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U.S. Centers for Disease Control and Prevention
National Center for Immunization and Respiratory Diseases

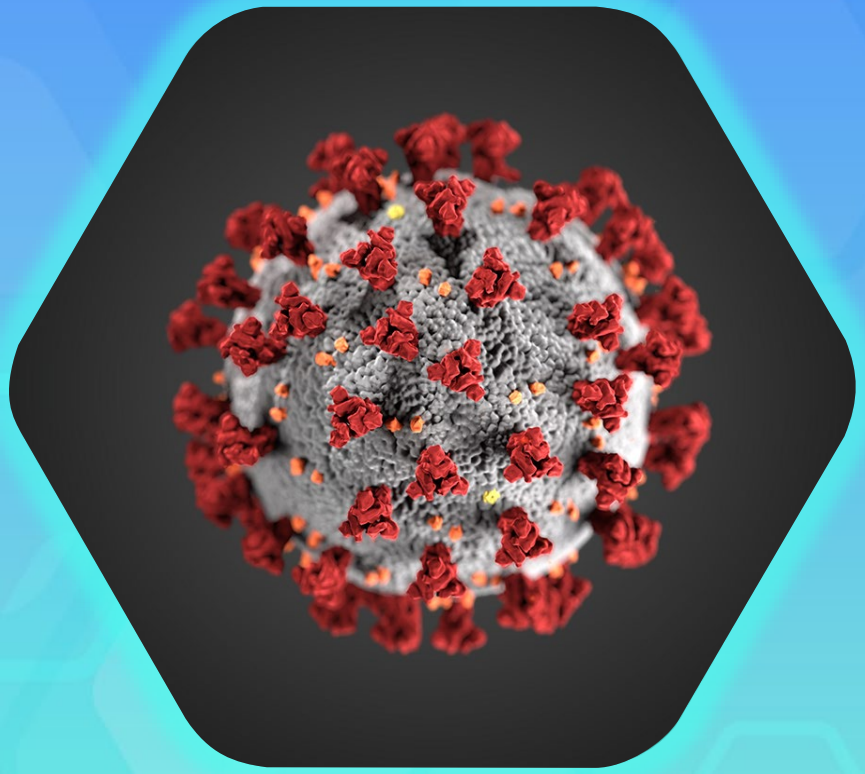
Update on Current Epidemiology of COVID-19 and SARS-CoV-2 genomics

Natalie J. Thornburg, PhD

Chief, Laboratory Branch

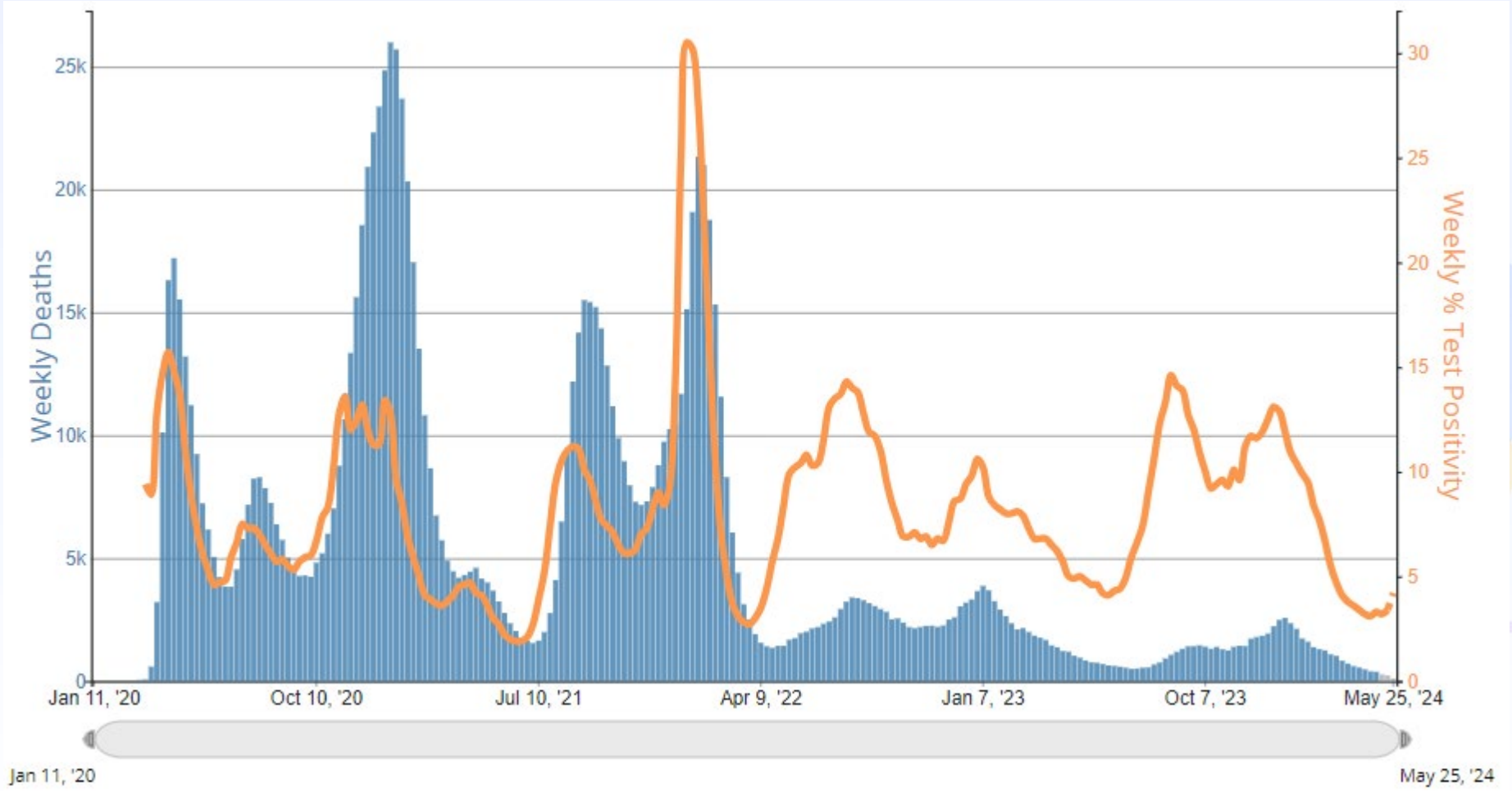
Coronaviruses and Other Respiratory Viruses Division

