

# Omicron

## Update Dec. 26, 2021

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### Contents:

- Slide 2: The common mutational pattern in Omicron Spikes
- Slides 3-9: Dynamic transitions towards Omicron prevalence by continent and some regional highlights
- Slides 10-13: Emerging Omicron variants, and a potential sequencing issue with respect to the insertion at 214 among common Omicron variants

# Mutation list of the most common form of Spike among Omicron sequences

For common B.1.1.529 and BA.1 Pango lineage forms compared to the Wuhan reference sequence

## NTD

A67V **H69- V70-** T95I **G142D V143- Y144- Y145-** **N211-** L212I **+214EPE**

## RBD

G339D S371L S373P S375F K417N N440K G446S S477N T478K E484A

Q493R G496S Q498R N501Y Y505H

Near furin (cleavage enhancing)

Heptad Repeat 1

T547K D614G **H655Y N679K P681H** N764K D796Y N856K **Q954H N969K L981F**

Full mutation list:

A67V **H69- V70-** T95I G142D **V143- Y144- Y145-** **N211-** L212I **+214EPE** G339D S371L S373P S375F K417N N440K G446S  
S477N T478K E484A Q493R G496S Q498R N501Y Y505H T547K D614G **H655Y N679K P681H** N764K D796Y N856K Q954H  
N969K L981F

Enabled by data from

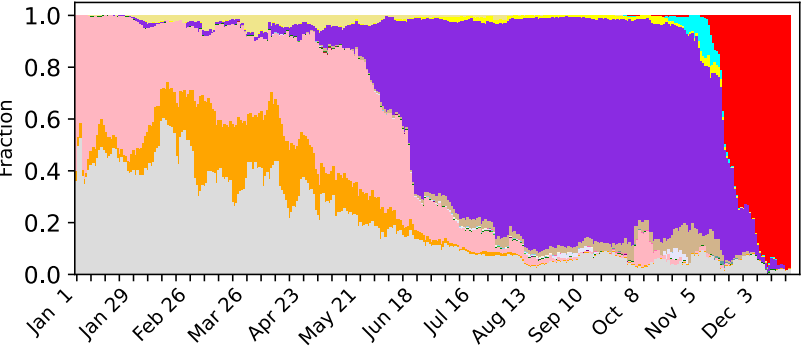


**INDELS BOLD: + indicates an insertion - a deletion**

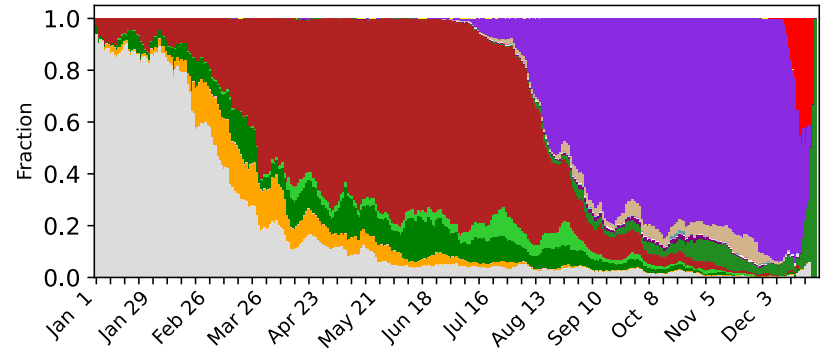
# Fraction of Sars-CoV-2 sequences of distinct lineages averaged by week through 2021 by continent.



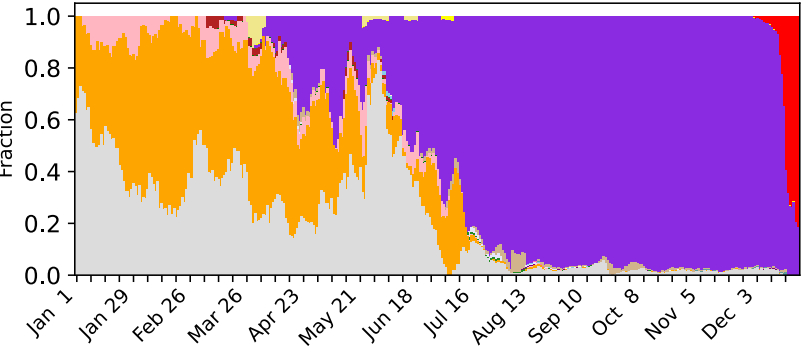
Africa: 33508 sequences



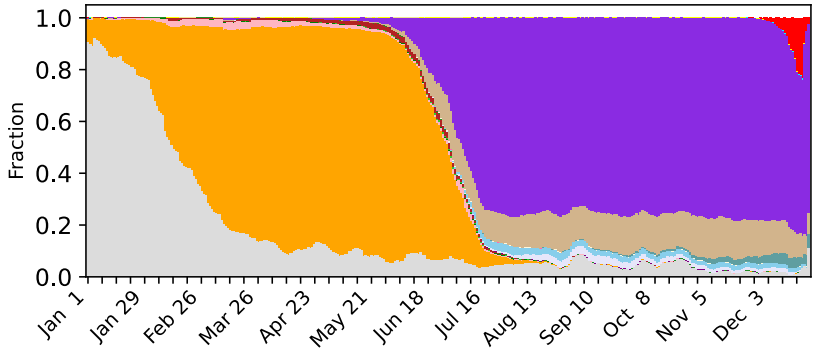
South-America: 77927 sequences



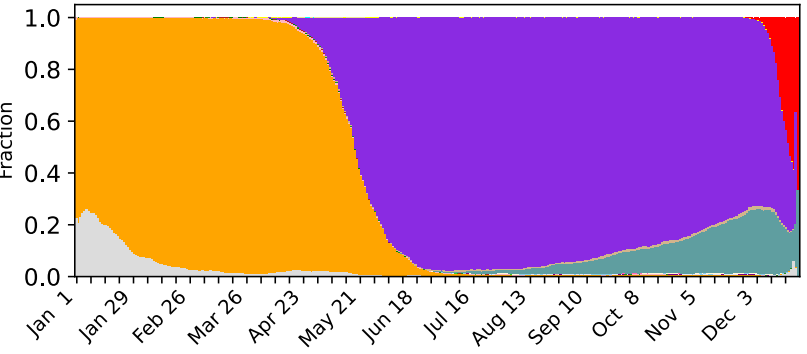
Oceania: 14606 sequences



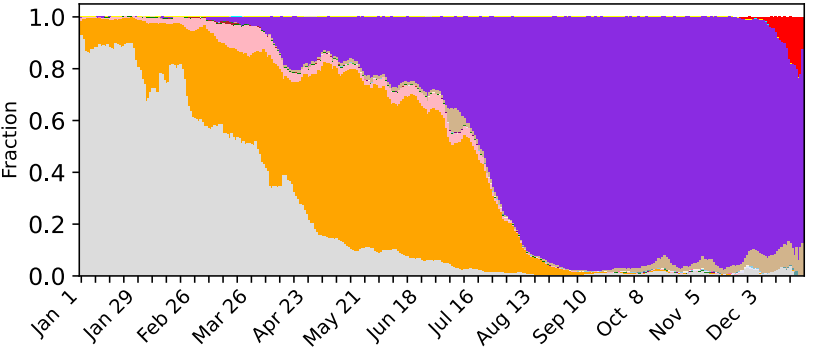
Europe w/o United-Kingdom: 1286362 sequences



