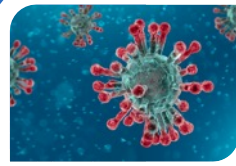


Omicron: Black Clouds and Silver Linings

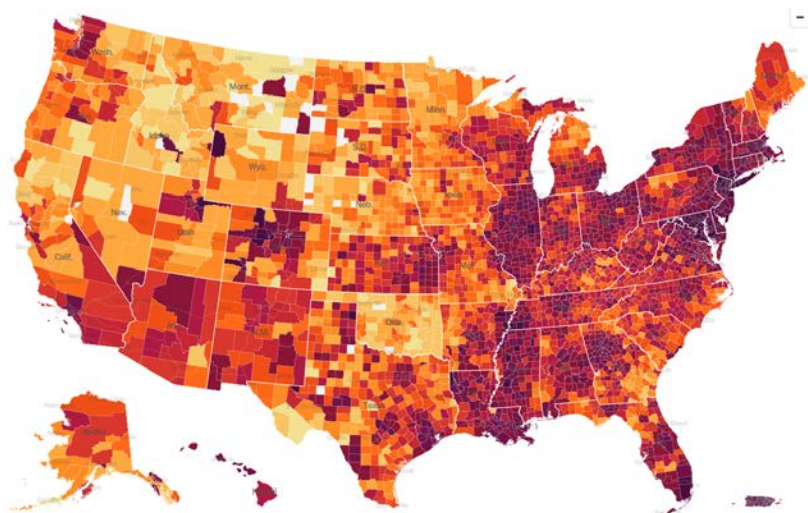
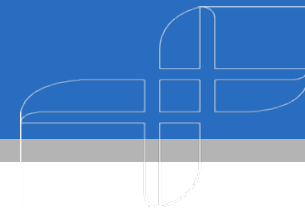
D. Engelthaler
TGen
01/04/2022

Thanksgiving 2021



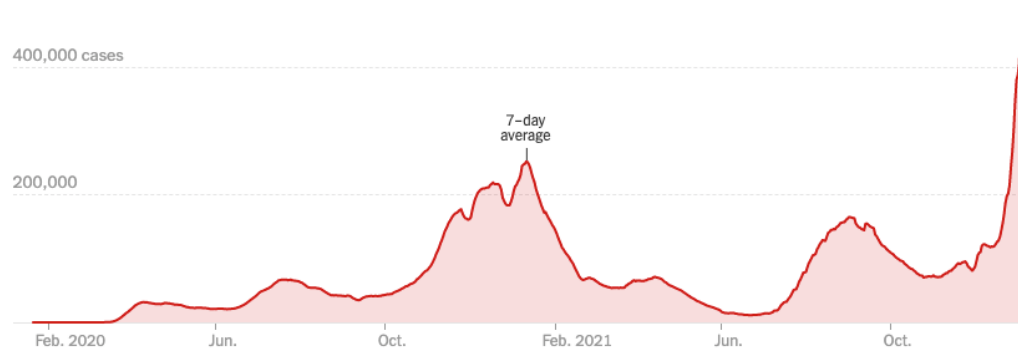
- South African Officials alerted the world that a new variant was rapidly spreading in the region
 - Seemed to outcompete Delta
 - Spread faster than Delta
 - Evade some immunity from vaccines
 - Infecting younger populations
 - Seemed to cause milder illness over all
- World promptly banned travel from South Africa to stop the spread ...

