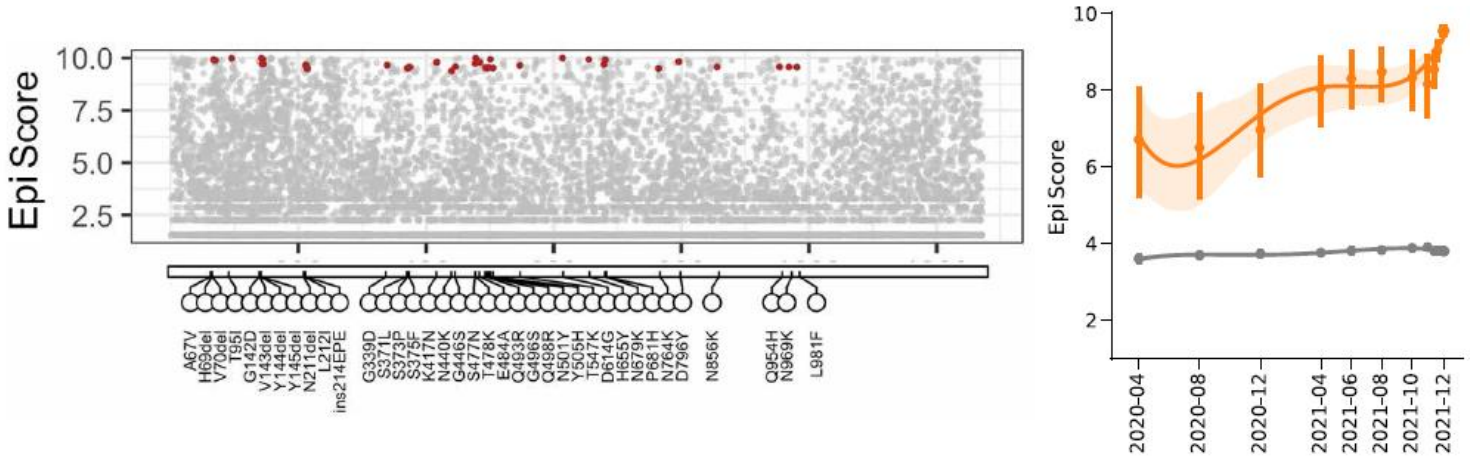
Maher et al., Sci. Transl. Med. 14, 23 February 2022

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

CORONAVIRUS

Predicting the mutational drivers of future SARS-CoV-2 variants of concern

M. Cyrus Maher[1]*, Istvan Bartha[1], Steven Weaver[2], Julia di Iulio[1], Elena Ferri[1], Leah Soriaga[1], Florian A. Lempp[1], Brian L. Hie[3,4], Bryan Bryson[4,5], Bonnie Berger[3,6], David L. Robertson[7], Gyorgy Snell[1], Davide Corti[1], Herbert W. Virgin[1,8,9], Sergei L. Kosakovsky Pond[2], Amalio Telenti[1]*



To predict which existing amino acid mutations in SARS-CoV-2 might contribute to future variants of concern, we tested the predictive value of features comprising epidemiology, evolution, immunology, and neural network–based protein sequence modeling and identified primary biological drivers of SARS-CoV-2 evolution.

The most predictive variable in this feature category was "**Epi Score**," the exponentially weighted mean ranking across the other epidemiological variables calculated from GISAID.

- It is possible to forecast the driver mutations that could appear in emerging SARS-CoV-2 variants of concern.
- This score captures both lineage expansion and recurrent mutations that occurs in multiple variant lineages by convergent evolution