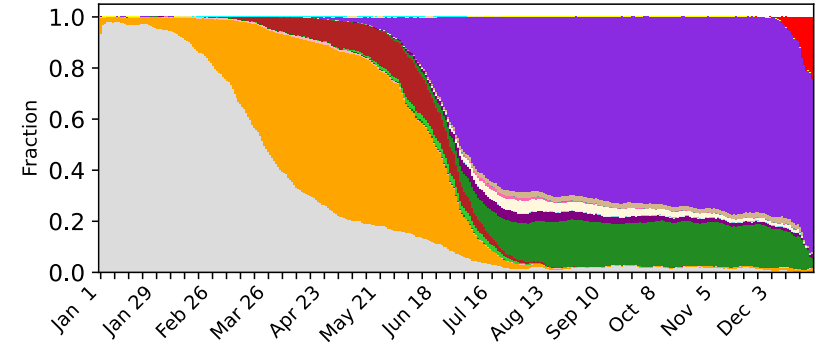
United-Kingdom: 1324802 sequences



Asia: 222743 sequences



North-America: 1653047 sequences



- Omicron
- B.1.640
- B.1.1.318
- C.1.2
- Delta
- Delta\_AY.122
- Delta\_AY.4.2
- Delta\_AY.35
- Delta\_AY.47
- Delta\_AY.98.1
- Delta\_AY.33
- Delta\_AY.26
- Delta\_AY.25
- Gamma
- Mu
- Lambda
- Beta
- Alpha
- other

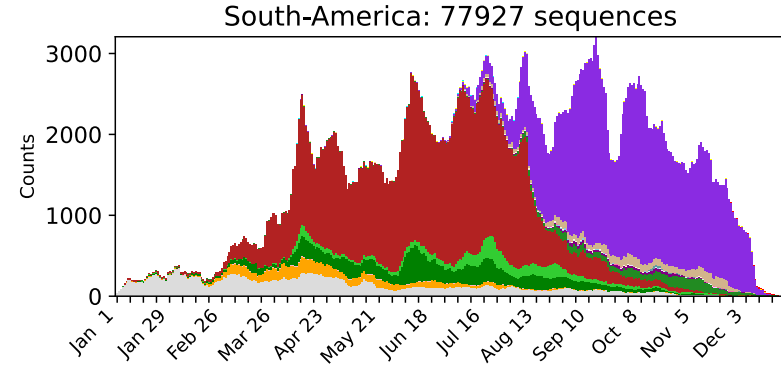
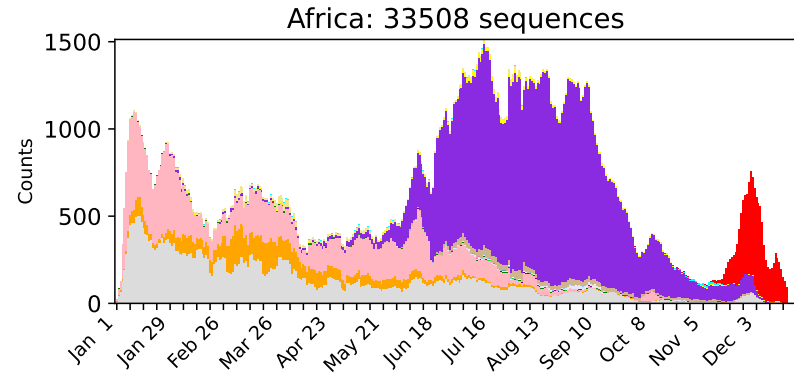
First half of 2021:  
Relatively gradual transitions towards Alpha, Gamma (S. America) or Beta (Africa).

Late spring/summer:  
Relatively accelerated transition to Delta.

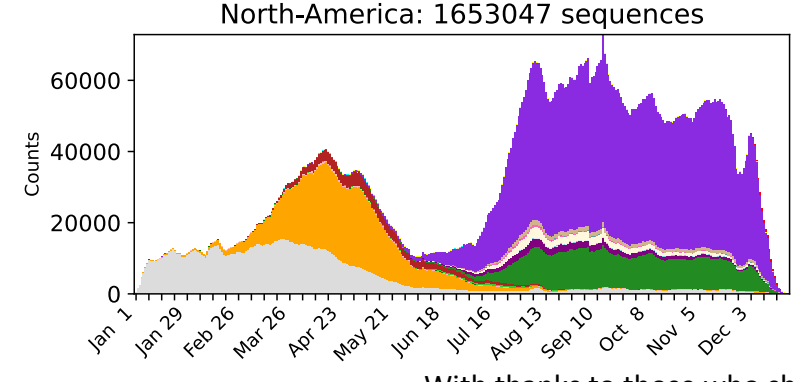
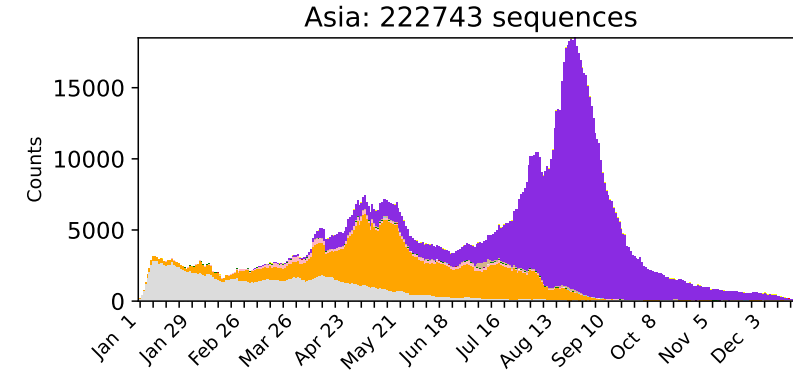
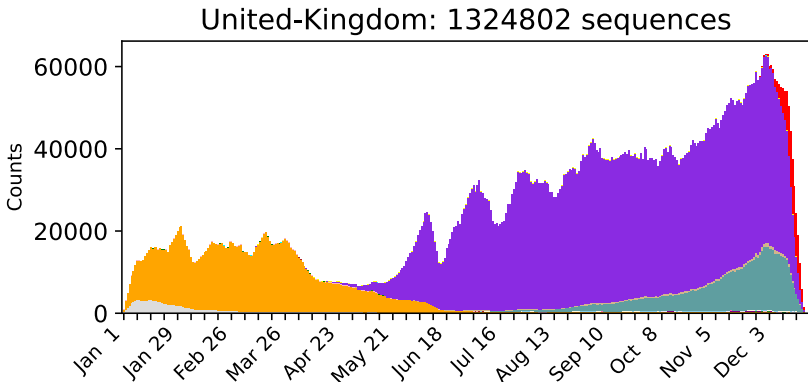
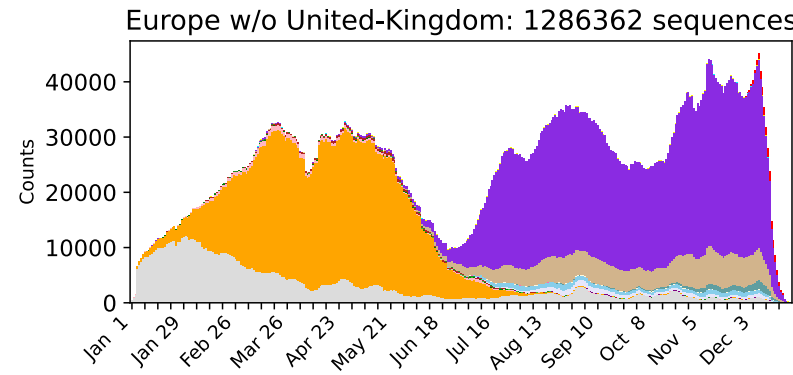
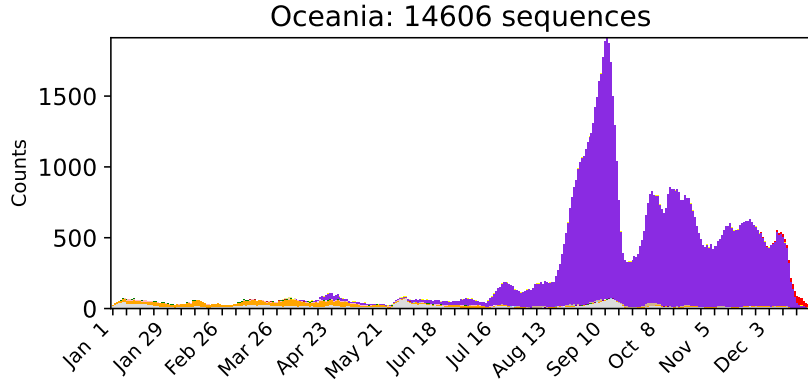
Nov/December:  
Rapid transitions to Omicron.

With thanks to those who share sequences through GISAID

Same data as the previous slide plotted as counts of distinct lineages averaged by week through 2021 by continent.