Current epidemiology of COVID-19



CDC | **NCIRD** | Coronavirus and Other Respiratory Viruses Division

Weekly trends in COVID-19 deaths and percent positivity, United States March 14, 2020- May 25, 2024

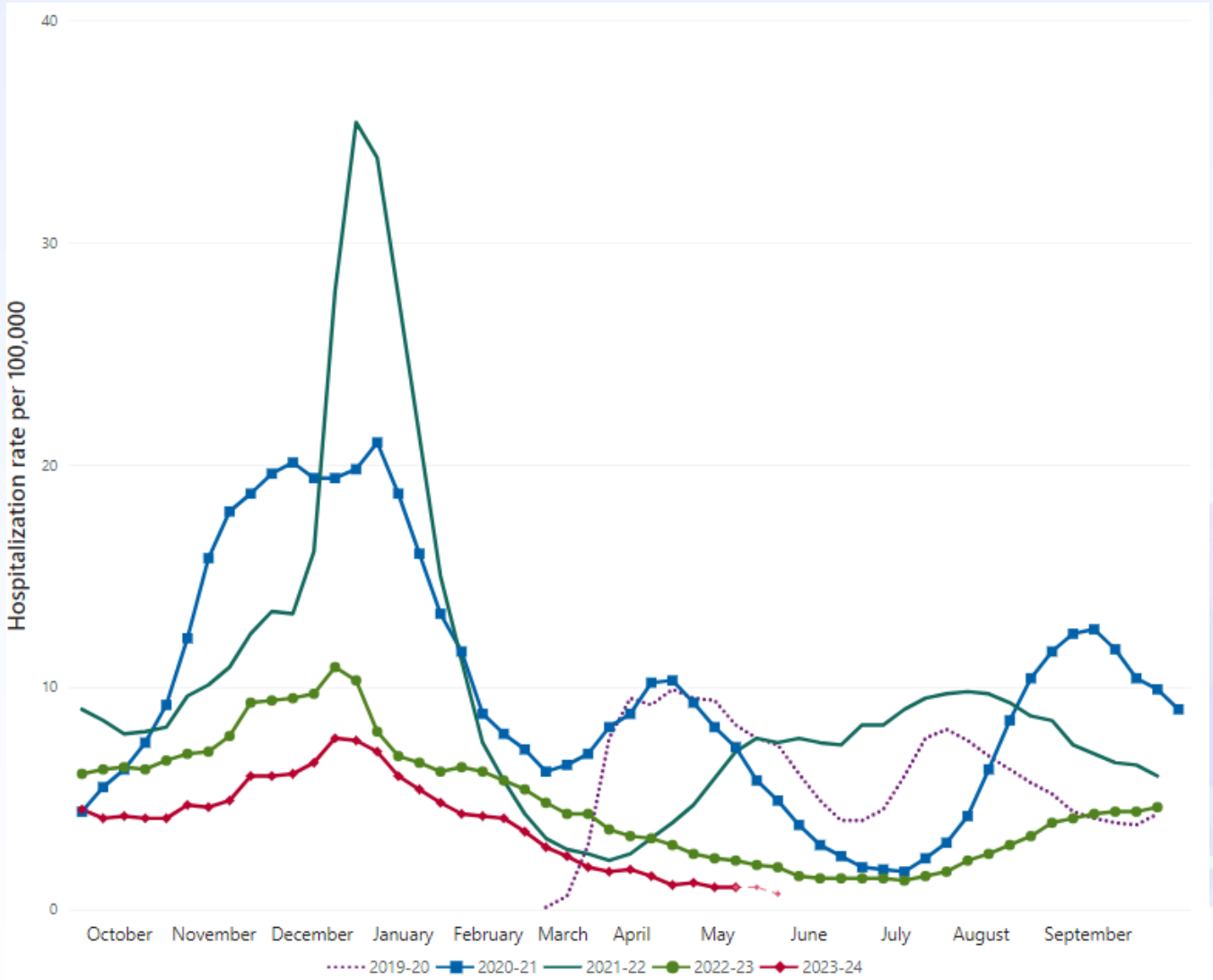


Source: National Center for Health Statistics (NCHS) National Vital Statistics Surveillance (NVSS) and National Respiratory and Enteric Virus Surveillance System