Maher et al., Sci. Transl. Med. 14, 23 February 2022

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

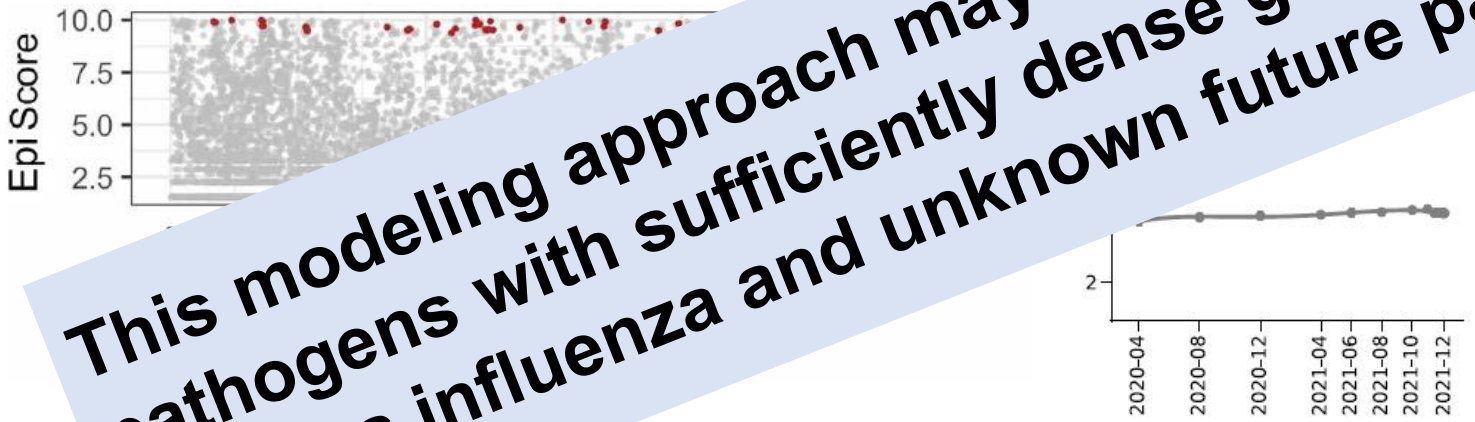
CORONAVIRUS

Predicting the mutational drivers of future SARS-CoV-2 variants of concern

M. Cyrus Maher[1]*, Istvan Bartha[1], Steven Weaver[2], Julia di Iulio[1], Elena Ferri[1], Leah Soriaga[1], Florian A. Lempp[1], Brian L. Hie[3,4], Bryan Bryson[4,5], Bonnie Berger[3,6], David L. Robertson[7], Gyorgy Snell[1], Davide Corti[1], Herbert W. Virgin[1,8,9], Sergei L. Kosakovsky Pond[2], A...

This modeling approach may be applied to any rapidly evolving pathogens with sufficiently dense genomic surveillance data, such as influenza and unknown future pandemic viruses

To predict which c... mutations i... cont... ...n, ...es ...twork–based ...odeling and identified ...gical drivers of SARS-CoV-2 ...ion.



The most predictive variable in this feature category was "**Epi Score**," the exponentially weighted mean ranking across the other epidemiological variables calculated from GISAID.