- Omicron
- B.1.640
- B.1.1.318
- C.1.2
- Delta
- Delta\_AY.122
- Delta\_AY.4.2
- Delta\_AY.35
- Delta\_AY.47
- Delta\_AY.98.1
- Delta\_AY.33
- Delta\_AY.26
- Delta\_AY.25
- Gamma
- Mu
- Lambda
- Beta
- Alpha
- other

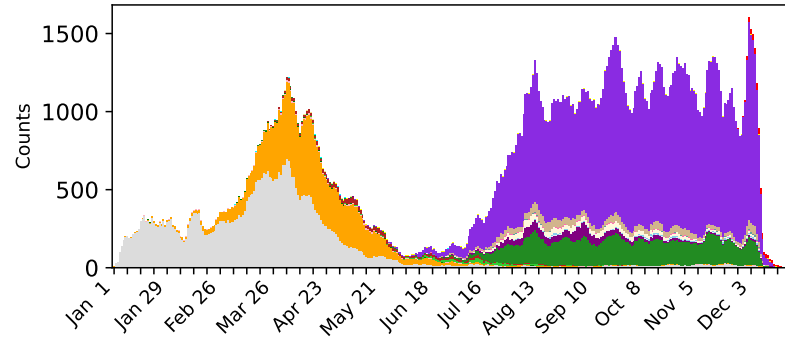


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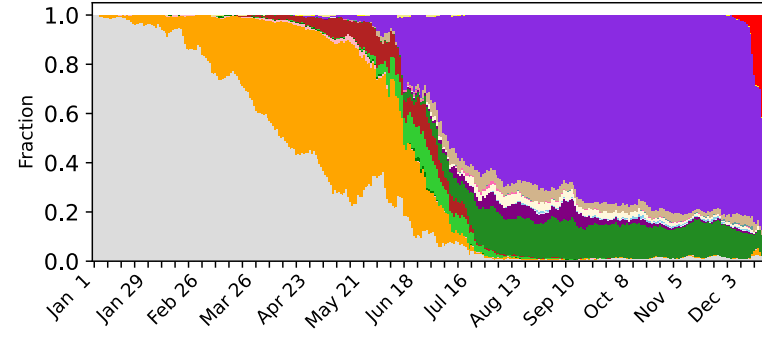
# Omicron: B.1.1.529 and BA.\*

## Examples of North American transitions

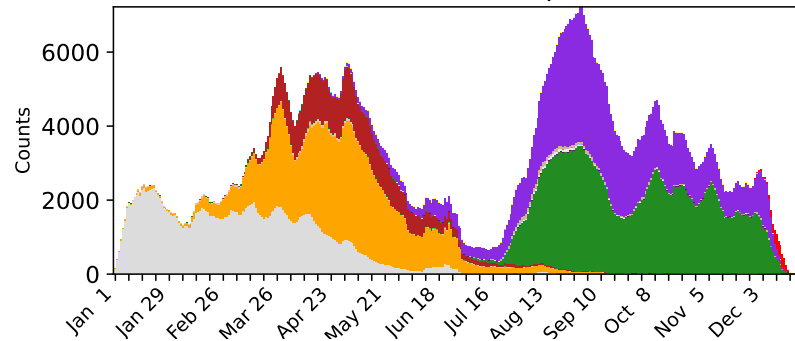
USA.New-York: 33513 sequences



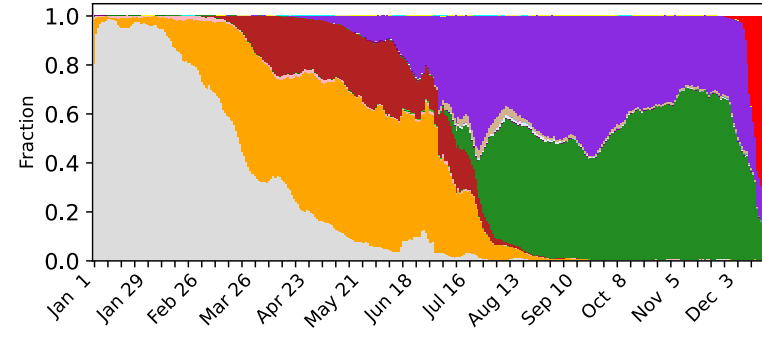
USA.New-York: 33513 sequences



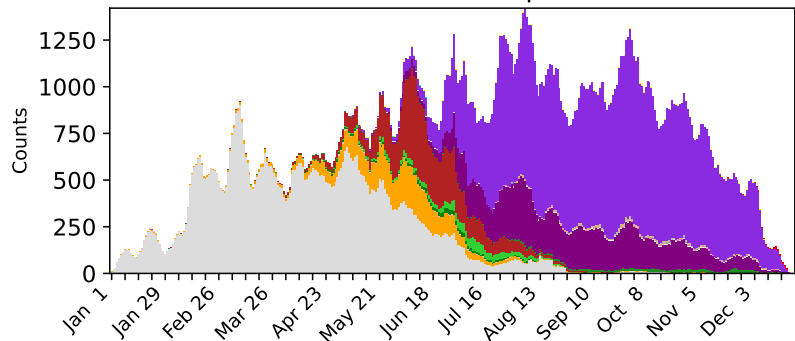
Canada: 158073 sequences



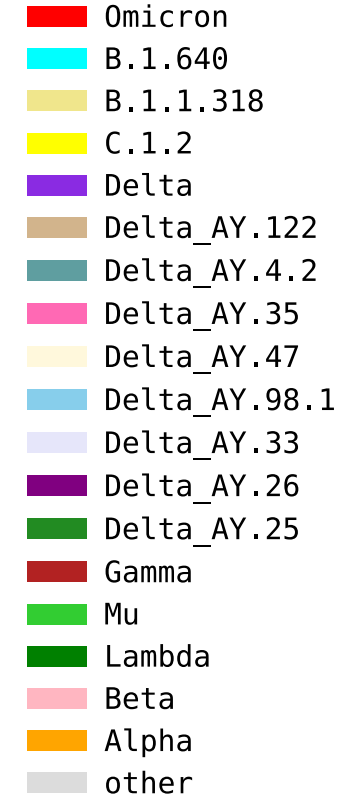
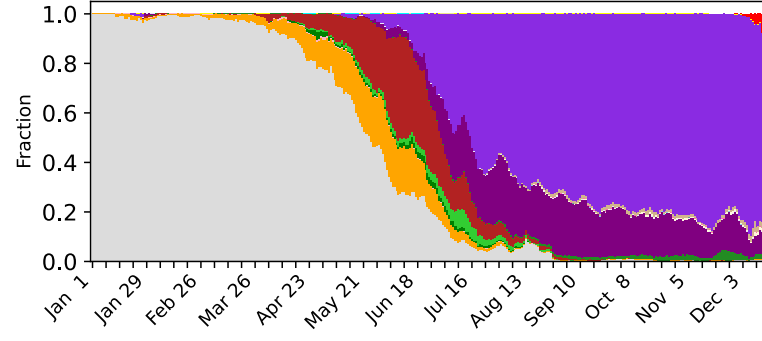
Canada: 158073 sequences