CDC COVID Data Tracker: Trends by Geographic Area

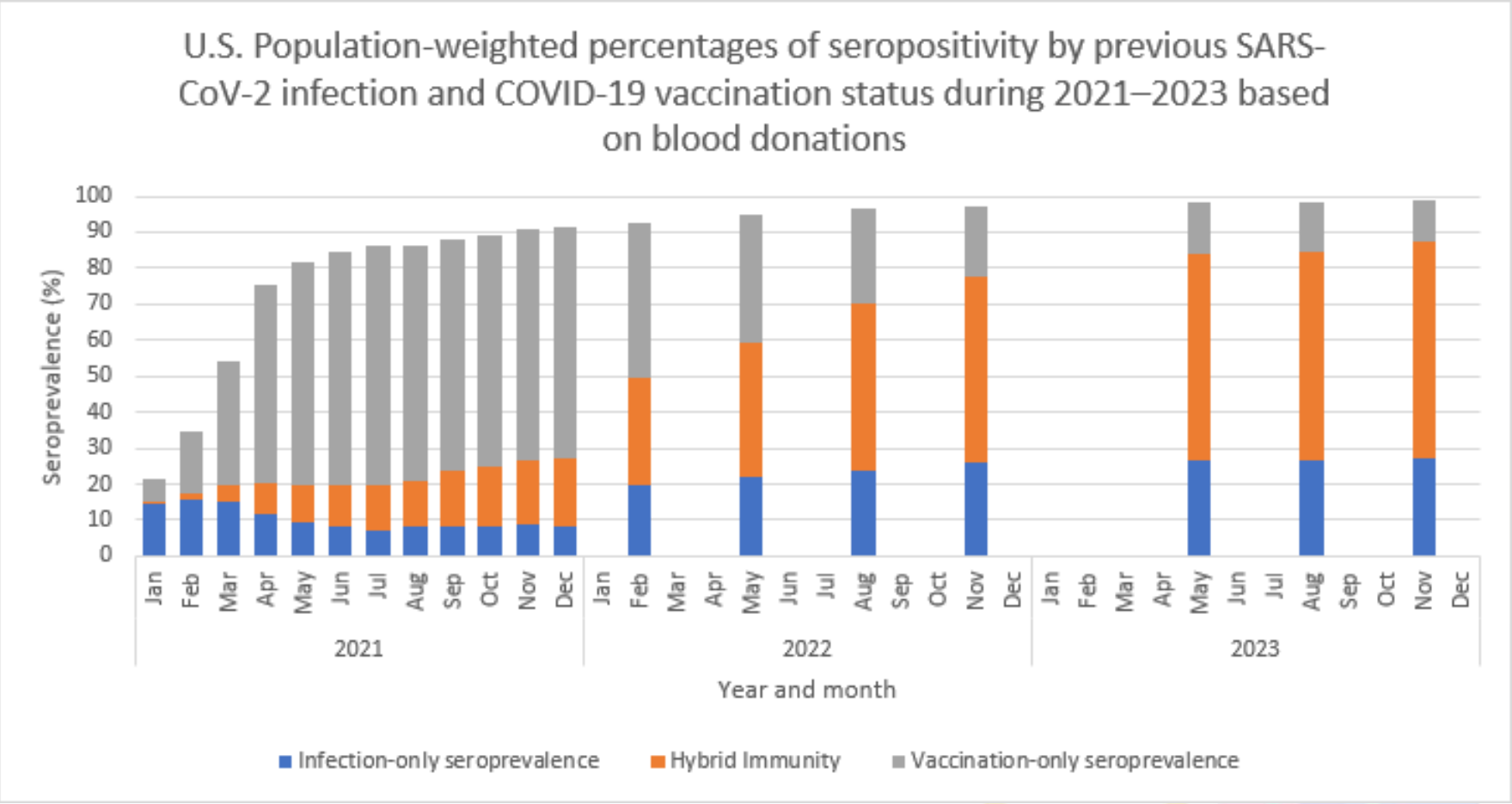
Updated 5/30/2024

Trends in COVID-19 associated hospitalization rates by year: 2020-2024



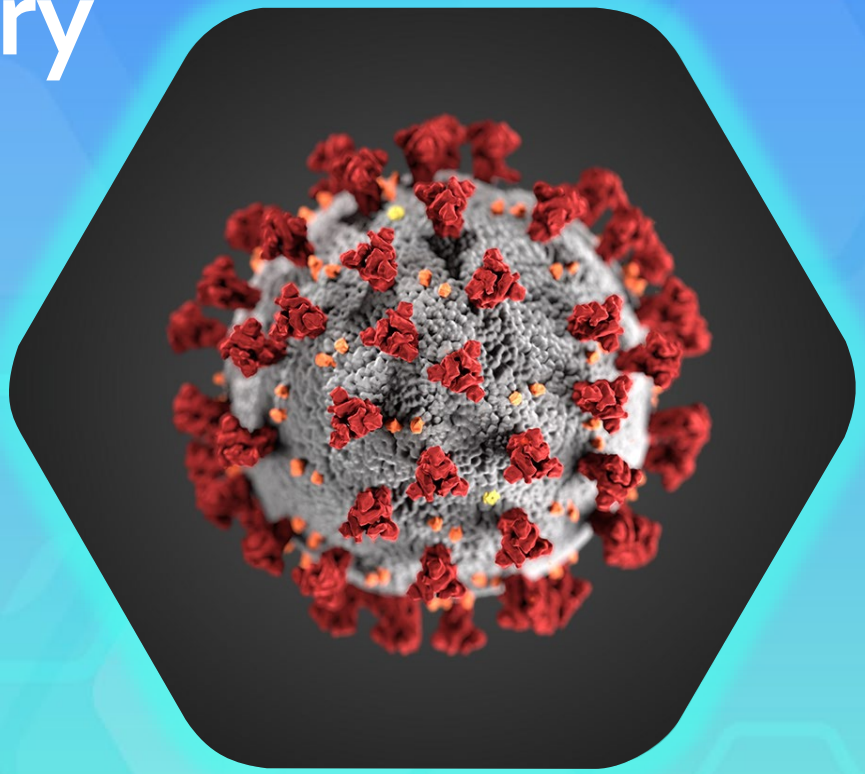
Data source: COVID-NET CDC COVID Data Tracker: COVID-NET Hospitalization Surveillance Network Updated 5/30/2024

Prevalence of Vaccine-Induced, Infection-Induced, and Hybrid* Immunity† Against SARS-CoV-2 Among Blood Donors Aged ≥16 years — United States, January 2021 – November 2023