Omicron in the US - 01/04/2022

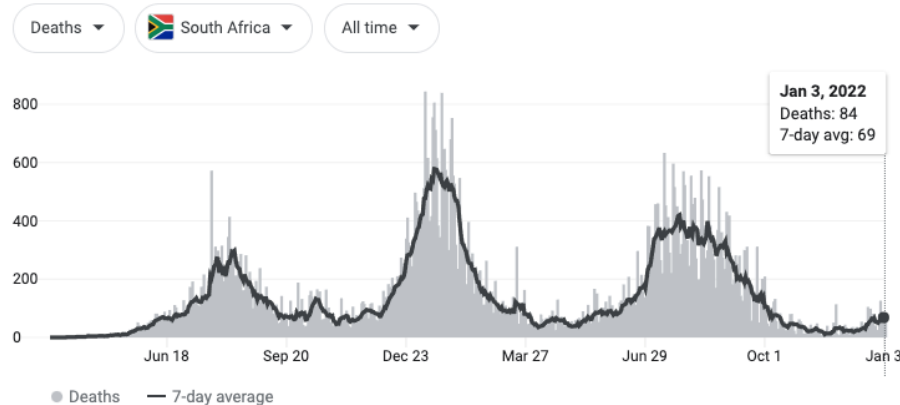
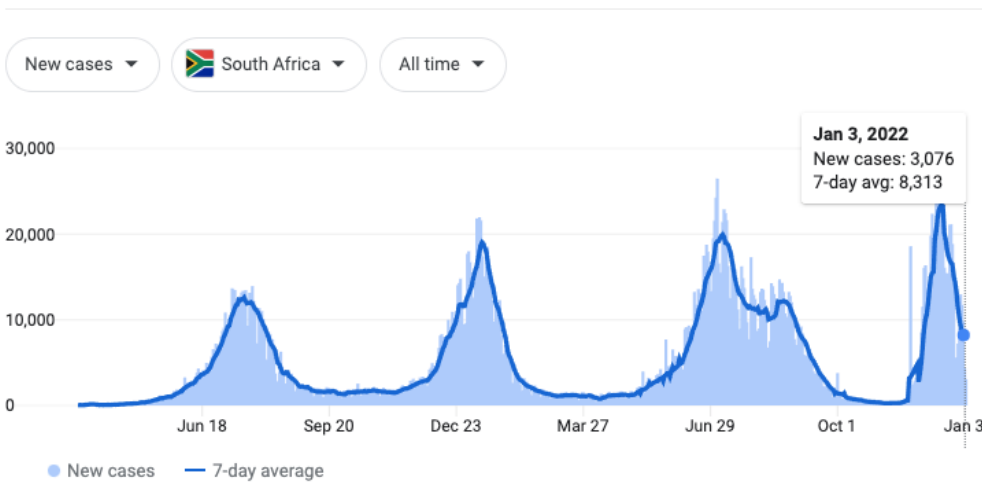
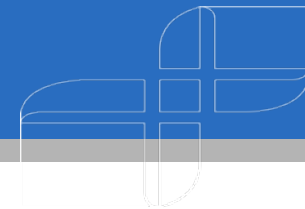


