

New analyses regarding Spike 452 mutations in BA.2 update 2022/04/16

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- There are three L452 mutations common in a BA.2 backbone that appear to be increasing in frequencies : Q, M and R. Representative of each of these are now included in our spreadsheet.
- L452Q in BA.2 backbone is coming quickly up in frequency in the US, with New York at the lead.
 - BA.2 L452Q is most often found in combination with S704L in the Pango lineage BA.2.12.1. This lineage is increasing relatively quickly in New York, as well as in many other states and in Canada.
- Many BA.4 and BA.5 sequences in GISAID are only partial in Spike, and carry with long strings of Ns, making a definitive most common form of Spike difficult to resolve. The most common form is shared between sequences with BA.4 and BA.5, carries L452R, and is included here, but the situation is in flux.
 - There are also subset of L452R carrying Spikes in a BA.2 backbone that are distinct from the BA.4 and BA.5 lineages.
- **Recombination:**
 - The Pango lineages beginning with X indicate recombinants.
 - We have been tracking one since February, that is now designated XD by the Pango group. It is still very rare, but an interesting form with a section of Delta in the Spike NTD in a BA.1 backbone.
 - Most of the Pango X-recombinant lineages involving Omicron have breakpoints outside of Spike, so are not included here; e.g. XE has a baseline BA.2 spike, and XF has a baseline line BA.1 Spike. We are tracking several other possible recombinant sequences within Spike that might be natural or artificial in origin that.



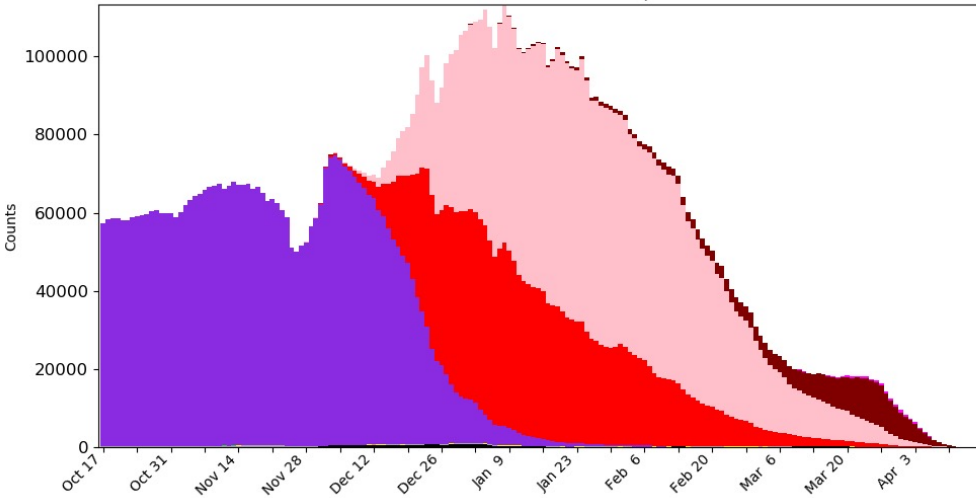
LA-UR-21-28226

Thanks to Anna Niewiadomska for helpful discussion and for providing some of her early L452-mutation alignments, helping define these new forms.