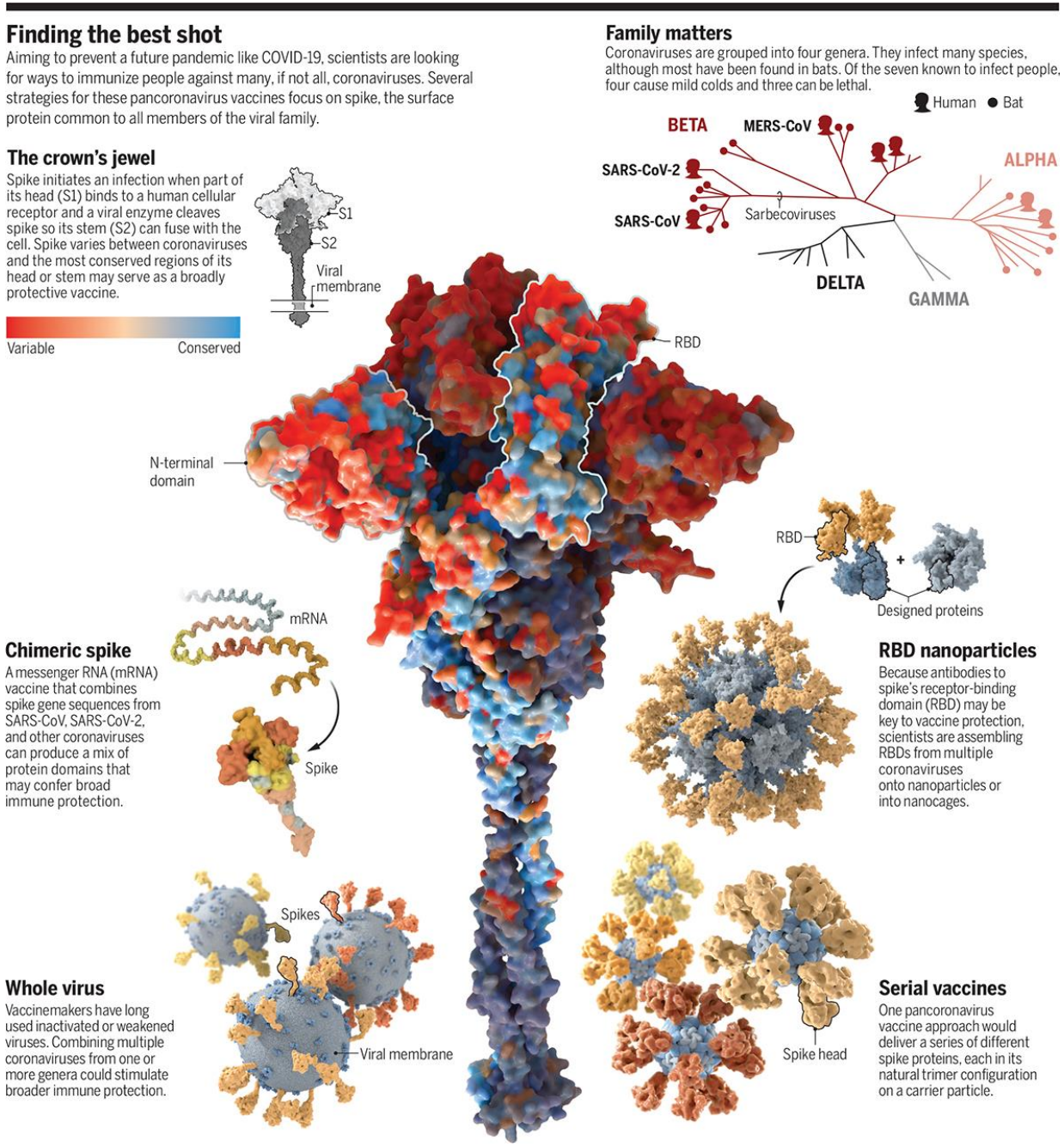
- It is ...cast the driver mutations that could appear in emerging SARS-CoV-2 variants of concern.
- This score captures both lineage expansion and recurrent mutations that occurs in multiple variant lineages by convergent evolution

Maher et al., Sci. Transl. Med. 14, 23 February 2022

The pan-coronavirus vaccine race

Several options

- Mix diverse Spike antigens in one formulation
- Design chimeric Spike antigens
- Sequential injection of different Spike antigens
- Optimize Spike sequence to overcome virus diversity
- Use antigens conserved in various coronaviruses (i.e.N)
- Whole inactivated virus mixed preparations



Jon Cohen, The dream vaccine. Science16 Apr 2021: 227-231. https://doi.org/10.1126/science.372.6539.227

The future of COVID-19

US researchers, using influenza pandemics as a model for the future development of COVID-19, considered three scenarios:

- **Ongoing severe** disease manifestations combined with high levels of infected individuals which foster further evolution of the virus;