Jones JM et al. Unpublished data

SARS-CoV-2 genomics summary



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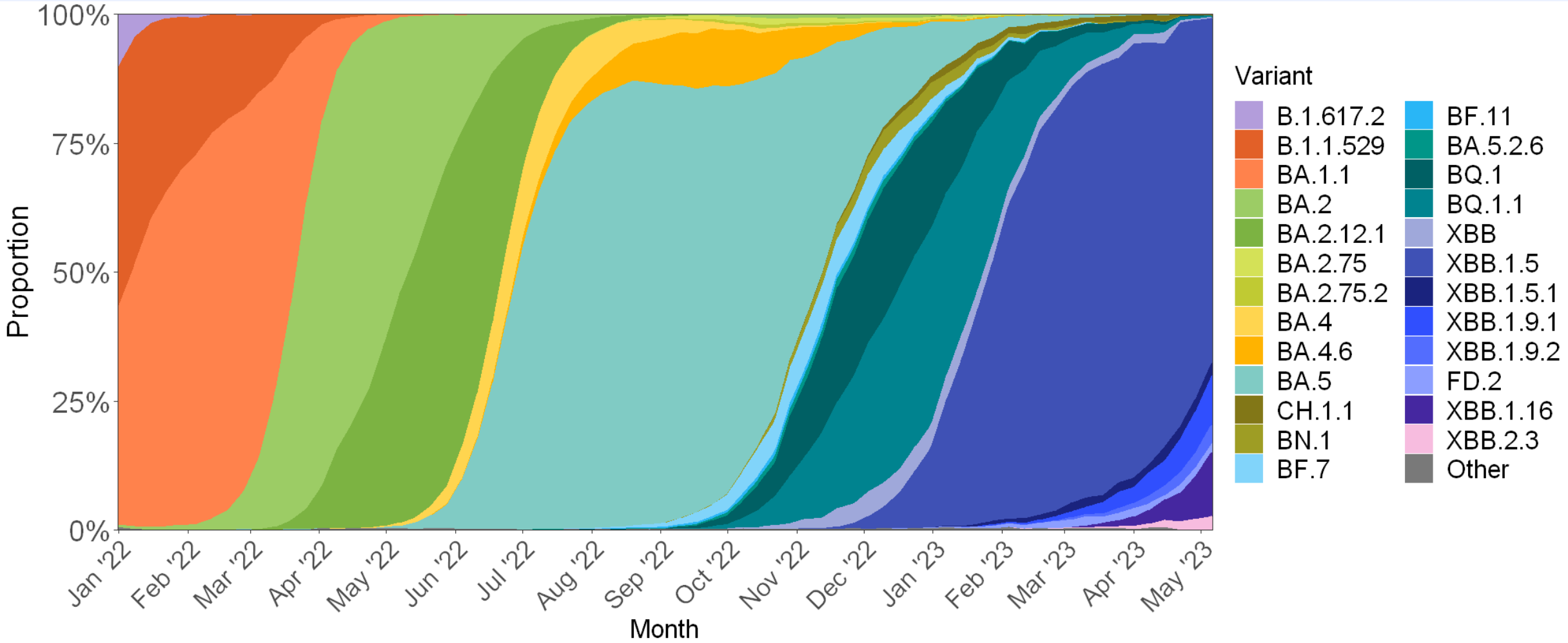
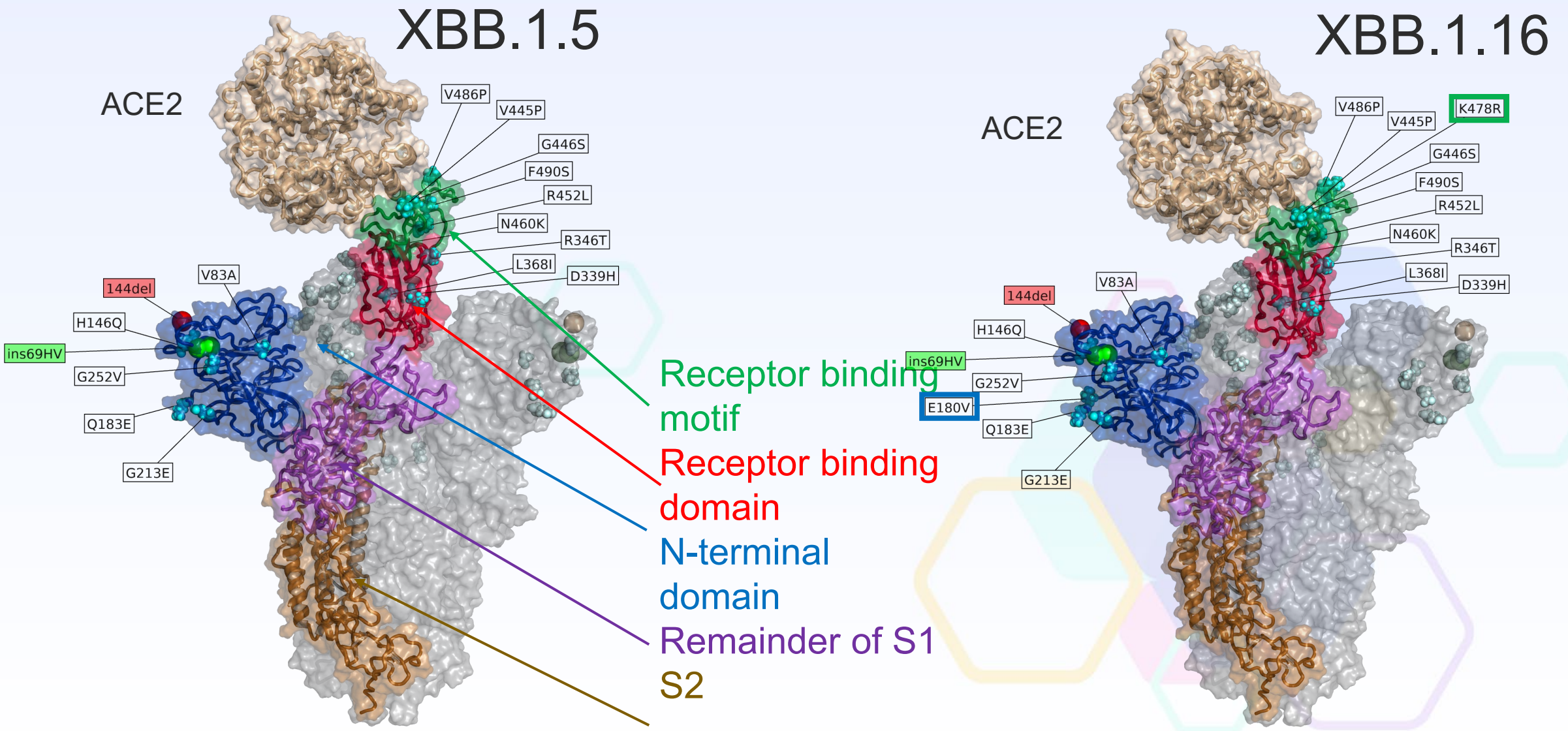
In winter 2022-2023, we observed strain replacement: BA5-lineages to XBB.1.5 lineage