Mexico: 36327 sequences



Mexico: 36327 sequences

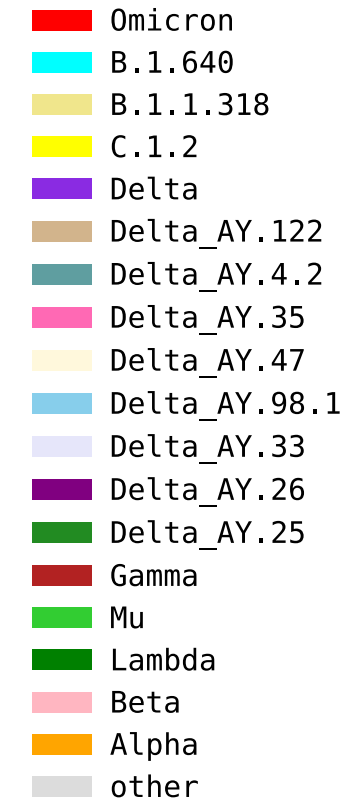
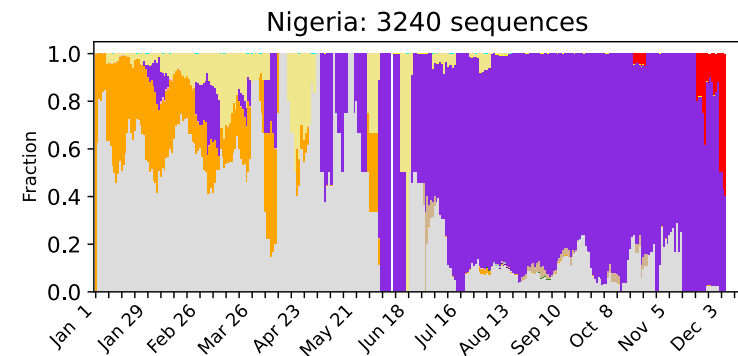
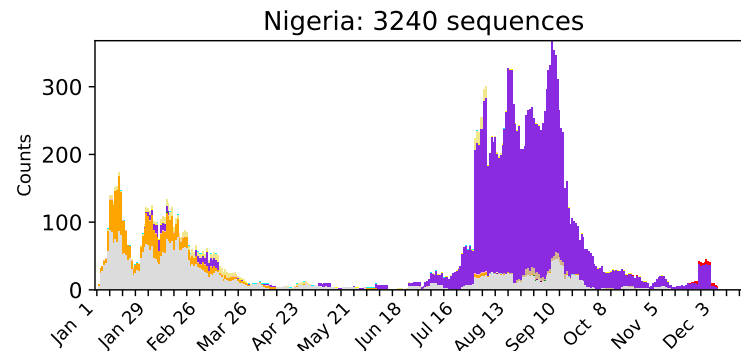
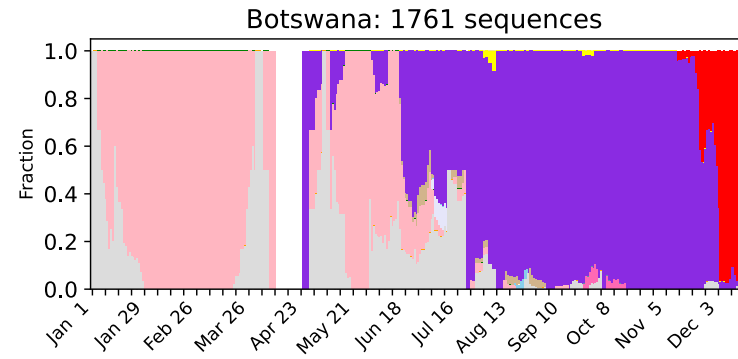
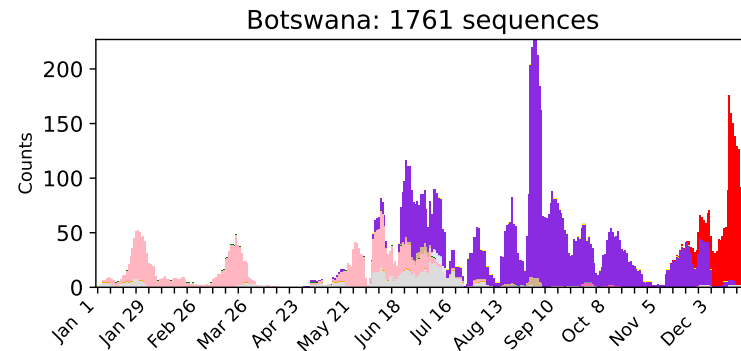
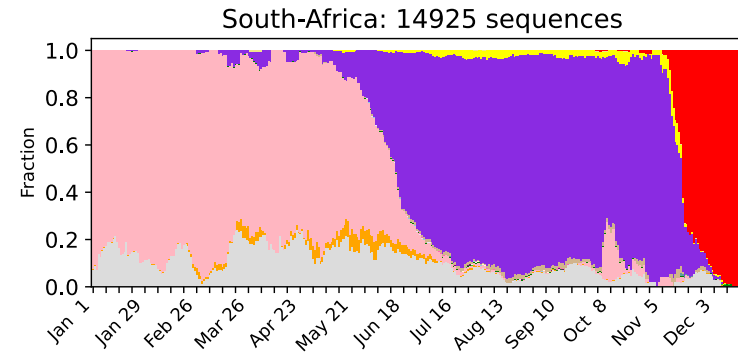
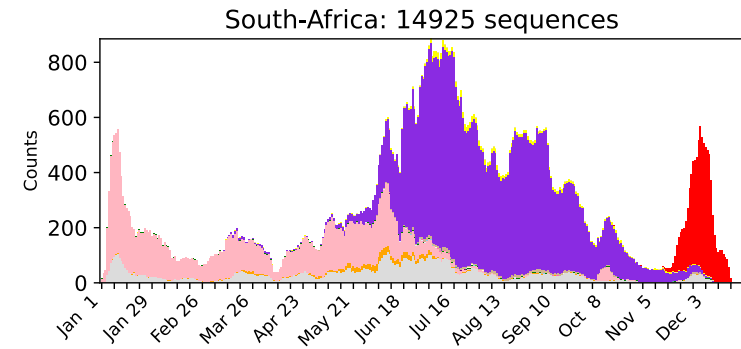