New reported cases

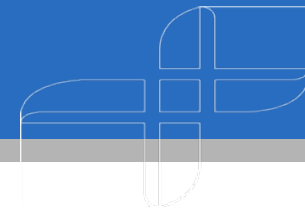
All time Last 90 days



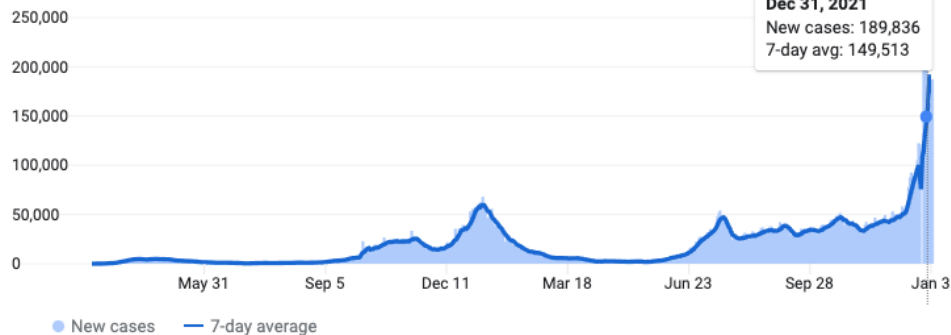
Omicron in South Africa - 01/04/2022



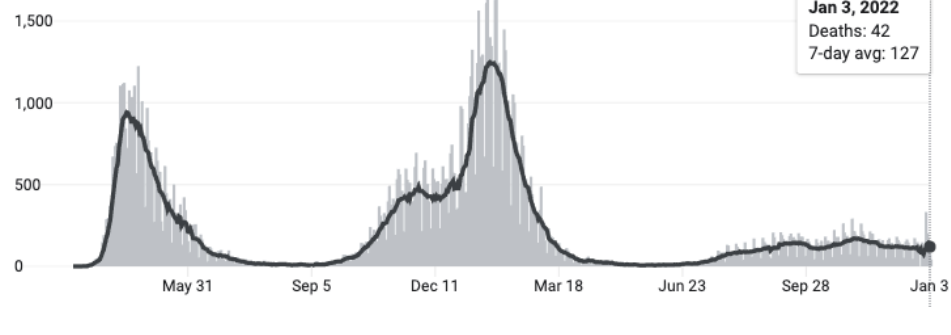
Omicron in UK - 01/04/2022



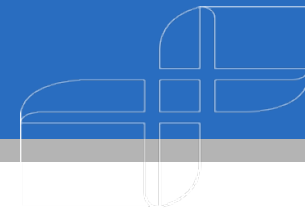
New cases ▾ United Kingdom ▾ All regions ▾ All time ▾