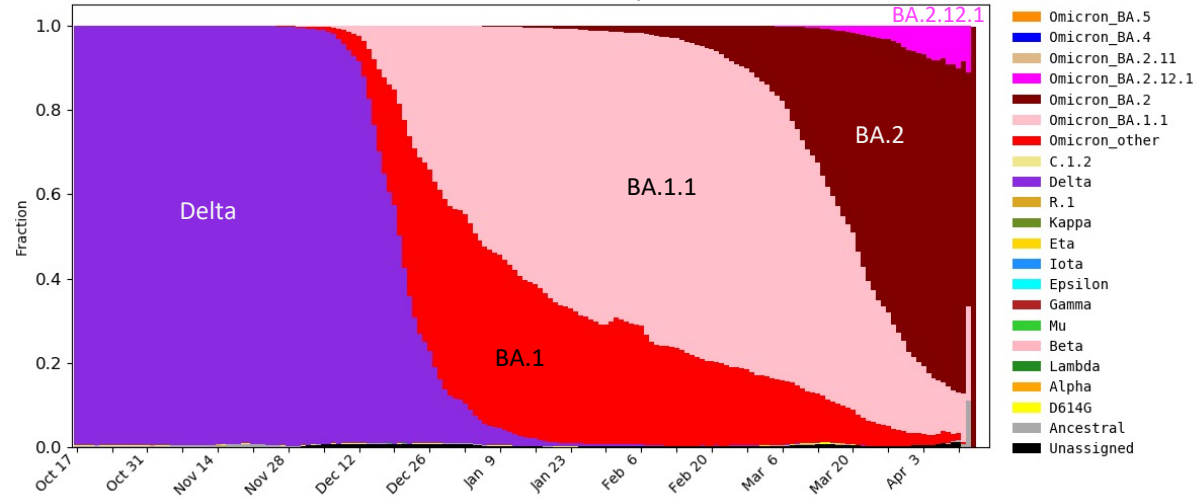


BA.2.12.1 sampling is increasing in N. America, BA.4 and BA.5 in Africa

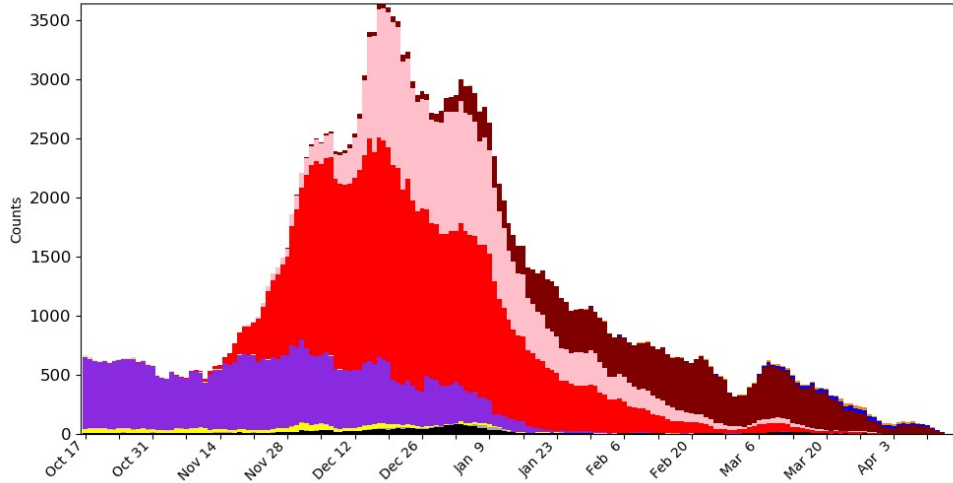
North-America: 1567846 sequences



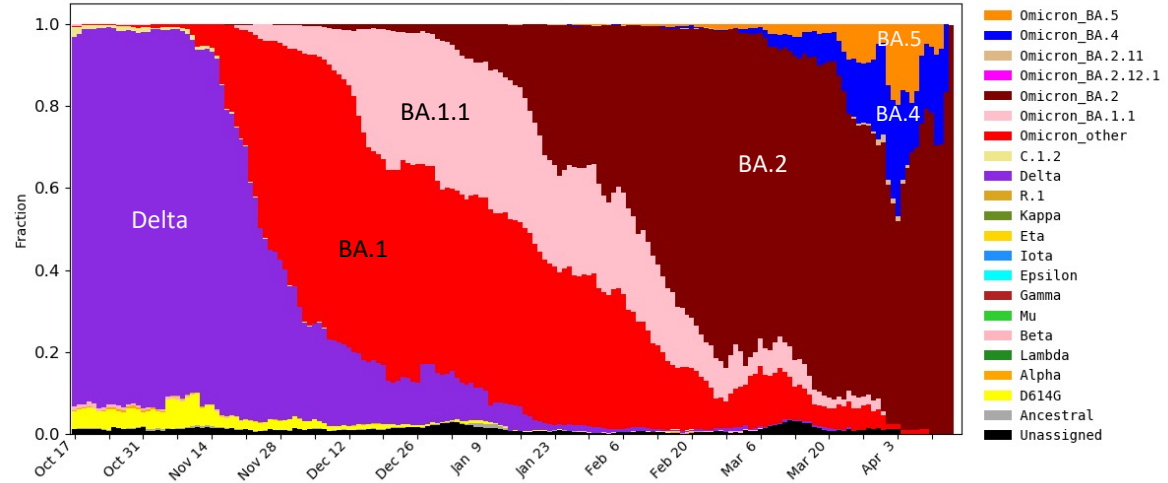
North-America: 1567846 sequences



Africa: 30777 sequences



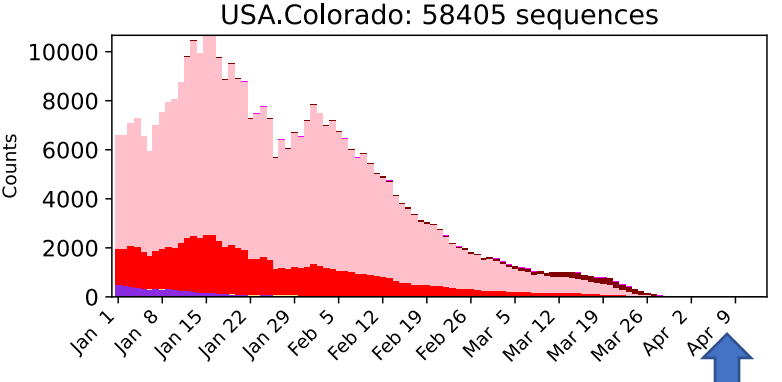
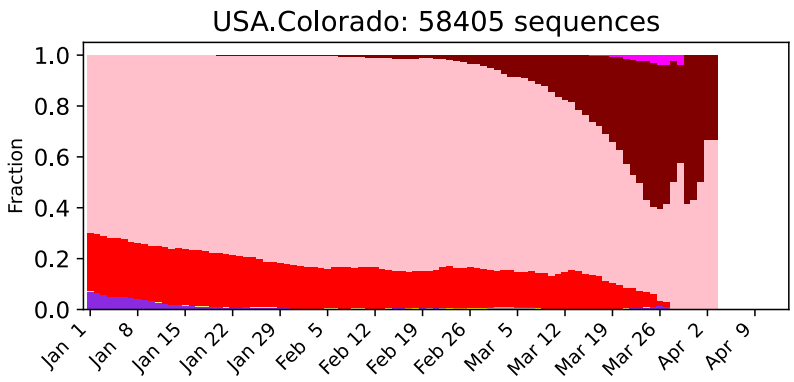