With thanks to those who share sequences through GISAID



# Omicron: B.1.1.529 and BA.\*

## Examples of African transitions

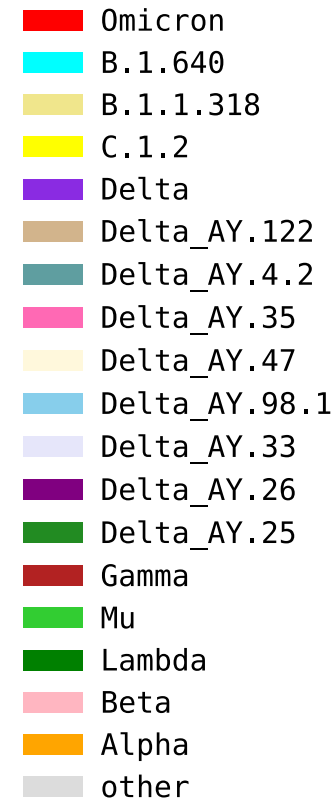
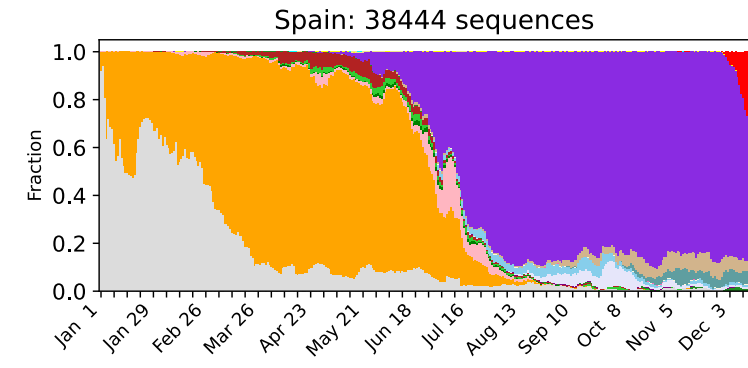
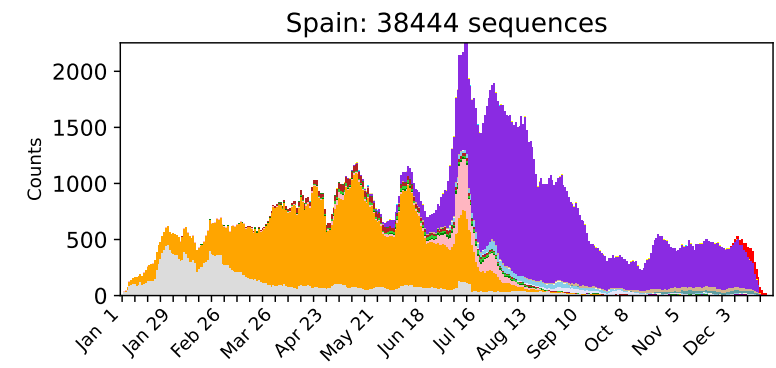
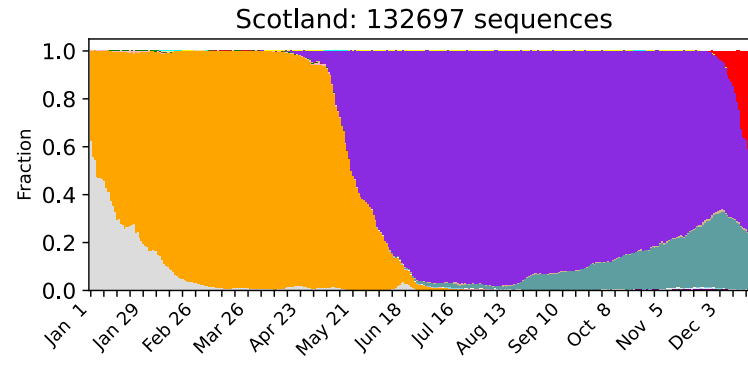
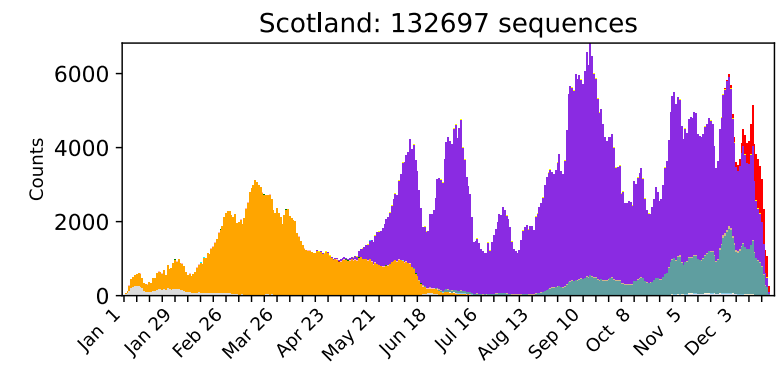
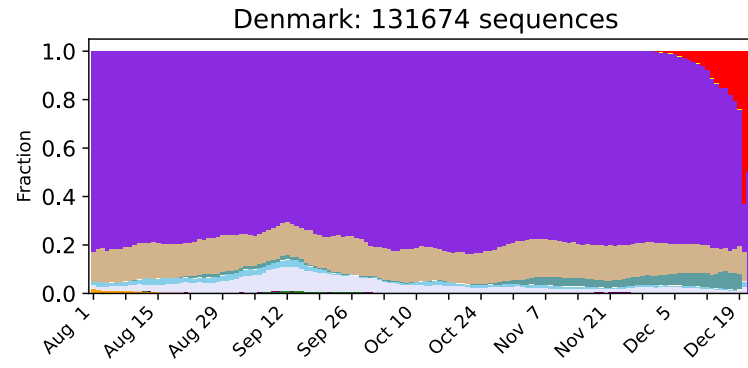
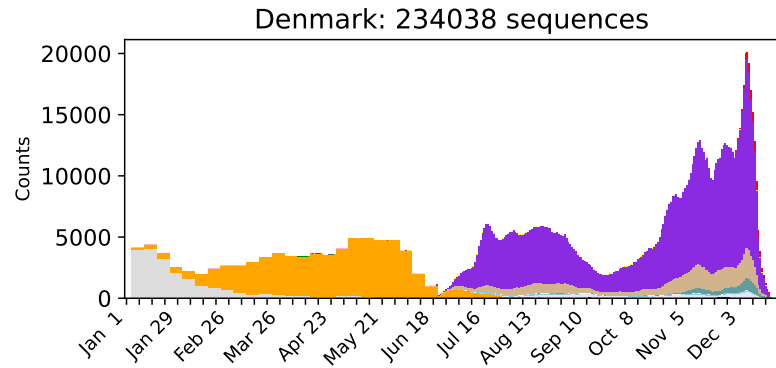


With thanks to those who share sequences through GISAID



# Omicron: B.1.1.529 and BA.\*

## Examples of UK/European transitions



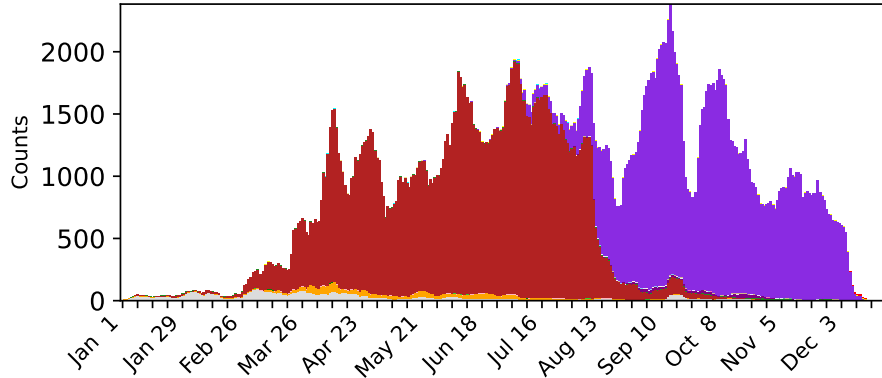
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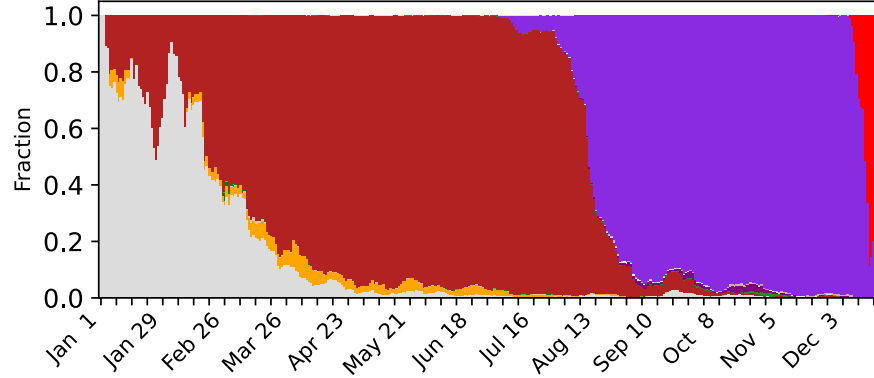
# Omicron: B.1.1.529 and BA.\*

## Examples of South American transitions

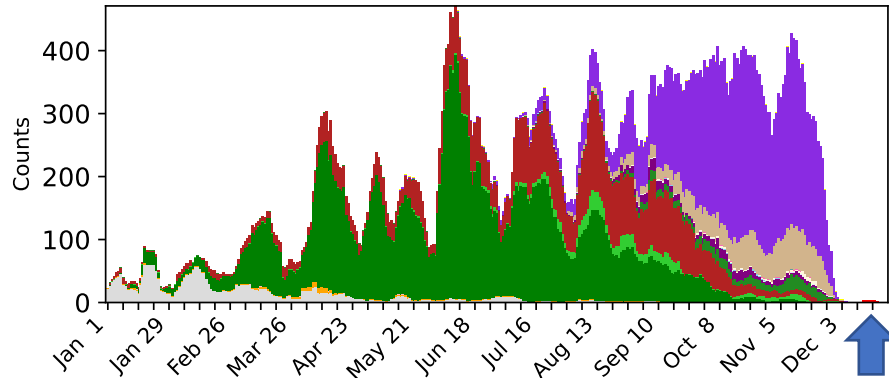
Brazil: 47000 sequences



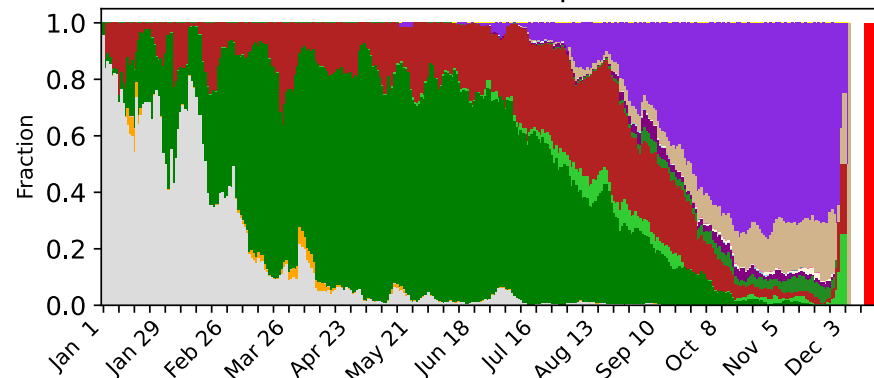
Brazil: 47000 sequences



Peru: 10397 sequences



Peru: 10397 sequences



- Omicron
- B.1.640
- B.1.1.318
- C.1.2
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- Delta\_AY.33
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- Delta\_AY.25
- Gamma
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- Lambda
- Beta
- Alpha
- other