Deaths ▾ United Kingdom ▾ All regions ▾ All time ▾



The Omicron Trajectory



■ Cases ■ Hospitalizations ■ Deaths

New York

300% of last winter's peak

200%

100%

July 1, 2021

Jan. 3

New Jersey

300% of last winter's peak

200%

100%

July 1, 2021

Jan. 3

Massachusetts

300% of last winter's peak

200%

100%

July 1, 2021

Jan. 3

Florida

300% of last winter's peak

200%

100%

July 1, 2021

Jan. 3

Arizona

300% of last winter's peak

200%

100%

July 1, 2021

Jan. 3

New Mexico

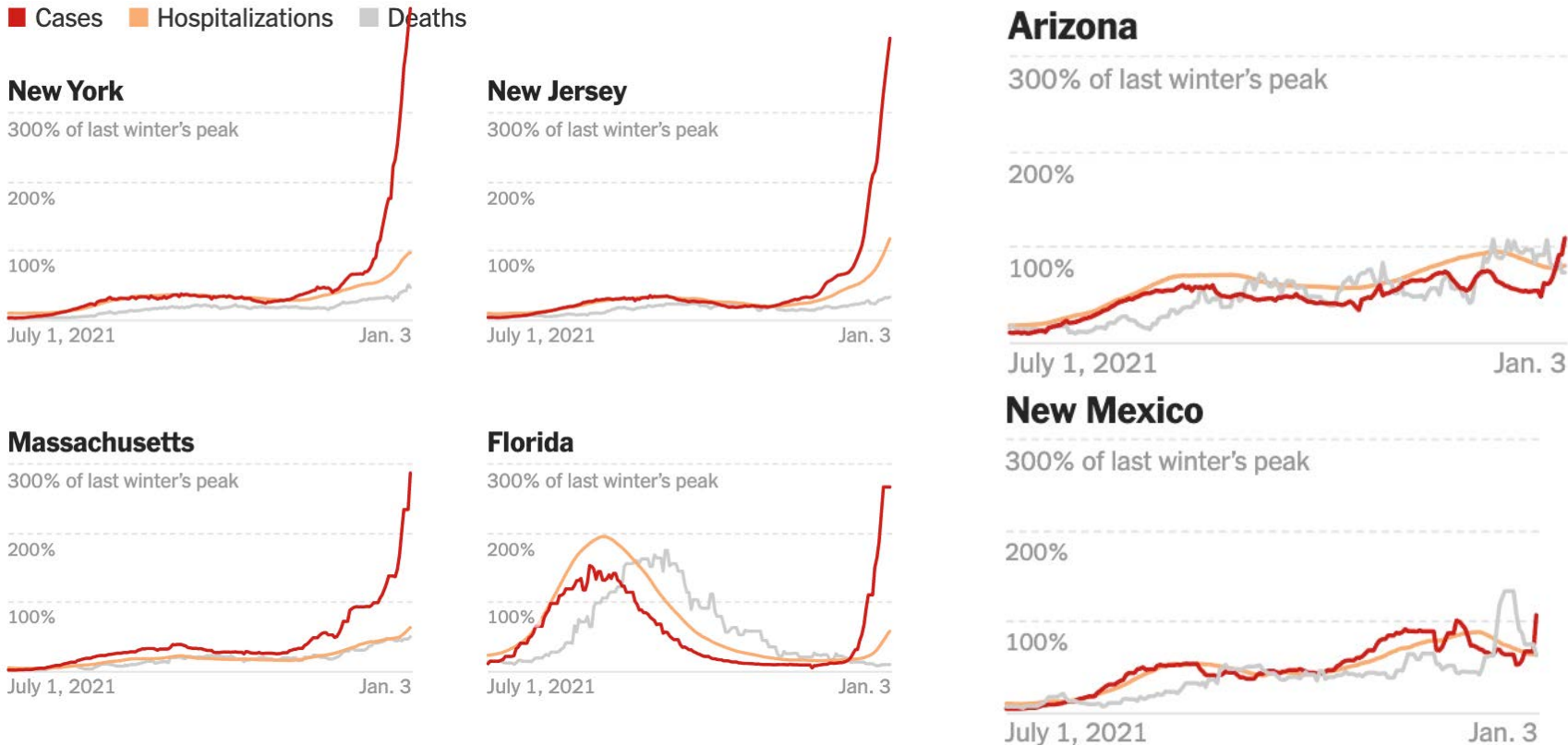
300% of last winter's peak

200%

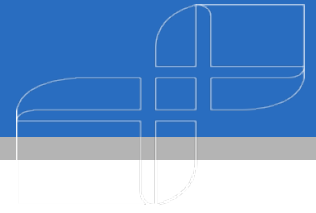
100%

July 1, 2021

Jan. 3

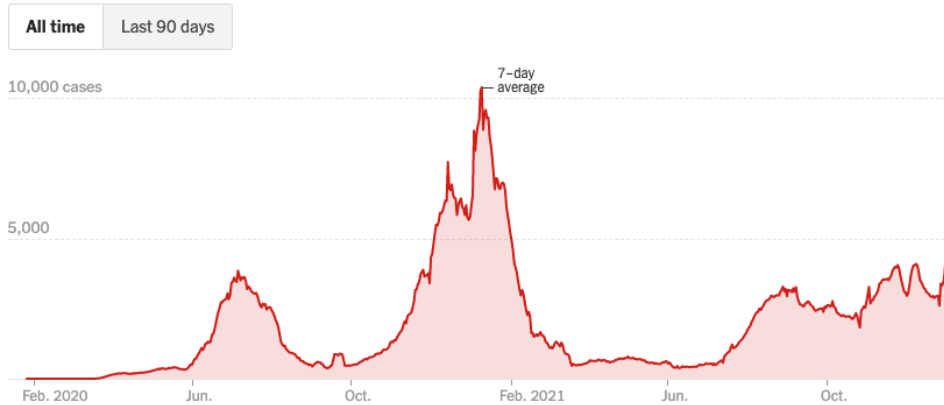


COVID: AZ and Coconino



Arizona

New reported cases

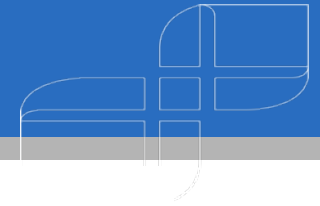


Coconino

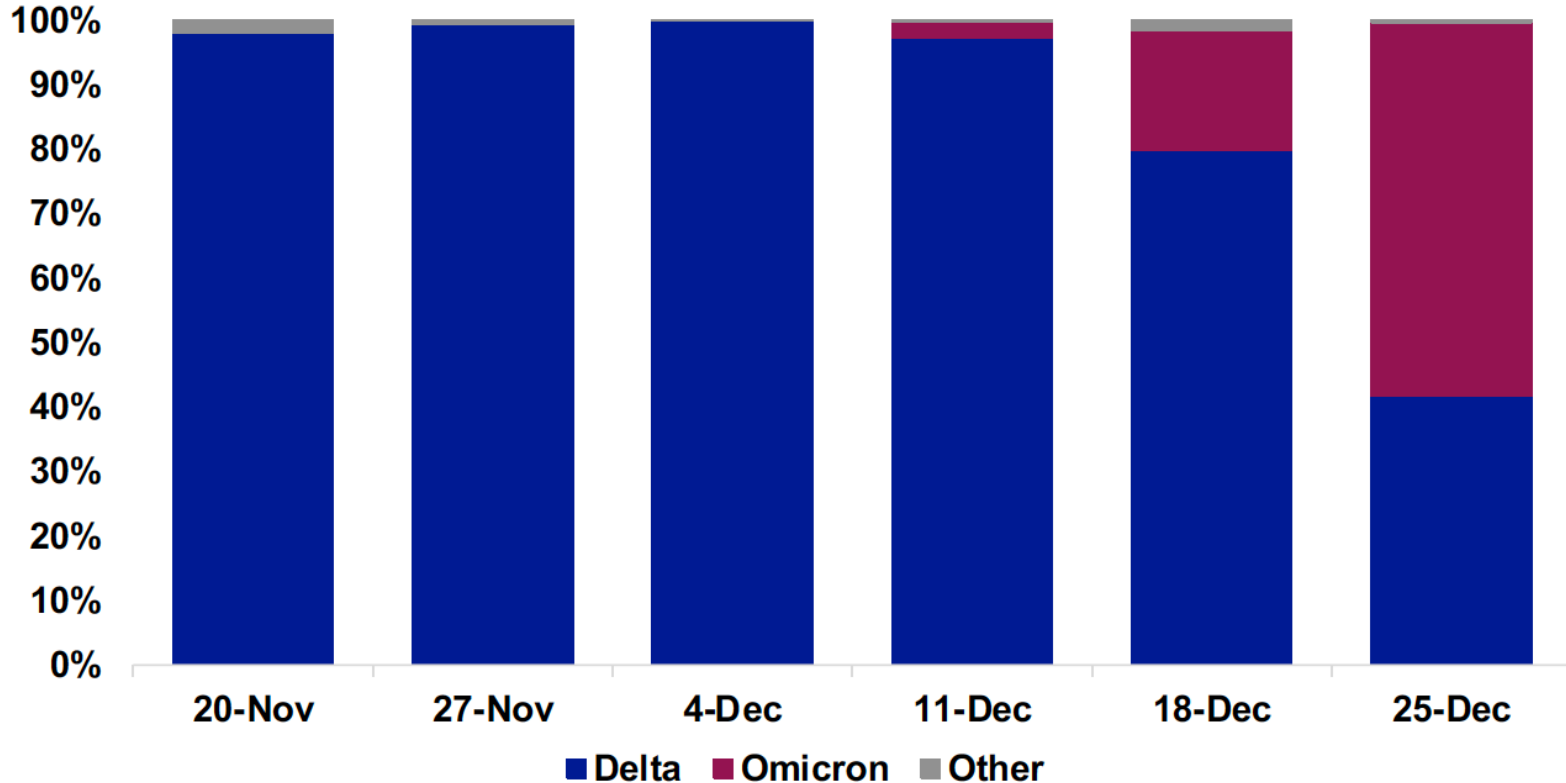
New reported cases throughout the pandemic



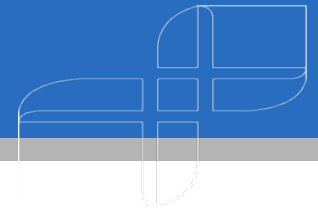
AZ Variant Surveillance



Proportion of Circulating Variants by Week



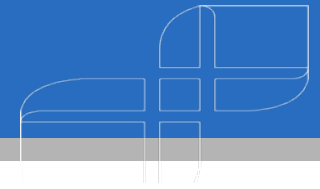
AZ Omicron by Week (01/04/2022)