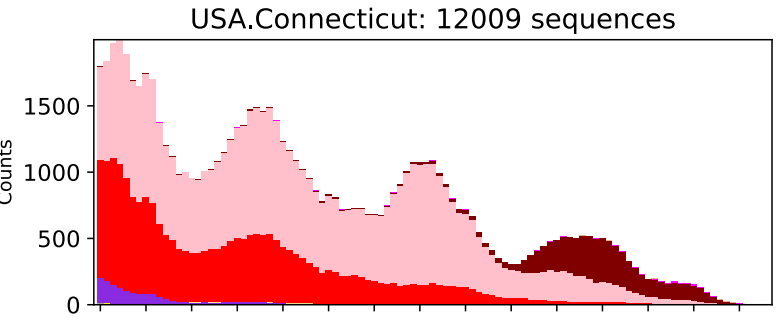
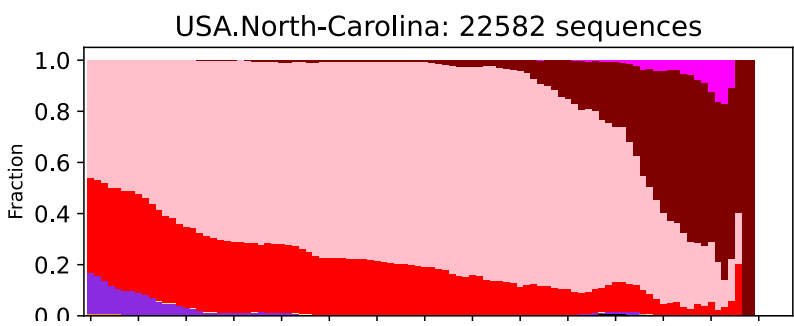
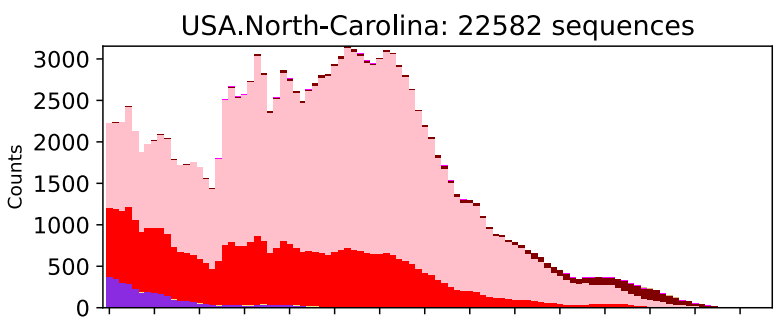
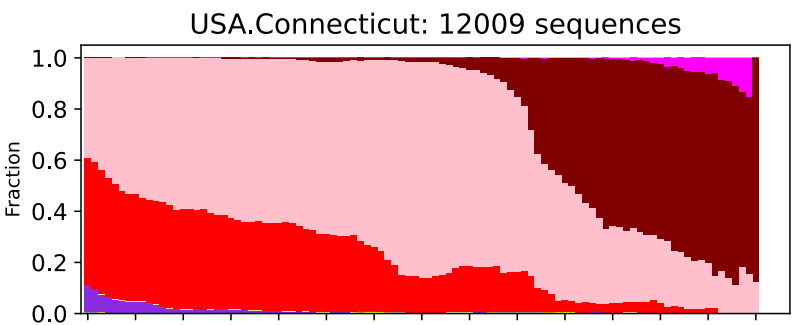
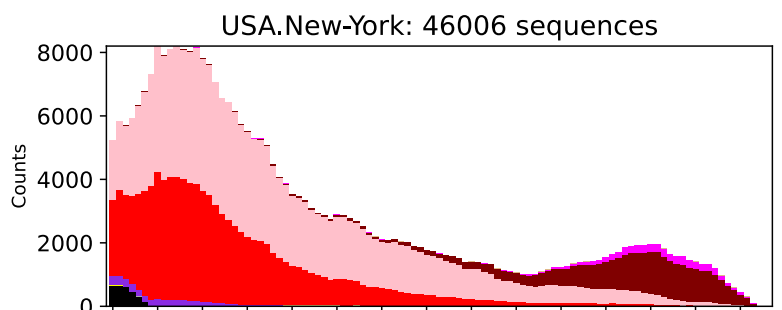
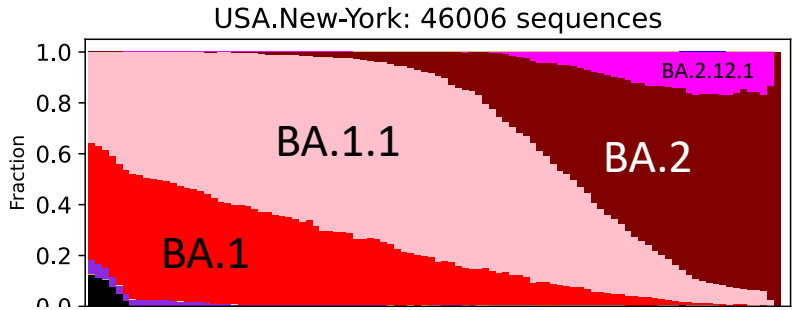
Africa: 30777 sequences



BA.2.12.1 is coming up relative to BA.2 in multiple US states, and this Pango lineages tracks closely with Spike BA.2 + L452Q + S704L.