Limited sampling



With thanks to those who share sequences through GISAID

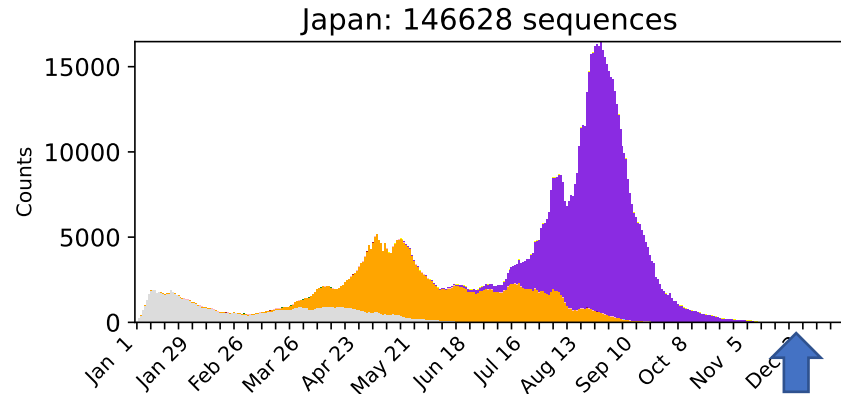




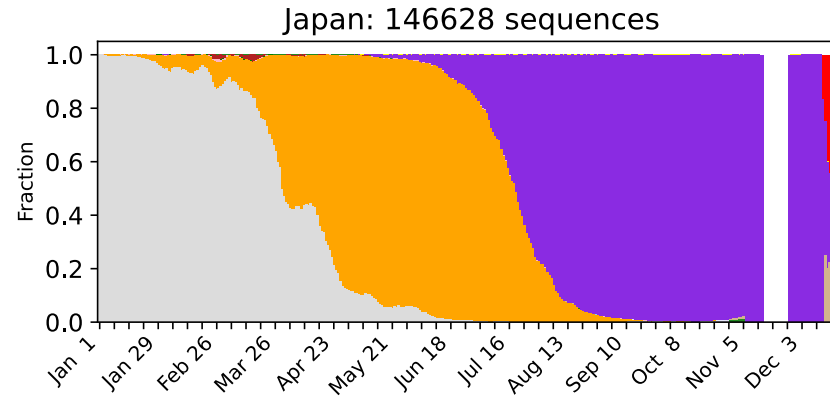
# Omicron: B.1.1.529 and BA.\*

## Examples of Asian transitions

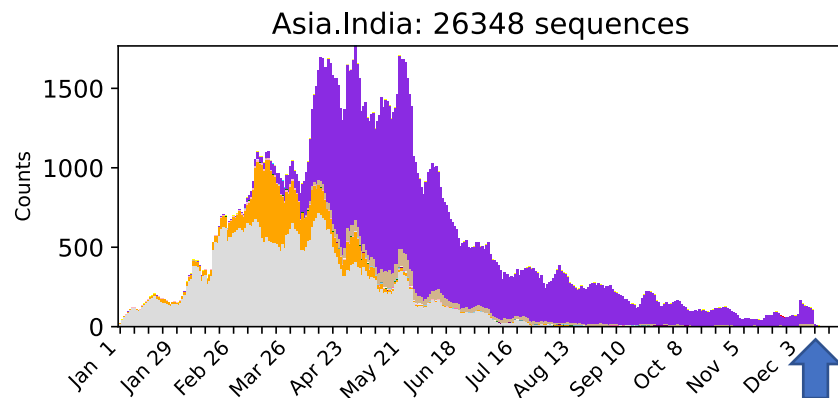
Limited sampling in Japan, but clear presence



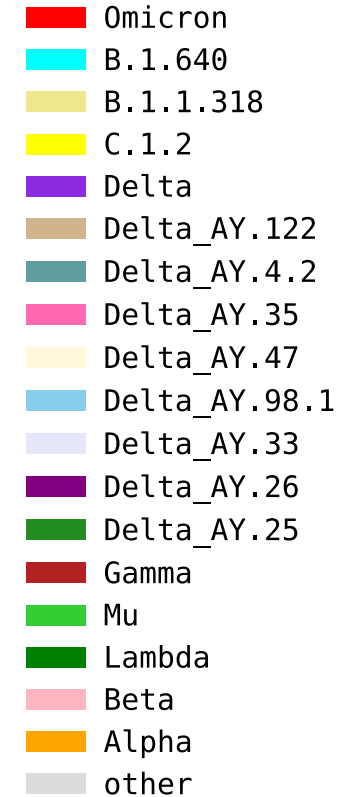
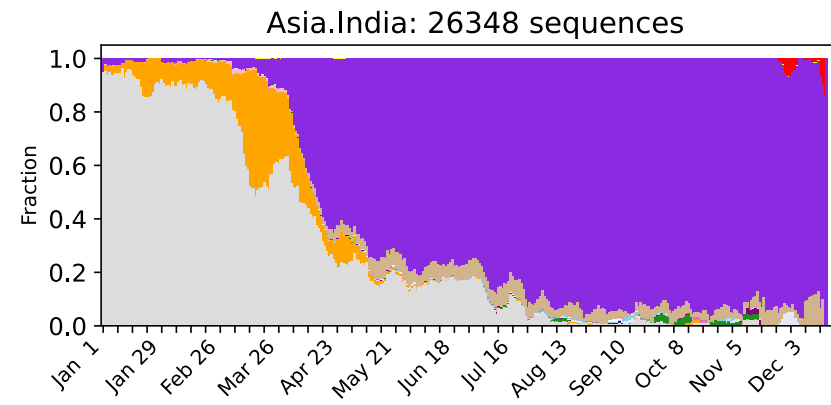
Limited sampling



Just beginning to be sampled in India



Limited sampling



With thanks to those who share sequences through GISAID

# Omicron Variants

Most Omicron Spike sequences have stretches of ambiguous based calls. These variants were the most commonly found among the essentially complete Spike sequences, sampled 12/23/2021

Amino acids that reverted to ancestral are indicated by a blank. Red indicates an amino acid altering mutation.



Counts  
Lineage Form Spike form as mutation string relative to the Wuhan reference sequence.