Count and Proportion of Circulating Variants by Week

Date (end of week)	Omicron Count	Omicron Proportion	Delta Count	Delta Proportion	Total Weekly Genomes
20-Nov	0	0.00%	1814	98.11%	1849
27-Nov	0	0.00%	1497	99.40%	1506
4-Dec	0	0.00%	1622	99.88%	1624
11-Dec	26	2.37%	1067	97.35%	1096
18-Dec	169	18.69%	722	79.87%	904
25-Dec	324	57.86%	234	41.79%	560

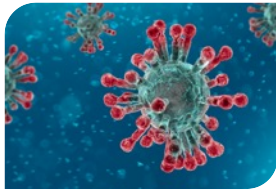
AZ Omicron by County (01/04/2022)



Count and Proportion by County – December 2021

Proportion represents # of Omicron genomes out of total genomes sequenced for given timeframe.

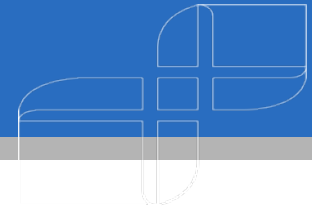
County	# Omicron (Month)	Total Genomes* (Month)	Proportion (Month)	# Omicron (12/19-1/1)	Total Genomes* (12/19-1/1)	Proportion (12/19-1/1)
Coconino	170	530	32.1%	98	132	74.2%
Maricopa	262	1707	15.3%	185	306	60.5%
Pima	20	257	7.8%	16	35	45.7%
Pinal	1	43	2.3%	1	6	16.7%
Gila	1	23	4.3%	1	1	100.0%
Yavapai	1	9	11.1%	0	0	0.0%
Unknown	67	1508	4.4%	26	60	43.3%
Total	522	3976	---	327	540	---



Why is Omicron so Different?