- Omicron_BA.5
- Omicron_BA.4
- Omicron_BA.2.11
- Omicron_BA.2.12.1
- Omicron_BA.2
- Omicron_BA.1.1
- Omicron
- C.1.2
- Delta
- R.1
- Kappa
- Eta
- Iota
- Epsilon
- Gamma
- Mu
- Beta
- Lambda
- Alpha
- D614G
- Ancestral
- None

Tracking Frequencies of Pango Lineage names from 1/13/2022 GISAID Data.



Sparse sampling in recent timepoints



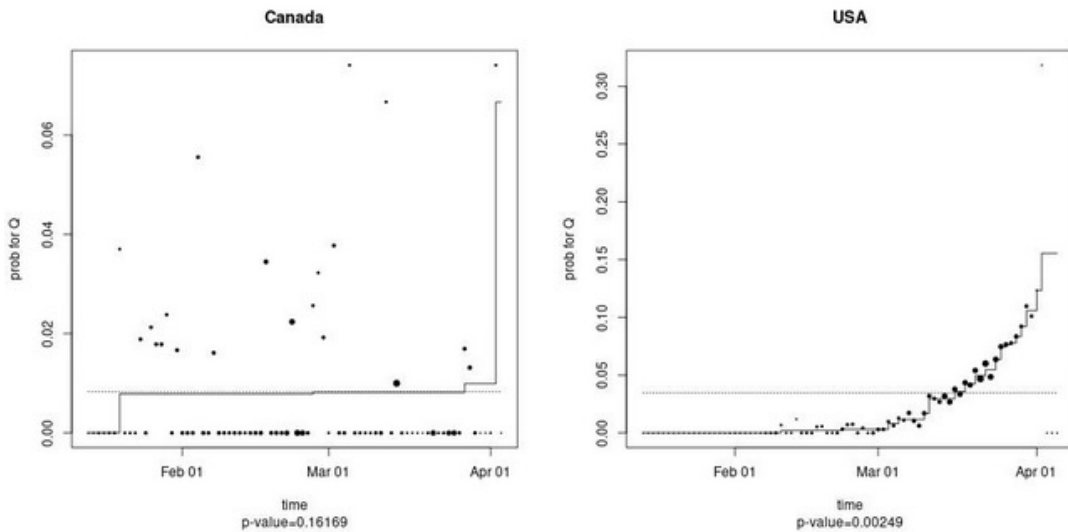
BA.2 + L452Q is increasing relative to other BA.2's in GISAID – mostly BA.1.12.1

L452Q is increasing in the US, but was first observed in Canada
Where it is still at low frequency, < 1%

Only two countries have BA.2 with 452Q sampled more than >10 times. The frequency of 452Q among BA.2s over time is graphed for each day sampled. The size of the circle reflects sampling size on that day. Low p-values indicate it is significantly increasing over time.

Country level

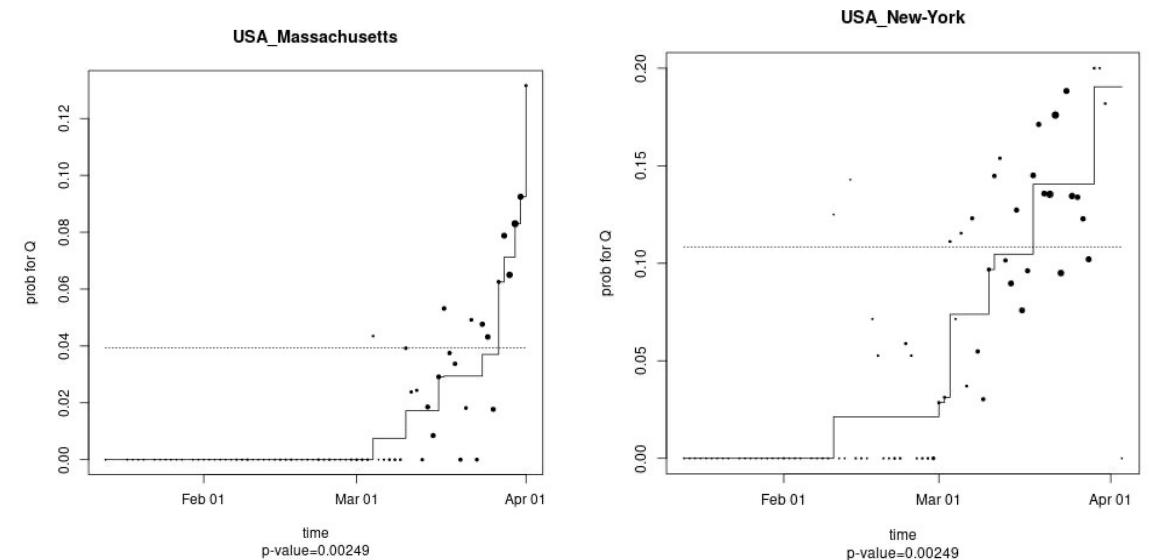
	# Q	# Others	Total	Q/Total (%)	# days	Time window	p-val
Canada	32	3837	3869	0.83	80	79	0.16169
USA	814	22591	23405	3.48	82	81	0.00249



Summary of all states/provinces where L452Q was found >10 times, the graphs show the 2 states L452Q was most sampled