Baseline:																																									
BA.1	3265	1454	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-	N211I	L212-	+214EPE	G339D	S371L	S373P	S375F	K417N	N440K	G446S	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	N764K	D796Y	N856K	Q954H	N969K	L981F		
BA.1	3265	219	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-	N211I	L212-		G339D	S371L	S373P	S375F	K417N	N440K	G446S	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	N764K	D796Y	N856K	Q954H	N969K	L981F		
BA.1	3265	229	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-	N211I	L212-	+214EPE	G339D	R346K	S371L	S373P	S375F	K417N	N440K	G446S	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	N764K	D796Y	N856K	Q954H	N969K	L981F	
BA.1	3265	23	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-	N211I	L212-		G339D	R346K	S371L	S373P	S375F	K417N	N440K	G446S	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	N764K	D796Y	N856K	Q954H	N969K	L981F	
BA.1	3265	137	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-	N211I	L212-	+214EPE	G339D	S371L	S373P	S375F					L452R	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	N764K	D796Y	N856K	Q954H	N969K	L981F
BA.1	3265	13	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-	N211I	L212-	+214EPE	G339D	S371L	S373P	S375F					L452R	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H		D796Y	N856K	Q954H	N969K	L981F
BA.1	3265	11	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-	N211I	L212-	+214EPE	G339D	S371L	S373P	S375F					L452X	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	N764K	D796Y	N856K	Q954H	N969K	L981F
BA.1	3265	95	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-	N211I	L212-	+214EPE	G339D	S371L	S373P	S375F	K417N	N440K	G446S	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	A701V	N764K	D796Y	N856K	Q954H	N969K	L981F	
BA.1	3265	36	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-	N211I	L212-		G339D	S371L	S373P	S375F	K417N	N440K	G446S	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	A701V	N764K	D796Y	N856K	Q954H	N969K	L981F	
BA.1	3265	42	A67V	H69-	V70-	T95I			L141F		N211I	L212-	+214EPE	G339D	S371L	S373P	S375F	K417N	N440K	G446S	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	N764K	D796Y	N856K	Q954H	N969K	L981F		
BA.1	3265	13	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-	N211I	L212-	+214EPE	G339D	S371L	S373P	S375F		N440K	G446S	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	N764K	D796Y	N856K	Q954H	N969K	L981F		
BA.1	3265	25	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-	N211I	L212-		G339D	S371L	S373P	S375F		N440K	G446S	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	N764K	D796Y	N856K	Q954H	N969K	L981F		
BA.1	3265	12	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-	N211I	L212-	+214EPE	G339D	S371L	S373P	S375F	K417X	N440K	G446S	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	N764K	D796Y	N856K	Q954H	N969K	L981F		
BA.1	3265	26	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-	N211I	L212-		G339D	S371L	S373P	S375F	K417X	N440K	G446S	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	N764K	D796Y	N856K	Q954H	N969K	L981F		
BA.1	3265	54	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-	N211I	L212-	+214EPE	G339D	S371L	S373P	S375F	K417N	N440K	G446S	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	N764K	D796Y	N856K	Q954H	N969K	L981F	D1146X	
BA.1	3265	10	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-	N211I	L212-		G339D	S371L	S373P	S375F	K417N	N440K	G446S	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	N764K	D796Y	N856K	Q954H	N969K	L981F	D1146X	
*BA.1	3265	13	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-				G339D	S371L	S373P	S375F	K417N	N440K	G446S	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	N764K	D796Y	N856K	Q954H	N969K	L981F	D1146X	
*BA.1	3265	11	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-				G339D	S371L	S373P	S375F	K417N	N440K	G446S	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	N764K	D796Y	N856K	Q954H	N969K	L981F		
BA.1	3265	11	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-	N211I	L212-	+214EPE	G339D	S371L	S373P	S375F	K417N	N440K	G446S	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	N764K	D796Y	N856K	Q954H	N969K	L981F	I1081V	
BA.1	3265	1454	A67V	H69-	V70-	T95I	G142D	V143-	Y144-	Y145-	N211I	L212-	+214EPE	G339D	S371L	S373P	S375F	K417N	N440K	G446S	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	N764K	D796Y	N856K	Q954H	N969K	L981F		
*B.1.1.529	25	5	A67V			T95I								G339D	S371L	S373P	S375F	K417N	N440K	G446S	S477N	T478K	E484A	Q493R	G496S	Q498R	N501Y	Y505H	T547K	D614G	H655Y	N679K	P681H	N764K	D796Y	N856K	Q954H	N969K	L981F		

Note: The 'EPE' insertion at 214 (+214EPE) comes and goes in conjunction with multiple distinct Spike mutations, as well as within the baseline form. This recurrent pattern in association with multiple common mutations suggests that the apparent loss of the insertion may be a sequencing artifact.

\*Loss of the insertion coupled with regional reversions to ancestral amino acids within a local region of Spike may be an indication of recombination.

# Omicron variants of interest:

Amino acids that reverted to ancestral are indicated by a blank. Red indicates an amino acid altering mutation.

Original counts on the left are from 12/23/2021 an alignment of complete Spike sequences; about 13% of the total Omicron Spike sequence were complete.

Count updates are from the 12/26/2021 GISAID search interface and includes all Spike sequences with the amino acid substitution specified.

## Counts

Lineage Form Spike form as mutation string relative to the Wuhan reference sequence.

### Baseline Omicron, BA.1:

BA.1 3265 1454 A67V H69- V70- T95I G142D V143- Y144- Y145- N211I L212- +214EPE G339D S371L S373P S375F K417N N440K G446S S477N T478K E484A Q493R G496S Q498R N501Y Y505H T547K D614G H655Y N679K P681H N764K D796Y N856K Q954H N969K L981F

Spike **A701V** is found in 11,015 of 60,083 Omicron sequences, ~18% of total, 12/26/2021.

BA.1 3265 95 A67V H69- V70- T95I G142D V143- Y144- Y145- N211I L212- +214EPE G339D S371L S373P S375F K417N N440K G446S S477N T478K E484A Q493R G496S Q498R N501Y Y505H T547K D614G H655Y N679K P681H **A701V** N764K D796Y N856K Q954H N969K L981F

BA.1 3265 36 A67V H69- V70- T95I G142D V143- Y144- Y145- N211I L212- G339D S371L S373P S375F K417N N440K G446S S477N T478K E484A Q493R G496S Q498R N501Y Y505H T547K D614G H655Y N679K P681H **A701V** N764K D796Y N856K Q954H N969K L981F

Spike **R346K** is found in 7,466 of 60,083 Omicron sequences ~12% of total, 12/26/2021.

BA.1 3265 229 A67V H69- V70- T95I G142D V143- Y144- Y145- N211I L212- +214EPE G339D **R346K** S371L S373P S375F K417N N440K G446S S477N T478K E484A Q493R G496S Q498R N501Y Y505H T547K D614G H655Y N679K P681H N764K D796Y N856K Q954H N969K L981F

BA.1 3265 23 A67V H69- V70- T95I G142D V143- Y144- Y145- N211I L212- G339D **R346K** S371L S373P S375F K417N N440K G446S S477N T478K E484A Q493R G496S Q498R N501Y Y505H T547K D614G H655Y N679K P681H N764K D796Y N856K Q954H N969K L981F

Spike **L452R** is found in 705 of 60,083 Omicron sequences, ~1% of total, 12/26/2021. (This sequence may be a laboratory artifact, this has yet to be resolved).

BA.1 3265 137 A67V H69- V70- T95I G142D V143- Y144- Y145- N211I L212- +214EPE G339D S371L S373P S375F **L452R** S477N T478K E484A Q493R G496S Q498R N501Y Y505H T547K D614G H655Y N679K P681H N764K D796Y N856K Q954H N969K L981F

BA.1 3265 13 A67V H69- V70- T95I G142D V143- Y144- Y145- N211I L212- +214EPE G339D S371L S373P S375F **L452R** S477N T478K E484A Q493R G496S Q498R N501Y Y505H T547K D614G H655Y N679K P681H D796Y N856K Q954H N969K L981F

BA.1 3265 11 A67V H69- V70- T95I G142D V143- Y144- Y145- N211I L212- +214EPE G339D S371L S373P S375F **L452X** S477N T478K E484A Q493R G496S Q498R N501Y Y505H T547K D614G H655Y N679K P681H N764K D796Y N856K Q954H N969K L981F

**The 3 common Omicron variants noted above (A701V, R346K or L452R)** are not found to be consistently increasing relative to baseline Omicron in countries where they are cocirculating, and both forms are sampled and sequenced at least 10 times each (see slide. This suggests their presence may be due to founder effects as Omicron spread.