Ma et al. MMWR published on June 15, 2023

Spike Substitutions Relative to BA.5



Convergent Evolution of Different XBB.1.5 Sub-lineages:

Key changes in the spike receptor binding domain (RBD) detected from Summer 2022-2023

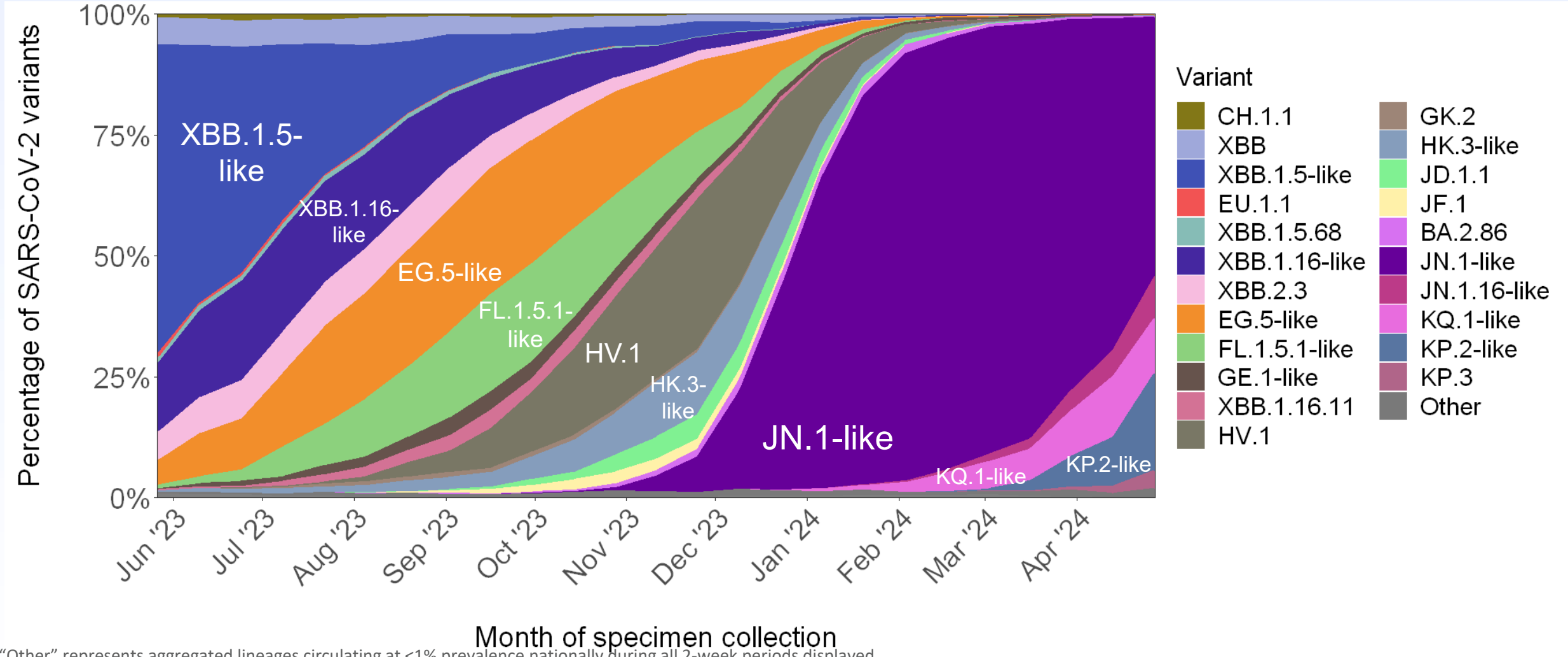
Lineage	Spike RBD (residues 333-527) amino acid substitutions											
	339 §	346 §,¶	368	444 §,¶	445 ¶	446 §,¶	452 §,¶	460 §,¶	478	486 §,¶	490 §,¶	521
Reference sequence: BA.4/BA.5	D	R	L	K	V	G	R	N	K	V	F	P
BA.4.6, BA.5.2.6, BF.7, BF.11	—	T	—	—	—	—	—	—	—	—	—	—
BQ.1	—	—	—	T	—	—	—	K	—	—	—	—
BQ.1.1	—	T	—	T	—	—	—	K	—	—	—	—
BA.2.75	H	—	—	—	—	S	L	K	—	F	—	—
BN.1	H	T	—	—	—	S	L	K	—	F	S	—
CH.1.1	H	T	—	T	—	S	—	K	—	S	—	—
XBB, XBB.1	H	T	I	—	P	S	L	K	—	S	S	—
XBB.1.5, XBB.1.5.1, FD.2, XBB.1.9.1, XBB.1.9.2	H	T	I	—	P	S	L	K	—	P	S	—
XBB.1.16, XBB.1.16.1	H	T	I	—	P	S	L	K	R	P	S	—
XBB.2.3	H	T	I	—	P	S	L	K	—	P	S	S

Ma et al. MMWR published on June 15, 2023

§ Indicates sites of independent substitutions in at least two different evolutionary lineages.