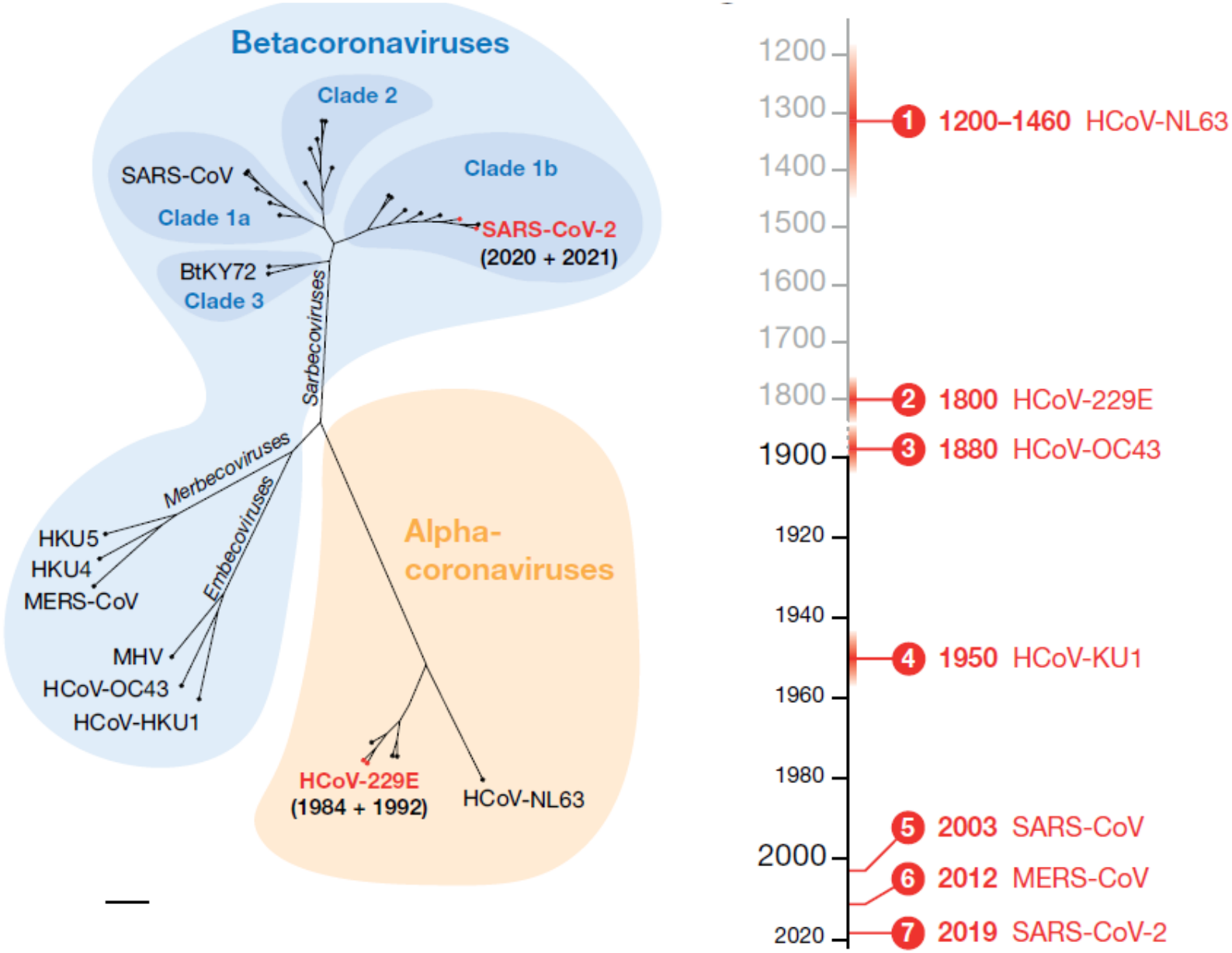
- A transition to an **epidemic seasonal** disease like influenza with an annual mortality burden of 250,000 to 500,000 people globally;

- An **endemic disease** similar to other human coronavirus infection that have a much lower disease impact than influenza.