**The very distinctive BA.2 and BA.3 continue to be very rare, update from 12/26/2021 GISAID search interface:**

BA.2 is found 55 times among 60,083 Omicron sequences, 0.03%

BA.3 is found 17 times among 60,083 Omicron sequences, 0.09%



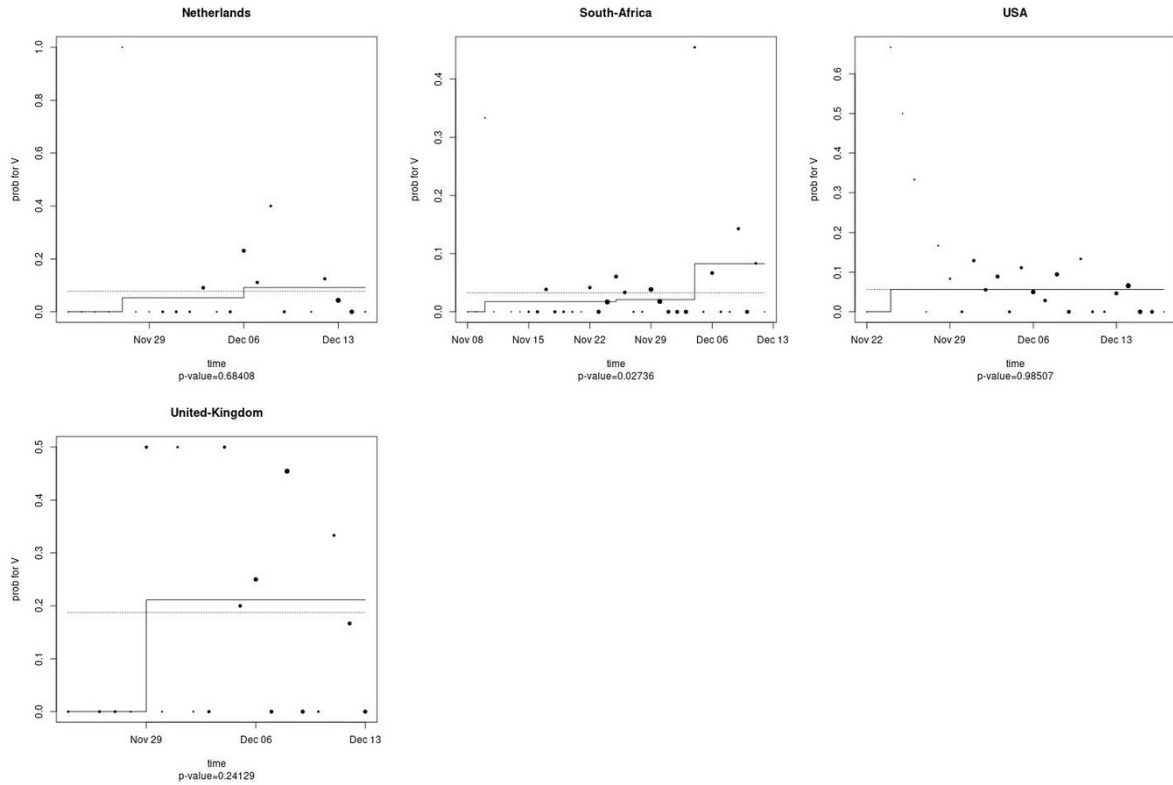
# Isotonic regression showing that the frequency of mutant forms relative to other Omicron sequences is not increasing in countries where they were found >10 times each.



## A701V is not consistently increasing sampled relative to other Omicron variants

Country level

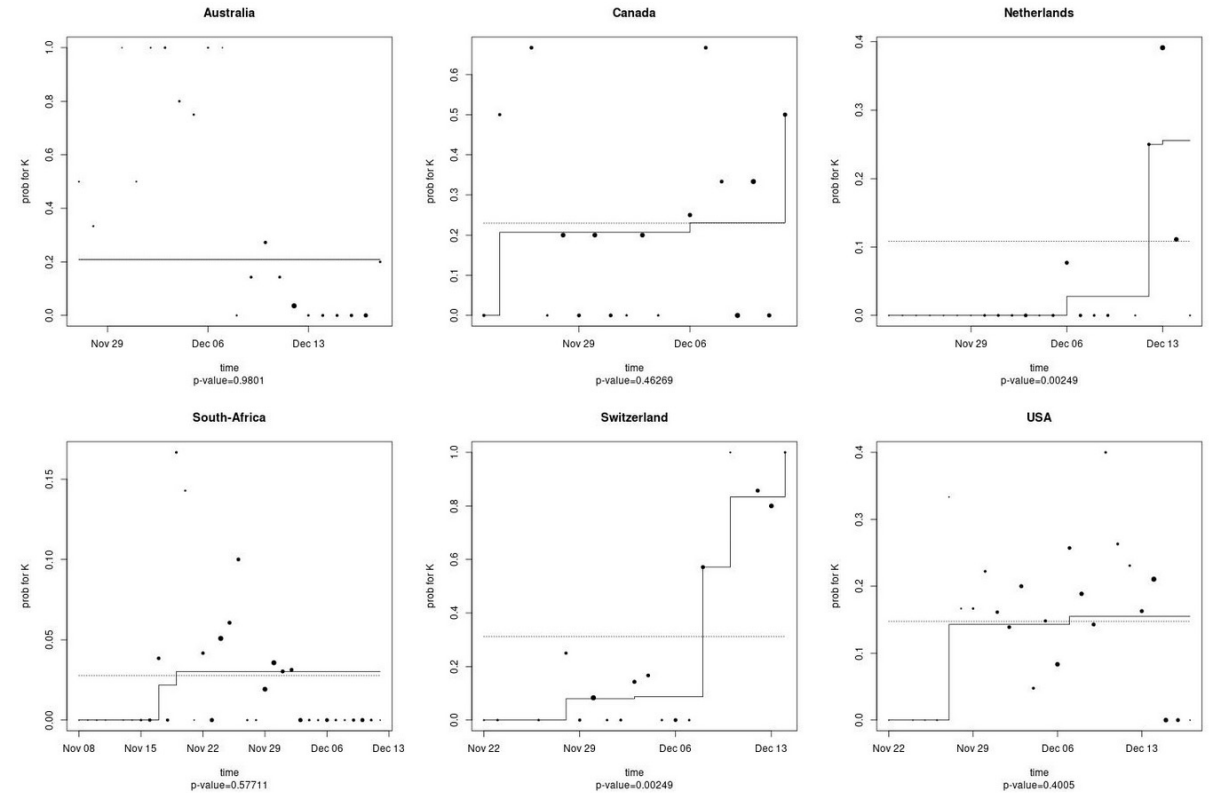
	# V	# Others	total	# days	time window	p-val
Netherlands	10	119	129	22	22	0.68408
South-Africa	21	627	648	34	34	0.02736
USA	38	633	671	25	25	0.98507
United-Kingdom	15	65	80	19	19	0.24129



## R346K is not consistently increasing sampled relative to other Omicron variants

Country level

	# K	# Others	total	# days	time window	p-val
Australia	29	110	139	21	21	0.9801
Canada	14	47	61	18	19	0.46269
Netherlands	14	115	129	22	22	0.00249
South-Africa	18	630	648	34	34	0.57711
Switzerland	25	55	80	18	22	0.00249
USA	99	572	671	25	25	0.4005



How to read: each dot is the sample for a given day, the size of the dot reflects the sample size on that day. All countries where the specified mutation was found >10 times are shown. The Y axis indicates the proportion of the Omicron sequences sampled that carried the mutation on a given day. The p-value is a one-sided test for increasing frequency of the mutation over time. Analyses were done using the isotonic regression tool at [cov.lanl.gov](http://cov.lanl.gov), GISAID sample date: 12/24/2021; this includes only QC'd near complete Omicron sequences.

L452R may be increasing sampled relative to other Omicron variants in the UK, at least among the QC controlled sequences.

Geographically, it is only commonly sampled in Houston County, Texas, and in sequences from the UK.

L452R is often found in conjunction with K417 N440 G446 each being ancestral, rather than Omicron's typical K417N N440K G446S.

This pattern is suggestive of an Omicron recombination with Delta, Delta found in the stretch spanning the region encoding Spike 417-452.

*A recombinant sequence can either be the result of an in vitro artifact, due to cross-contamination or primer issues, or can happen naturally.*

This precise form of the Spike has been found in multiple laboratories (USA: Houston, Ohio, Arizona, Pennsylvania, England, Scotland, Australia).

#### Country level

	# R	# Others	total	# days	time window	p-val
USA	66	605	671	25	25	0.39303
United-Kingdom	44	36	80	19	19	0.00249