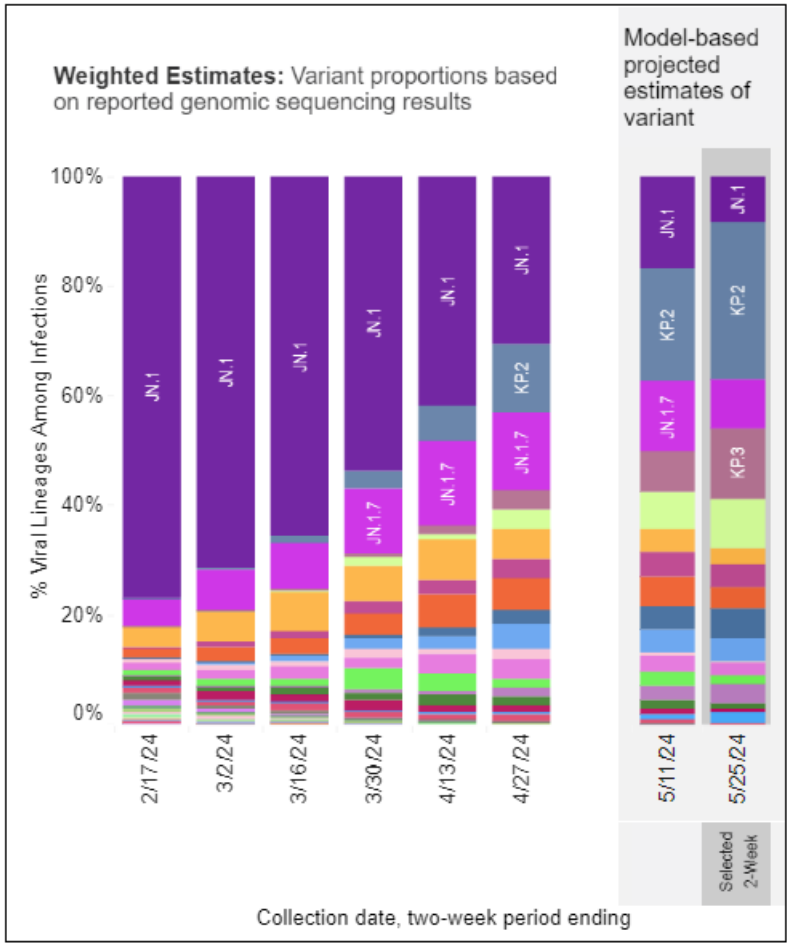
¶ Indicates sites identified in a previous study associated with *in vitro* reductions in binding by monoclonal antibodies that were previously FDA-authorized.

In winter 2023-2024, we observed strain replacement: XBB.1.5-lineages to JN.1 lineages



"Other" represents aggregated lineages circulating at <1% prevalence nationally during all 2-week periods displayed.
Lineages were ordered by date of first appearance on CDC's COVID data tracker (https://covid.cdc.gov/covid-data-tracker/#variant-proportions). Lineages with identical spike receptor binding domain amino acid sequences (residues 332 to 527) were grouped with a representative lineage and denoted as "representative lineage-like."

Weighted and Nowcast estimates in the United States of the 2-week periods ending 2/4 - 5/25/2024