Telenti et al., 2021

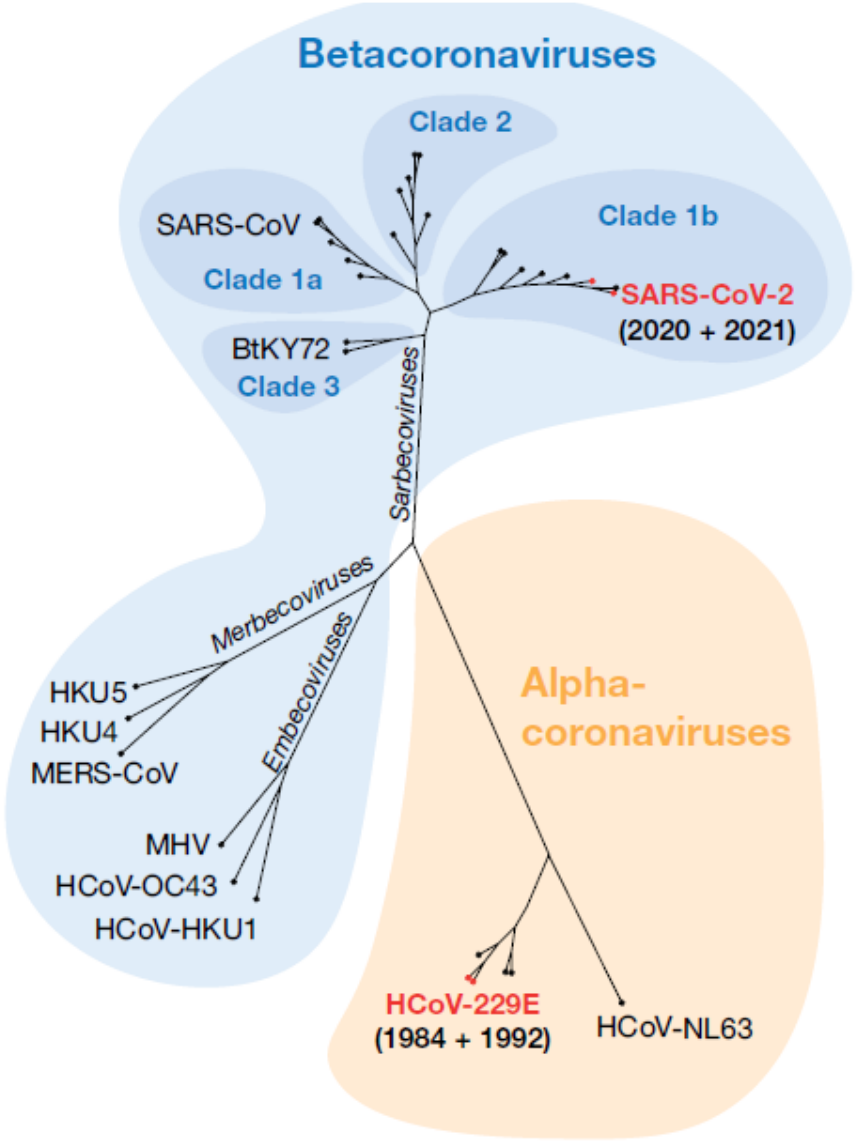
Timeline of the emergence of human coronaviruses based on molecular clock dating