State level

	# Q	# Others	Total	Q/Total (%)	# days	Time window	p-val
Canada_Alberta	12	905	917	1.31	62	62	0.32587
Canada_British-Columbia	11	1360	1371	0.80	43	42	0.57214
USA_California	13	3010	3023	0.43	81	80	0.00249
USA_Colorado	11	604	615	1.79	58	68	0.00498
USA_Connecticut	20	488	508	3.94	58	75	0.00249
USA_Florida	21	1333	1354	1.55	64	70	0.00498
USA_Illinois	15	980	995	1.51	63	76	0.00498
USA_Massachusetts	111	2712	2823	3.93	73	77	0.00249
USA_New-Hampshire	12	90	102	11.76	34	70	0.03483
USA_New-Jersey	59	1697	1756	3.36	64	69	0.00249
USA_New-York	365	3002	3367	10.84	76	79	0.00249
USA_North-Carolina	15	309	324	4.63	59	75	0.00498
USA_Pennsylvania	39	688	727	5.36	59	67	0.00249
USA_Vermont	61	326	387	15.76	33	66	0.00249
USA_Wisconsin	18	457	475	3.79	66	74	0.00249



Pango lineage BA.2.12.1 is increasing, as it carries Spike BA.2+ (L452Q + S704L)

<https://github.com/cov-lineages/pango-designation/issues/499>

Isotonic Regression shows an increasing frequency of Pango lineage BA.2.12.1 relative to BA.2 in the US.

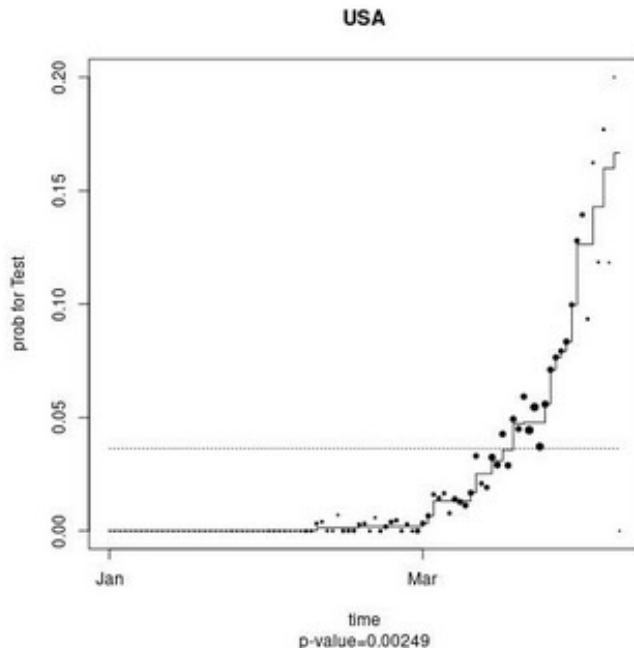
The USA was the only country where BA.2.12.1 was found more than 10 times, based on 2022/04/14 data. This shows fraction of BA.2.12.1 among BA.2s plotted by day since 2022/01/01 in the US – it is approaching 15%.



Country level

There were 1,379 sequences that matched your search term, the following summarizes the form in locations where it was found more than 10 times.

	# Test	# Others	Total	Test/Total (%)	# days	Time window	p-val
USA	1366	36207	37573	3.64	97	96	0.00249



Note: The number of BA.2.12.1 sequences is higher than the the number of samples for L452Q on the previous slide because Pango lineage data was just from the names, and so all GISAID data could be used.

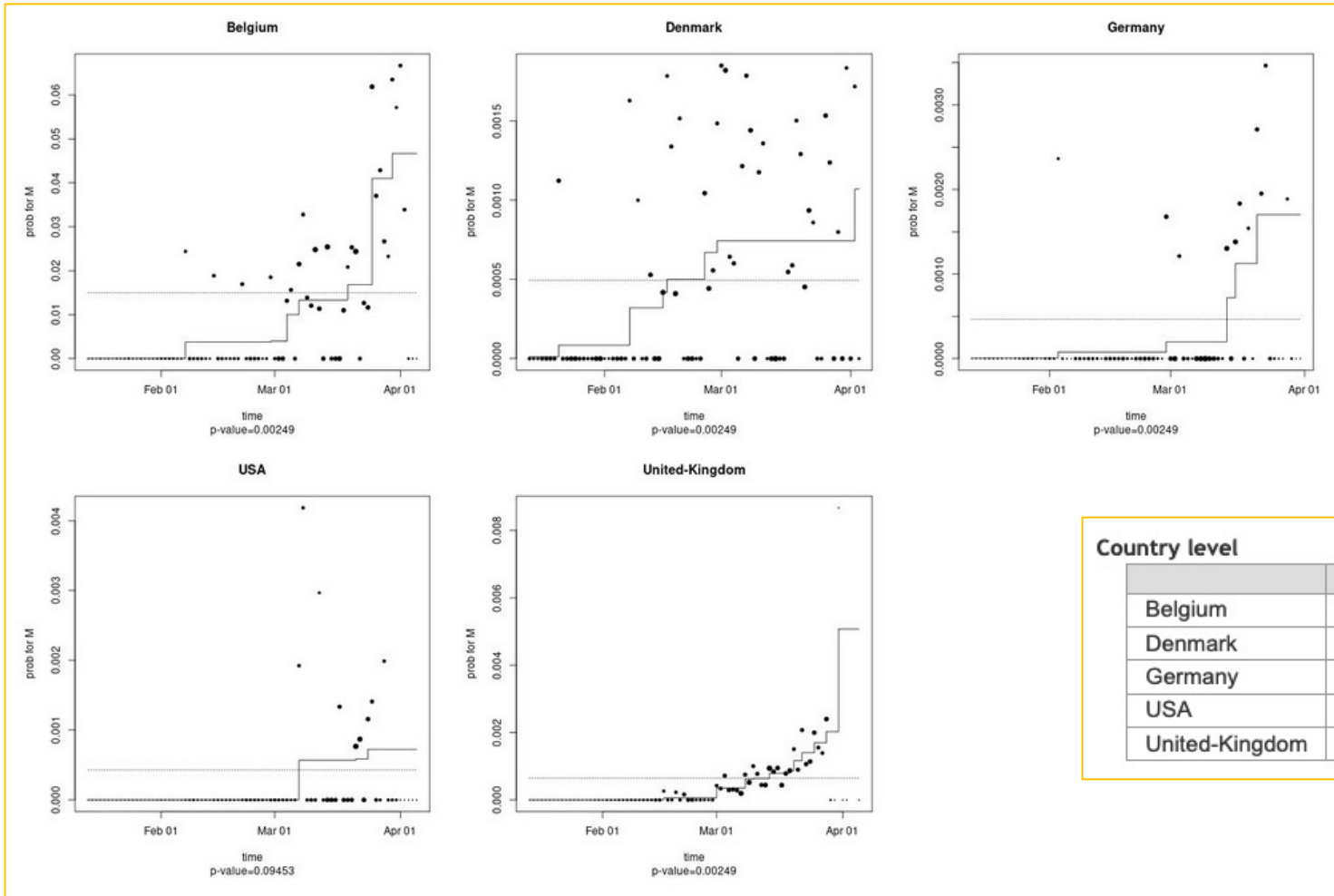
The sequence-based analysis on the previous page filters out incomplete data, and so the number of counts is smaller.