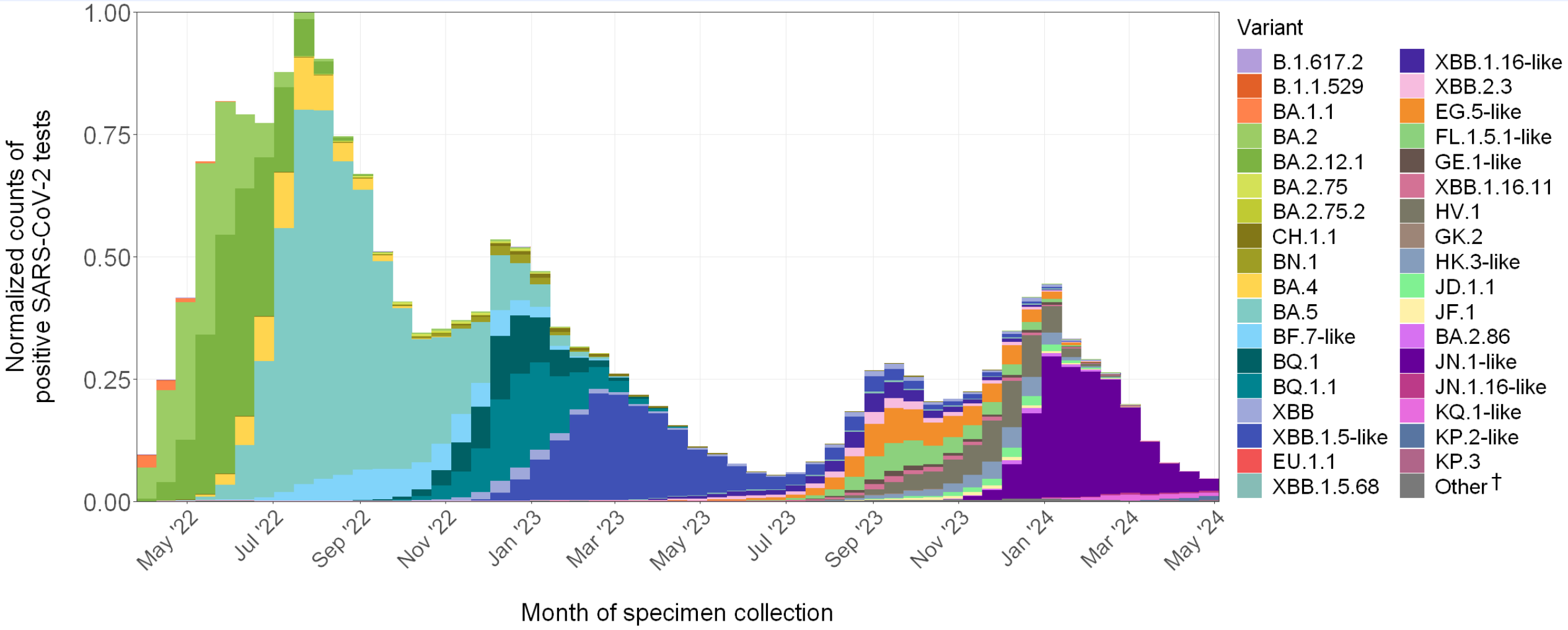
USA

WHO label	Lineage #	%Total	95%PI
Omicron	KP.2	28.5%	23.0-34.7%
	KP.3	12.7%	7.8-19.6%
	JN.1.7	9.2%	7.3-11.6%
	KP.1.1	9.2%	6.5-12.8%
	JN.1	8.4%	6.8-10.3%
	JN.1.16.1	5.4%	3.3-8.8%
	JN.1.16	4.2%	2.6-6.8%
	JN.1.13.1	4.0%	2.8-5.7%
	JN.1.11.1	3.9%	2.6-5.9%
	KS.1	3.5%	2.0-6.1%
	JN.1.8.1	2.7%	2.0-3.6%
	KQ.1	2.2%	1.2-4.0%
	KW.1.1	1.7%	0.7-4.2%
	JN.1.18	1.7%	1.1-2.5%
	JN.1.32	1.0%	0.7-1.5%
	XDP	0.6%	0.4-1.0%
	KV.2	0.4%	0.2-0.7%
	GE.1	0.0%	0.0-0.0%
	BA.2	0.0%	0.0-0.1%
	BA.2.86	0.0%	0.0-0.0%
	JG.3	0.0%	0.0-0.0%
	HV.1	0.0%	0.0-0.0%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one 2-week period. "Other" represents the aggregation of lineages which are circulating <1% nationall during all 2-week periods displayed.
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
# XDP was aggregated to JN.1.4(same spike as JN.1, but recombinants are always difficult), While all lineages are tracked by CDC, those named lineages not enumerated in this graphic are aggreg

*Covid data tracker: CDC COVID Data Tracker: Variant Proportions updated 5/24/2024

SARS-CoV-2 Variant Proportions Scaled by Normalized Counts of Positive Tests* from the National Respiratory and Enteric Virus Surveillance System (April 2022–April 2024)



* Counts of positive SARS-CoV-2 tests from NREVSS (https://www.cdc.gov/surveillance/nrevss/index.html) were normalized to the maximum, which occurred in the 2-week period ending July 23, 2022.
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Lineages were ordered by date of first appearance on CDC's COVID data tracker (https://covid.cdc.gov/covid-data-tracker/#variant-proportions). Lineages with identical spike receptor binding domain amino acid sequences (residues 332 to 527) were grouped with a representative lineage and denoted as "representative lineage-like."

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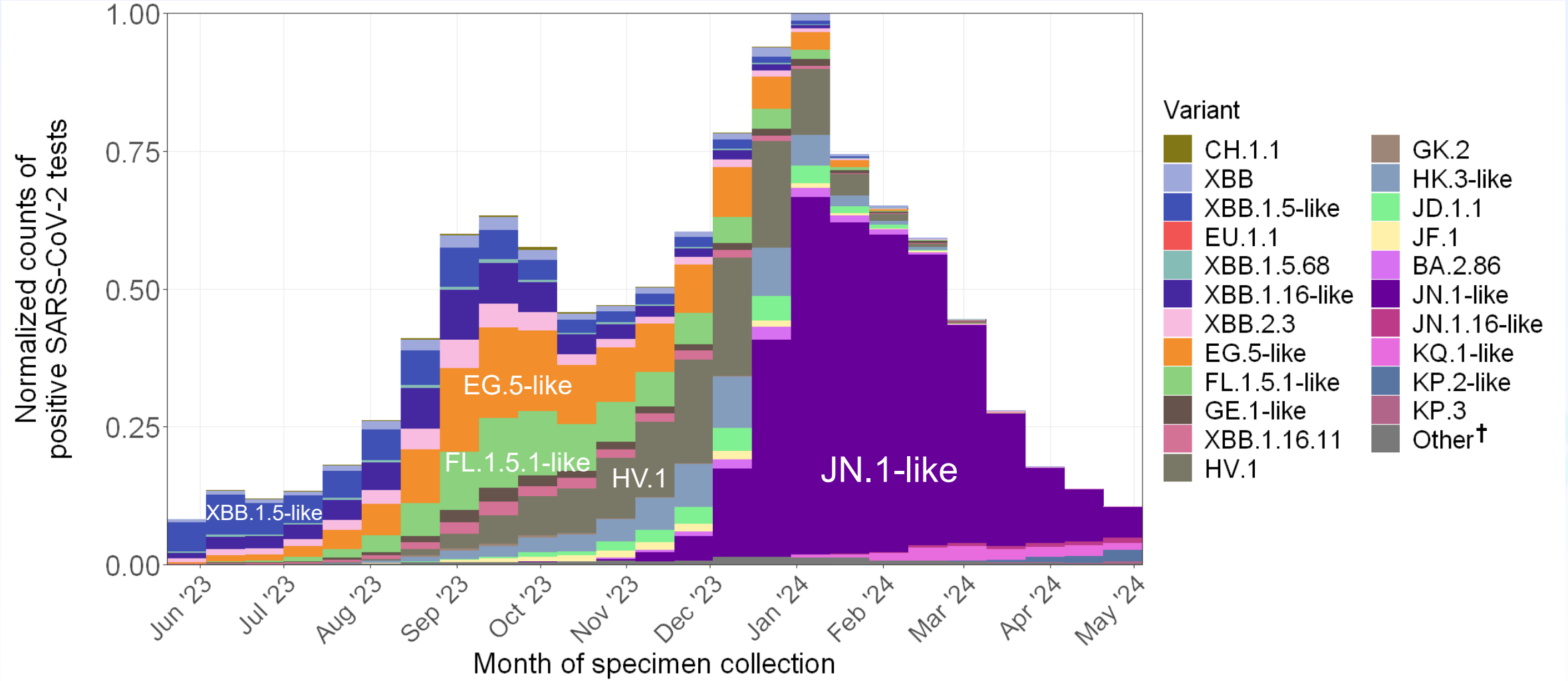