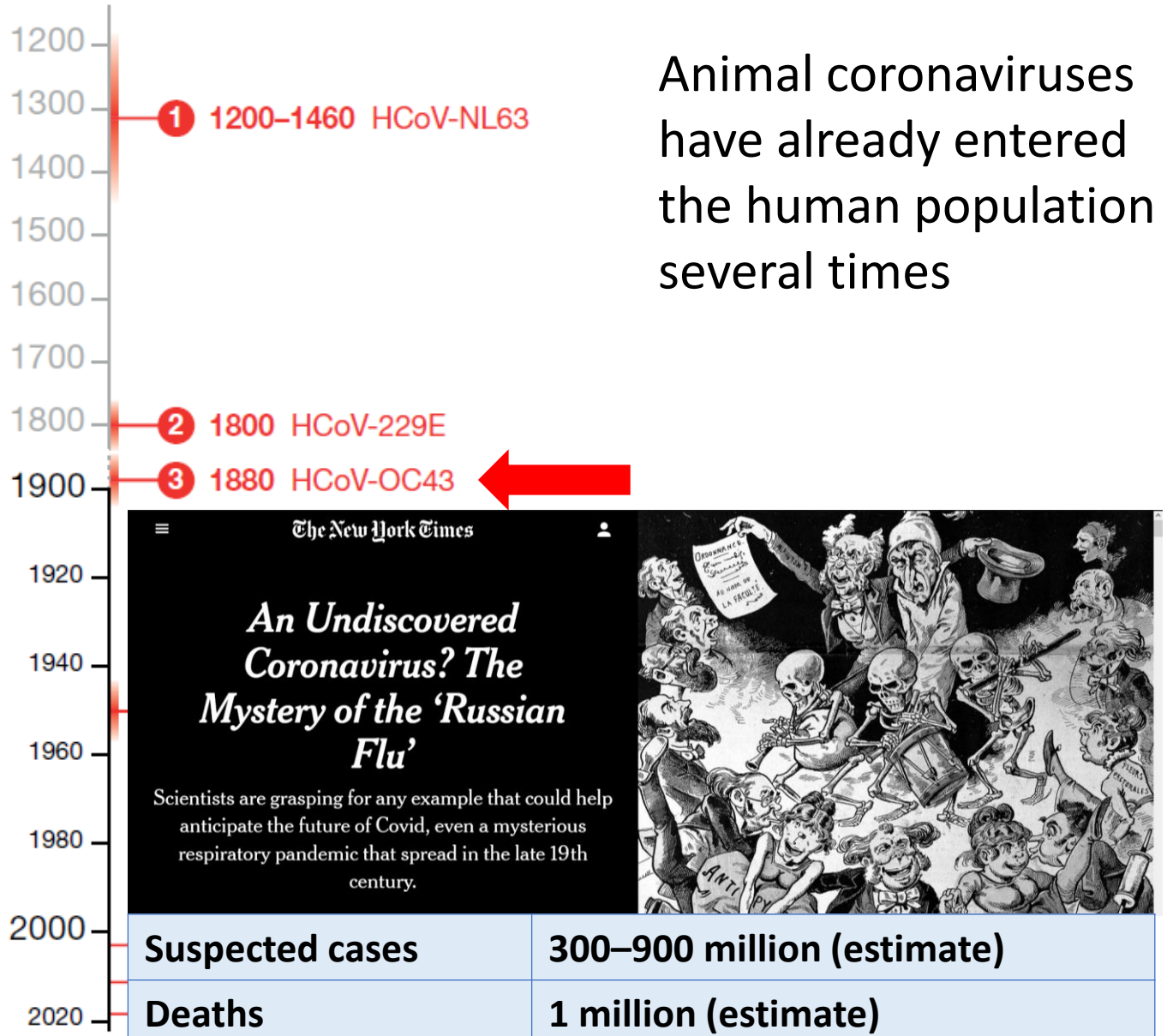


Animal coronaviruses have already entered the human population several times

Telenti A. et al. Nature 2021

Timeline of the emergence of human coronaviruses based on molecular clock dating





Animal coronaviruses have already entered the human population several times

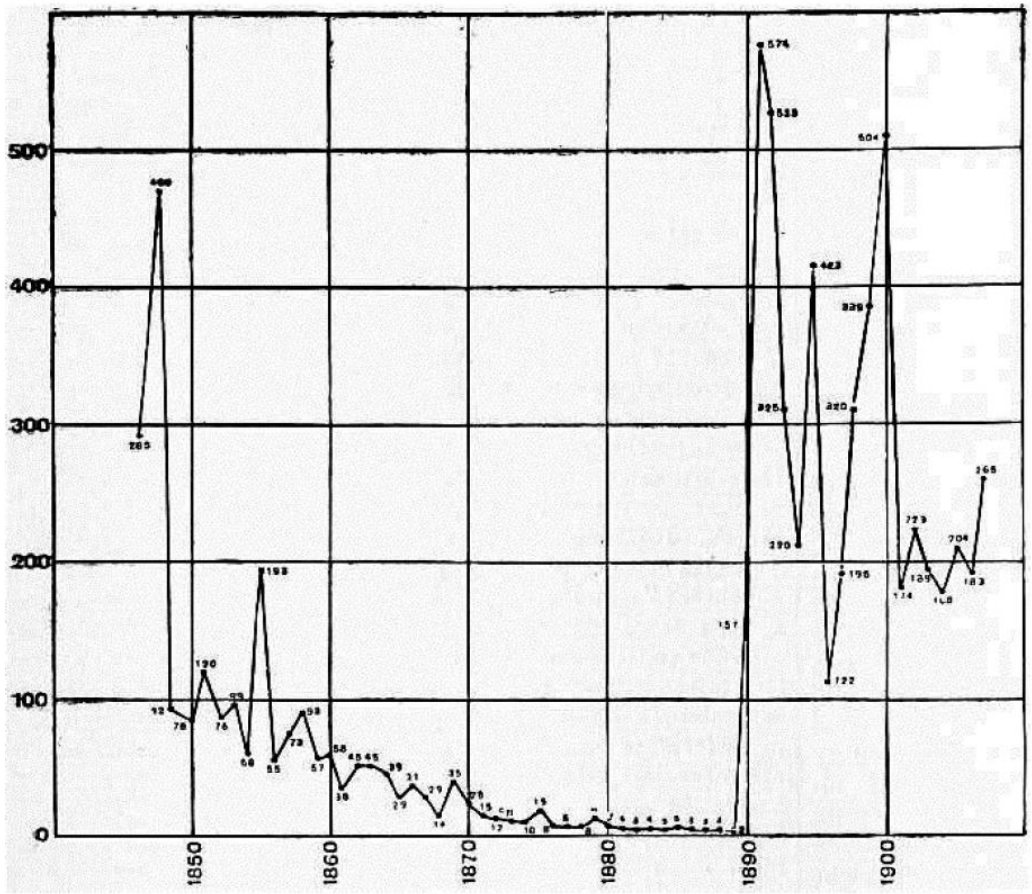
Suspected cases	**300–900 million (estimate)**
Deaths	**1 million (estimate)**