The trajectory of increase is consistent between the two analyses.

Spike L452M is still very rare, but is also increasing relative other BA.2's in GISAID:



All countries L452M was found more than 10 times, fraction of L452M Spikes among BA.2s plotted by day since 2022/01/01.



L452M is increasing, and recently found in ~ 5% of the samples in Belgium, but is <1% in other countries.

Country level

	# M	# Others	Total	M/Total (%)	# days	Time window	p-val
Belgium	55	3608	3663	1.50	82	81	0.00249
Denmark	61	123412	123473	0.05	80	79	0.00249
Germany	20	43196	43216	0.05	77	76	0.00249
USA	10	23395	23405	0.04	82	81	0.09453
United-Kingdom	192	298461	298653	0.06	80	81	0.00249

Based on Isotonic Regression, 4/14/2022: L452M frequency within BA.2

L452R is also still very rare relative to all other BA.2's in GISAID, but is also increasing, most notably in South Africa.

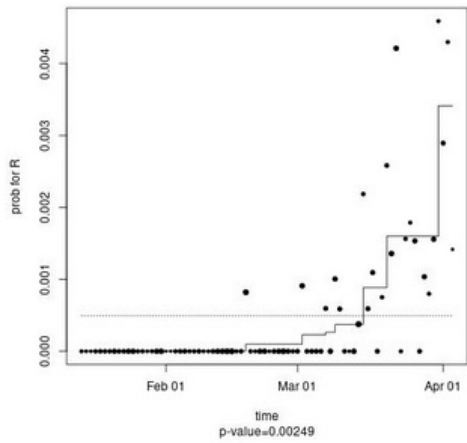
L452R is associated with Pango lineage BA.4 and BA.5, but also with other lineages a simpler BA.2 backdrop.



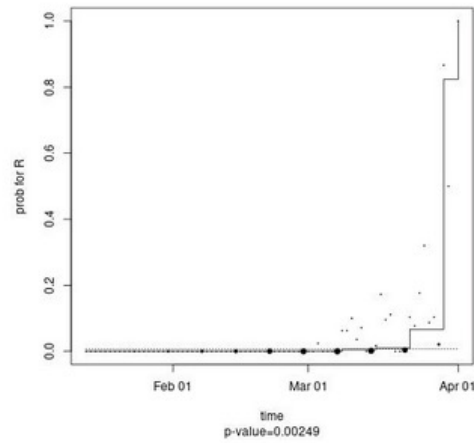
Country level

	# R	# Others	Total	R/Total (%)	# days	Time window	p-val
Denmark	61	123412	123473	0.05	80	79	0.00249
France	81	12584	12665	0.64	77	77	0.00249
South-Africa	61	1214	1275	4.78	76	78	0.00249
United-Kingdom	25	298628	298653	0.01	80	81	0.00746