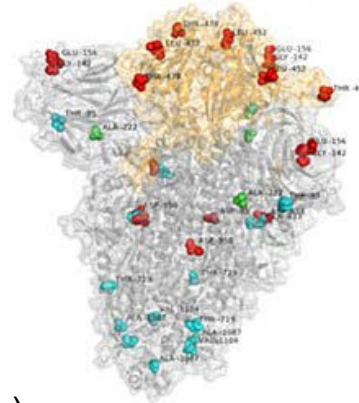
The Omicron Spike Mutations



(Top view of spike protein's receptor binding domain)

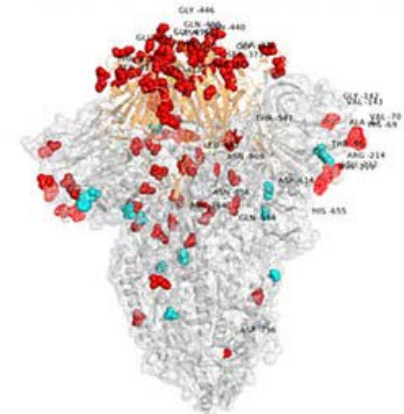
Delta

18 aa mutated residues in the Spike protein
8 residues in >60% of available sequences



Omicron

43 aa mutated residues in the Spike protein
34 residues in >60% of available sequences



The structure of SARS-CoV-2 spike protein showing the active site in orange and the residues coloured against different mutational rate.

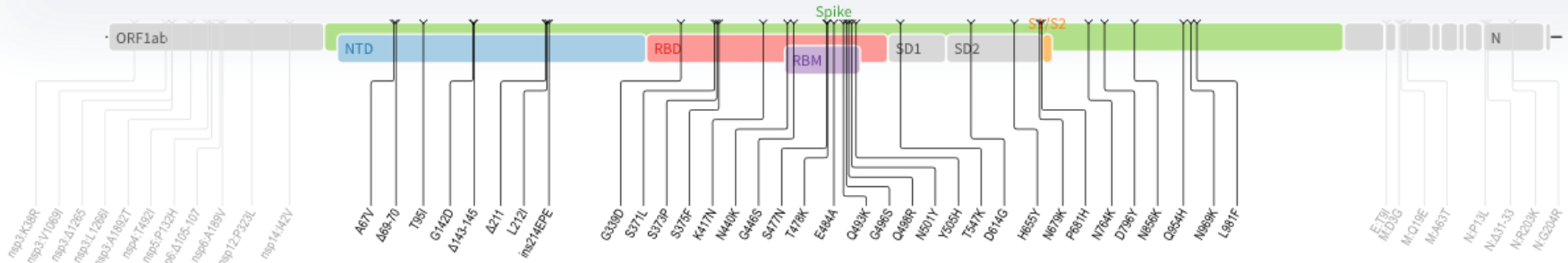
The Omicron Mutations



Omicron

B.1.1.529

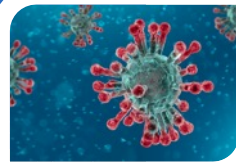
Outbreak.info B.1.1.529 Lineage Report ^[1]



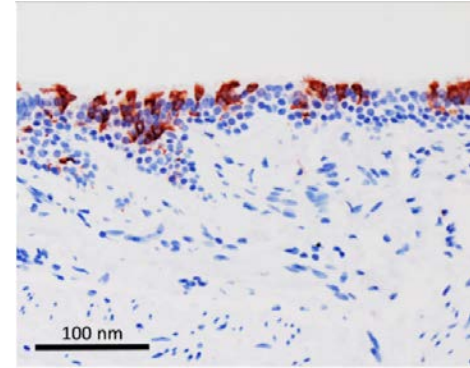
Adapted from outbreak.info

- S: Q498R and H501Y greatly enhance ACE2 affinity
- S: E484A may allow for immune evasion
- S: H665Y, N679K, P681H cluster at S1/S2 furin cleavage site – may increase transmissibility
- ORF1a: 105-107del may inhibit part of cellular immune response
- N: R203K and G204R have been associated with subgenomic RNA expression – may lead to lower Ct