Telenti A. et al. Nature 2021

microbial biotechnology
Open Access
Lilliput

What we can learn from the dynamics of the 1889 'Russian flu' pandemic for the future trajectory of COVID-19

Brüssow H. 2021



microbial biotechnology
Open Access
Lilliput

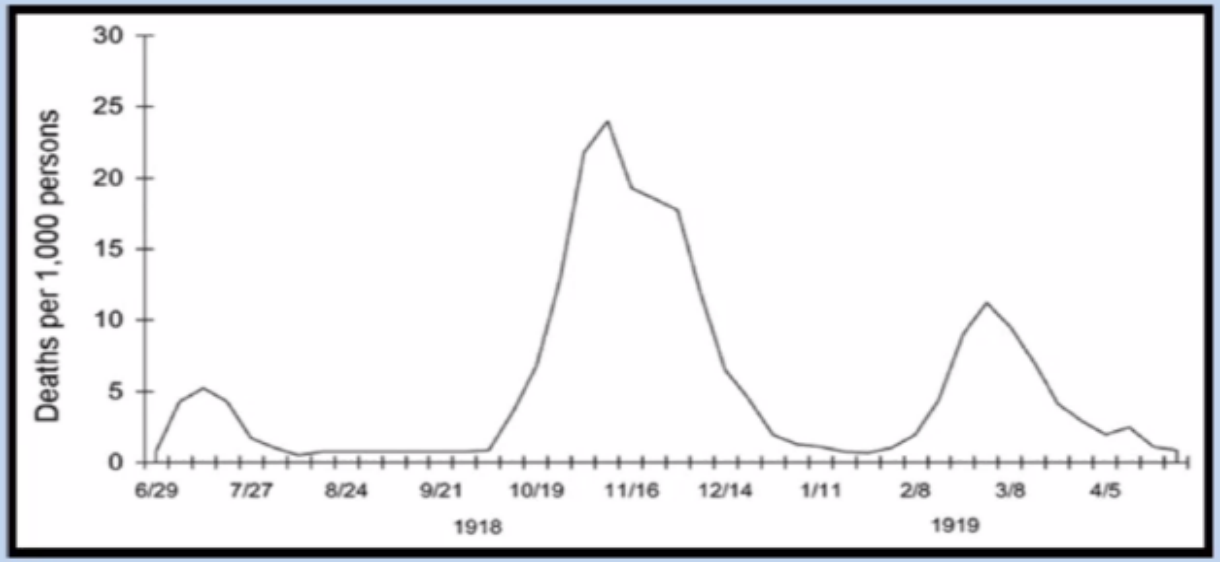
Clinical evidence that the pandemic from 1889 to 1891 commonly called the Russian flu might have been an earlier coronavirus pandemic

The pandemic starting in 1889 can serve as a paradigm for the future evolution of the COVID-19 pandemic.