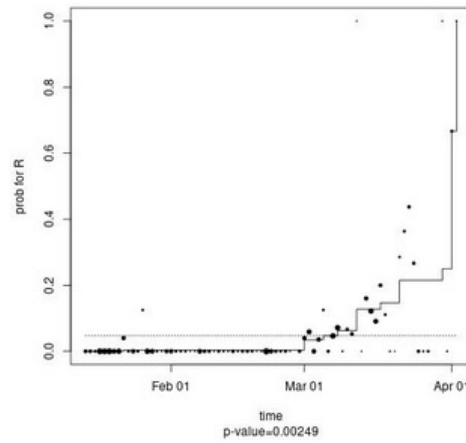
Denmark



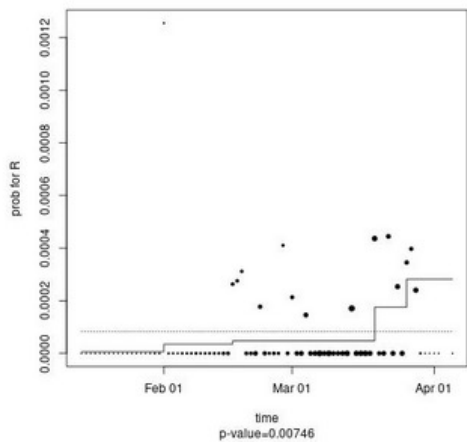
France



South-Africa



United-Kingdom



All countries where L452R is found more than 10 times, including BA.4 and BA.5 in South Africa

Isotonic Regression, 4/14/2022: L452R frequency within BA.2

Pango lineage BA.4 and BA.5 Spike forms



The Spike forms in these lineages are complex lineages, and many of the sequences have stretches of N.

The consensus form of Spike is the same in both (Q493_ is the ancestral form at 493):

BA.2 + H69-,V70,L452R,F486V,Q493_

We have included this form to represent both BA.4 and BA.5 for now, but the situation is still in flux.

Pango Lineage Form Form
Lineage Count Count Pct HD [Form as mutation string]

BA.4

Lineage	Count	Count	Pct	HD	Form as mutation string
BA.2 backbone					[T19I,L24-,P25-,P26-,A27S, G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K, S477N,T478K,E484A, Q493R, Q498R,N501Y,Y505H,D614G,H655Y, N679K,P681H,N764K,D796Y,Q954H,N969K]
BA.4	49	13	26.5%	0	[V3G,T19I,L24-,P25-,P26-,A27S,H69-,V70-,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452R,S477N,T478K,E484A,F486V, Q498R,N501Y,Y505H,D614G,H655Y, N679K,P681H,N764K,D796Y,Q954H,N969K]
BA.4	49	12	24.5%	2	[T19I,L24-,P25-,P26-,A27S,H69-,V70-,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452R,S477N,T478K,E484A,F486V, Q498R,N501Y,Y505H,D614G,H655Y,N658S,N679K,P681H,N764K,D796Y,Q954H,N969K]
BA.4	49	9	18.4%	1	[T19I,L24-,P25-,P26-,A27S,H69-,V70-,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452R,S477N,T478K,E484A,F486V, Q498R,N501Y,Y505H,D614G,H655Y, N679K,P681H,N764K,D796Y,Q954H,N969K] (consensus)
BA.4	49	4	8.2%	2	[V3G,T19I,L24-,P25-,P26-,A27S, G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452R,S477N,T478K,E484A,F486V, Q498R,N501Y,Y505H,D614G,H655Y, N679K,P681H,N764K,D796Y,Q954H,N969K]
BA.4	49	3	6.1%	1	[V3G,T19I,L24-,P25-,P26-,A27S,H69-,V70-,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452R,S477N,T478K,E484A,F486V, Q498R,N501Y,Y505H,D614G,H655Y,I670V,N679K,P681H,N764K,D796Y,Q954H,N969K]

There were 148 BA.4 sequences in the unfiltered set based on Pango designations, but only 49 had fully intact spikes. Overall V3G was present in about 1/3 of the sequences, and H69 V79 with no deletion was found 16 times, about 10%

BA.5

Lineage	Count	Count	Pct	HD	Form as mutation string
BA.2 backbone					[T19I,L24-,P25-,P26-,A27S, G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K, S477N,T478K,E484A, Q493R, Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K]
BA.5	39	17	43.6%	0	[T19I,L24-,P25-,P26-,A27S,H69-,V70-,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452R,S477N,T478K,E484A,F486V, Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K] (consensus)
BA.5	39	5	12.8%	2	[T19I,L24-,P25-,P26-,A27S,H69-,V70-,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N, K417N,N440K,L452R,S477N,T478K,E484A,F486V, Q498R,N501Y,Y505H,D614G, N679K,P681H,N764K,D796Y,Q954H,N969K]
BA.5	39	2	5.1%	1	[T19I,L24-,P25-,P26-,A27S,H69-,V70-,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N, K417N,N440K,L452R,S477N,T478K,E484A,F486V, Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K]
BA.5	39	2	5.1%	1	[T19I,L24-,P25-,P26-,A27S,H69-,V70-,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452R,S477N,T478K,E484A,F486V, Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K,A1020S]

There were 165 BA.5 Spike sequences in the unfiltered set just based on Pango designations. Only 39 had fully sequenced Spike, most had many "N"s". Among the full set of 165 sequences: The deletion at 69-70 was present in 64, but more often absent and ancestral, in 93, and X in 8 – so it is most often Ancestral, particularly in Ireland and India. L452R was absent and ancestral in 27, present in 58, and X in in 79. (present in 68%) The variants with L452 ancestral tended to be in the same sequences with 69-70 ancestral. The Q493_ ancestral and F486V were not consistent either.