The Latest Omicron Research

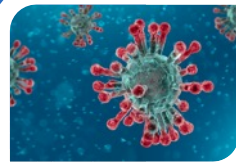


- Omicron preferentially invades upper airway cells versus lower airway (Delta is the opposite) (*Chi-wai, HKU, 2021*)
- Omicron results in significant decrease in hospitalization, severity and death (*Wolter, NICD S. Africa, 2021; Abdullah, SBAH, Cape Town; Ferguson, Imperial College, London, 2021*)
- Omicron evades antibodies from vaccination (J&J much worse than mRNA), previous infection better than vaccine, but boosters provide significant improvement for both (*Doria-Rose, NIAID, 2021*), but Omicron provides good protection against Delta
- Omicron does not evade T-cell immunity gained from vaccine or previous infection (*Keeton, U Cape Town, 2021; Tarke, La Jolla Inst, CA, 2021*)
- Omicron is also milder in children (*Rubin, Children's Hops Phil, 2022*)



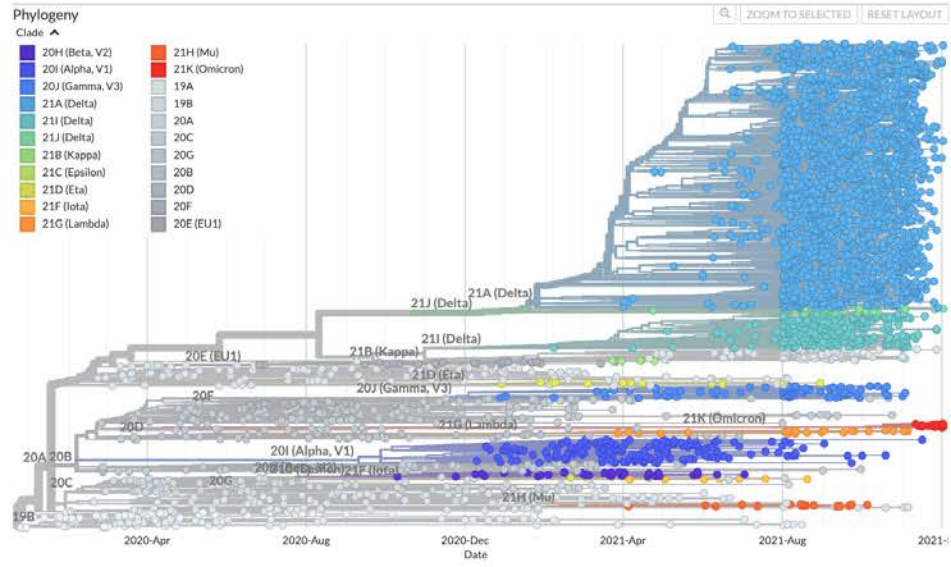
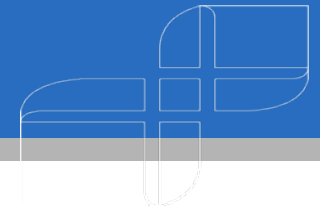
Omicron variant of SARS-CoV-2 (in red) infected human bronchus tissues.

Omicron: The Black Cloud and The Silver Lining

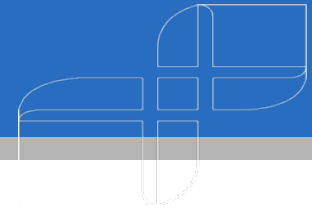


1. Omicron is quickly taking over as the dominant variant
2. Omicron will roll across us like a tidal wave and will roll back out again
3. Omicron will not be stopped by previous (>6 months) vaccination or infection; but they will stop serious illness and death
4. Omicron will likely lead to mostly mild and asymptomatic cases
5. We can lower Omicron spread by getting boosters
6. We need to ensure the highest at risk are highly immunized and stay somewhat isolated (for next few weeks)
7. We need to psychologically and socially accept that Omicron will wash over us and cause lots of cases,
 - But that this may be a good thing in the end – getting us closer to an endemic state