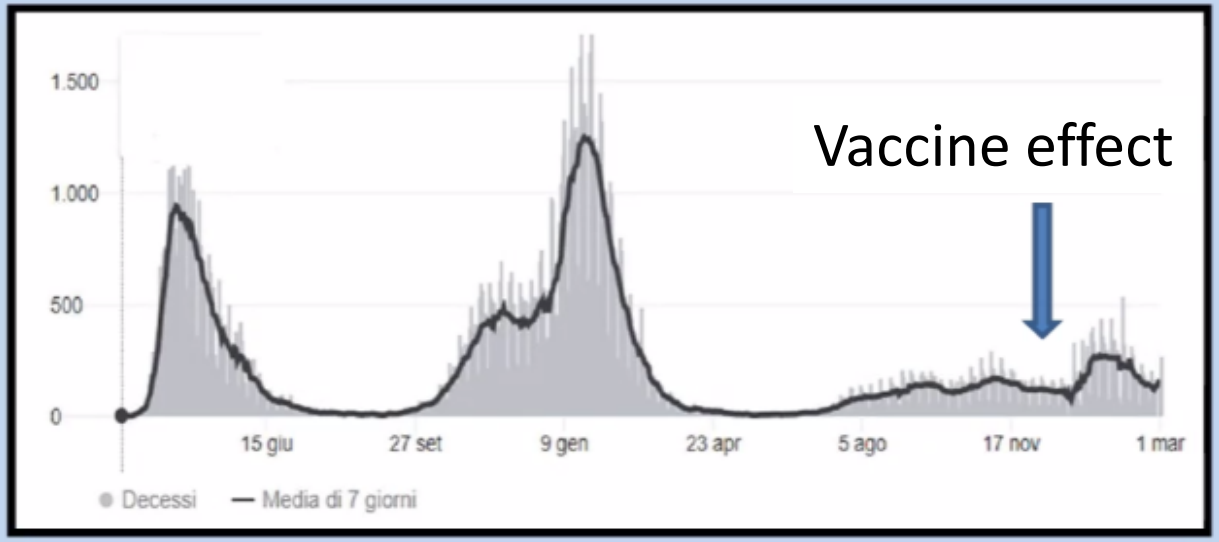
This historical event might provide an idea about the natural duration of such a pandemic.

From these data, one might deduce a **protracted 5-year course** for a COVID-19-like pandemic, suggesting that COVID-19 might occupy us well beyond 2022 **if the current vaccination campaigns does not change its 'natural' trajectory.**

Three pandemic waves: weekly mortality, Spanish Influenza vs. Covid , **United Kingdom**



1918-19



2020-22

Source: 1918 Influenza: the Mother of All Pandemics, Emerg Infect Dis. 2006 Jan; 12(1): 15–22.

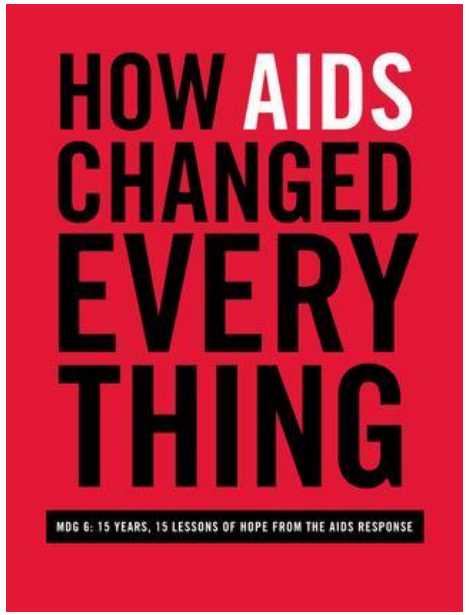
IL MONDO DOPO LA FINE DEL MONDO

Editori Laterza



31 Maggio 2020

HIV: strong clinical needs fueled prolific laboratory advancement



UNAIDS 2015

Unprecedented leap forward in the development of **molecular techniques**

- PCR and quantitative applications
- Sequencing
  - ✓**HIV first infection clinically managed on the basis of molecular monitoring (viral load and genotipic resistance)**
- Bioinformatics
  - ✓ Massive data analysis
  - ✓ Phylogenetic analysis pipelines
  - ✓ Genomic evolution pipelines
- Omics →**Systems biology**
  - ✓ Transcriptomics, Genomics, Proteomics, Lipidomics, Interactomics

Unprecedented leap forward in the development of **immunological techniques**

- Phenopypic and functionl assessment of immune cells
- Immunaging
- ….



GRAZIE