Spike amino acid mutation lists for BA.2 variants that carry L452 Q, M or R

The most common form of BA.2 variants with L452Q includes S704L

BA.2	Most common form	[T19I,L24S,P25-,P26-,A27-,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K, S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K] (consensus)	
BA.2	400947	656 0.2%	2 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452Q,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,S704L,N764K,D796Y,Q954H,N969K]
BA.2	400947	76 0.0%	3 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452Q,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,S704L,N764K,D796Y,A879V,Q954H,N969K]
BA.2	400947	14 0.0%	3 [T19I,L24-,P25-,P26-,A27S,G142D,N164K,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452Q,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,S704L,N764K,D796Y,Q954H,N969K]
BA.2	400947	12 0.0%	1 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452Q,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K]
BA.2	495585	9 0.0%	3 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N, L452Q,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,S704L,N764K,D796Y,Q954H,N969K]
BA.2	495585	3 0.0%	3 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,K417N,N440K, L452Q,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,S704L,N764K,D796Y,Q954H,N969K]
BA.2	495585	3 0.0%	3 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452Q,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681R,S704L,N764K,D796Y,Q954H,N969K]
BA.2	495585	2 0.0%	3 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452Q,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,S704L,N764K,D796Y,Q954H,N969K]
BA.2	495585	2 0.0%	4 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,P217T,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452Q,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,S704L,N764K,D796Y,A879V,Q954H,N969K]
BA.2	495585	2 0.0%	3 [L5F,T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452Q,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,S704L,N764K,D796Y,Q954H,N969K]
BA.2	495585	2 0.0%	3 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452Q,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,T547K,D614G,H655Y,N679K,P681H,S704L,N764K,D796Y,Q954H,N969K]
BA.2	495585	2 0.0%	6 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452Q,S477N,T478K,E484A,D614G,H655Y,N679K,P681H,S704L,N764K,D796Y,Q954H,N969K]
BA.2	495585	2 0.0%	4 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,L452Q,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,S704L,N764K,D796Y,A879V,Q954H,N969K]
BA.2.3	43540	41 0.1%	2 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452Q,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,S704L,N764K,D796Y,Q954H,N969K]
BA.2.3	43540	2 0.0%	1 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452Q,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K]
BA.2.3	43540	2 0.0%	2 [T19I,L24-,P25-,P26-,A27S,G142D,V213E,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452Q,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K]
BA.2.2	979	1 0.1%	1 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452Q,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K,I1221T]

The most common form of BA.2 variants with L452M includes just L452M

BA.2	Most common form	[T19I,L24S,P25-,P26-,A27-,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K, S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K] (consensus)	
BA.2	495585	241 0.0%	1 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452M,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K]
BA.2	495585	33 0.0%	2 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452M,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,D936Y,Q954H,N969K]
BA.2	495585	14 0.0%	5 [T19I, G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452M,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K]
BA.2	495585	9 0.0%	2 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452M,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K,G1099D]
BA.2	495585	2 0.0%	2 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452M,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,Q787H,D796Y,Q954H,N969K]
BA.2.3	43540	2 0.0%	1 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452M,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K]
BA.2.1	9480	5 0.1%	1 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452M,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K]

The most common form of BA.2 variants with L452R

BA.2	Most common form	[T19I,L24S,P25-,P26-,A27-,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K, S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K] (consensus)	
BA.2	495585	137 0.0%	1 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452R,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K]
BA.2	495585	10 0.0%	5 [T19I, G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452R,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K]
BA.2	495585	3 0.0%	2 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452R,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,I818V,Q954H,N969K]
BA.2	495585	2 0.0%	2 [T19I,L24-,P25-,P26-,A27S,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452R,S477N,T478K,E484A,Q493R,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,S689I,N764K,D796Y,Q954H,N969K]

Spikes also include L452R, and are associated with BA.4 and BA.5

BA.2	495585	15 0.0%	5 [T19I,L24-,P25-,P26-,A27S,H69-,V70-,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452R,S477N,T478K,E484A,F486V, Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K]
BA.2	495585	5 0.0%	7 [T19I,L24-,P25-,P26-,A27S,H69-,V70-,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N, K417N,N440K,L452R,S477N,T478K,E484A,F486V, Q498R,N501Y,Y505H,D614G,N679K,P681H,N764K,D796Y,Q954H,N969K]
BA.2	495585	3 0.0%	6 [T19I,L24-,P25-,P26-,A27S,H69-,V70-,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452R,S477N,T478K,E484A,F486V, Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K]
BA.2	495585	2 0.0%	6 [V3G,T19I,L24-,P25-,P26-,A27S,H69-,V70-,G142D,V213G,G339D,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,L452R,S477N,T478K,E484A,F486V, Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K]

This includes all Spike BA.2 452 mutational forms found more than twice, their counts, and the counts of the Pango lineage designated at the time of sampling. This data collected was just prior to the BA.2 Pango sublineage names being introduced into GISAID. These counts are based on complete Spike sequences in GISAID, excluding Spikes with strings of N's

Pango lineages related to BA.2 that have L452 mutations and the counts in GISAID on 2022/04/14:

	<u>Lineage</u>	<u>L452M</u>	<u>L452Q</u>	<u>L452R</u>
BA.2.12:	66,606	18	113	12
BA.2.12.1:	1,744	0	1,704	0
BA.2.9	331,807	493	4	69
BA.2.11	443	0	0	198
BA.4	192	0	0	153
BA.5*	168	0	0	60*

*Spike L452R is in about 2/3 of BA.5 sequences with the 452 codon sequenced, and about 1/3 ancestral L452. Most often there are stretches of N's spanning the bases in this codon.