SARS-CoV-2 Phylogeny: Omicron



SARS-CoV-2 Phylogeny: Omicron



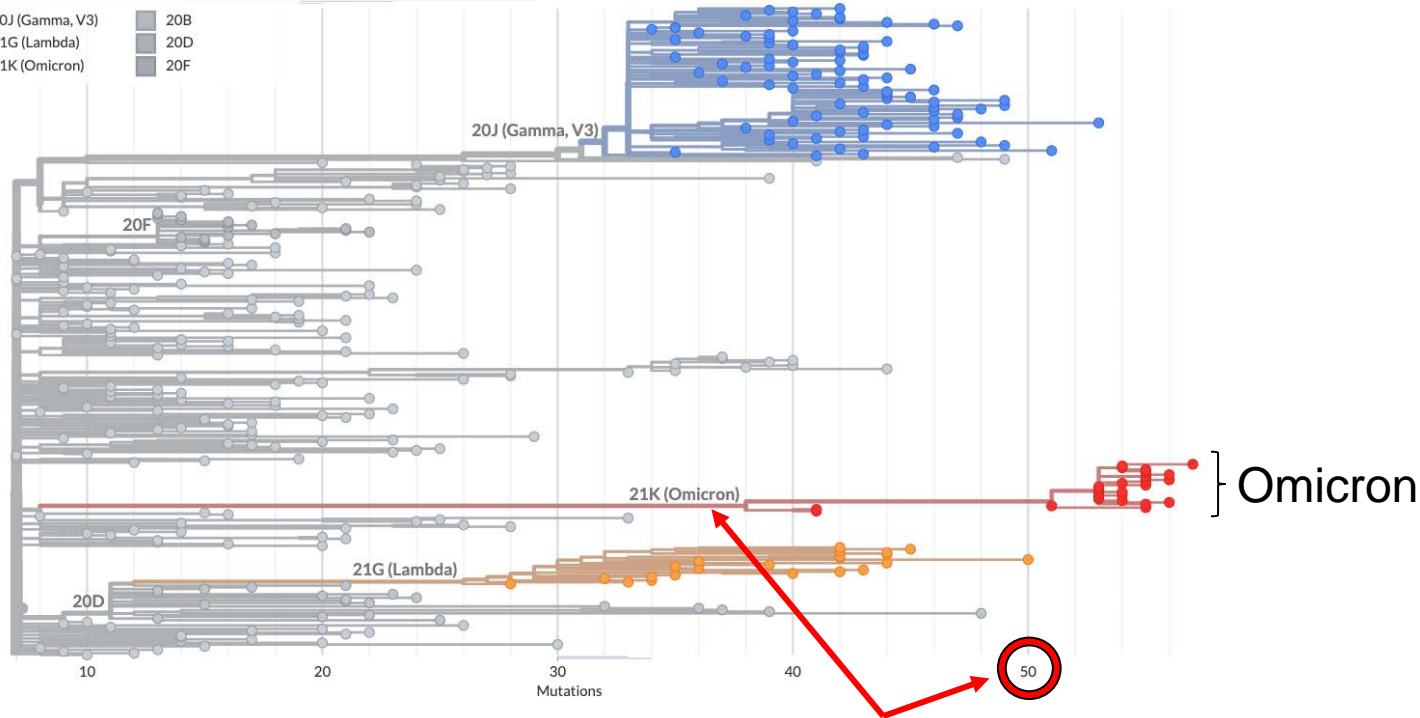
Phylogeny

Clade ▲

- 20J (Gamma, V3)
- 21G (Lambda)
- 21K (Omicron)
- 20B
- 20D
- 20F

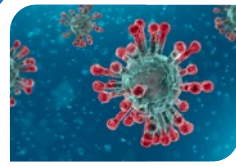
🔍 ZOOM TO SELECTED

🔄 RESET LAYOUT



Omicron branch has 50 Mutations
(Therefore has a significant separation from last known related strain)

Hypothetical Mechanisms for the Hyper-Mutations



- Long term/chronic infection, allowing for development of mutations in single host (*likely*)
 - Documented as most likely mechanism for past variants
- Animal spillover, followed by reverse spillover into humans (*possible*)
 - Have seen host based selection driving mutations in spillovers in mink
- Recombination between two or more coronaviruses in single host (*unlikely*)
 - Mutations appear to be mostly selected for, not accidental through recombination