* Counts of positive SARS-CoV-2 tests from NREVSS (https://www.cdc.gov/surveillance/nrevss/index.html) were normalized to the maximum, which occurred in the 2-week period ending January 6, 2024.
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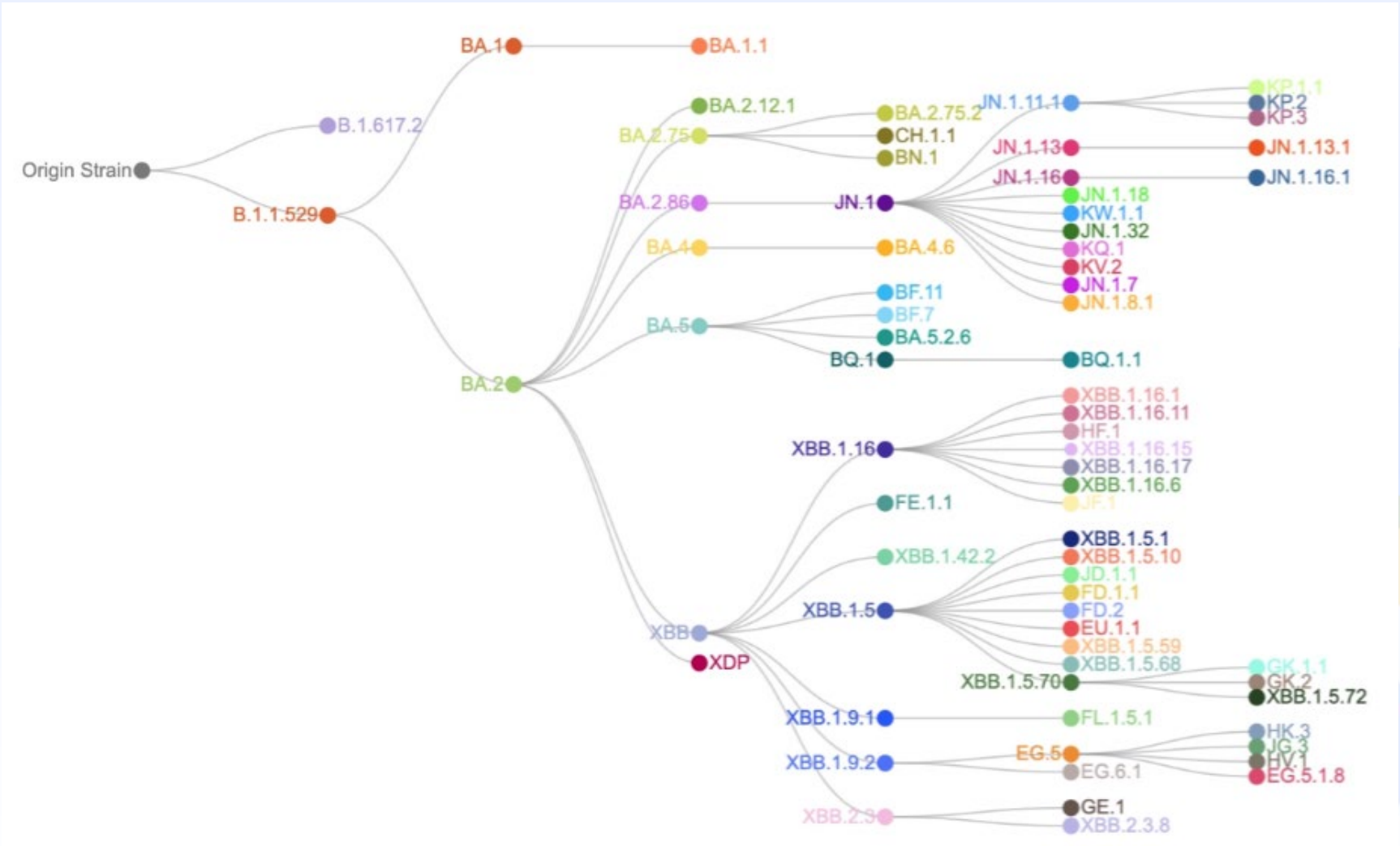
Lineages were ordered by date of first appearance on CDC's COVID data tracker (https://covid.cdc.gov/covid-data-tracker/#variant-proportions). Lineages with identical spike receptor binding domain amino acid sequences (residues 332 to 527) were grouped with a representative lineage and denoted as "representative lineage-like."

Relationship of recent SARS-CoV-2 lineages



Covid data tracker: [CDC COVID Data Tracker: Variant Proportions](#) updated 5/24/2024

Convergent Evolution of Different Omicron Sub-Lineages

Key changes in the spike receptor binding domain (RBD)* detected since May 2023

Lineage	332	346 §,¶	356	368	403	445 ¶	450 ¶	452 §,¶	455 §,¶	456 §,¶	475 ¶	478	481	483 ¶	484 ¶	486 §,¶	490 ¶	493 ¶	521
Reference sequence: XBB.1.5†	I	T	K	I	R	P	N	L	L	F	A	K	N	V	A	P	S	Q	P
XBB																S			
XBB.1.16-like (HF.1, XBB.1.16, XBB.1.16.1, XBB.1.16.17)												R							
XBB.2.3																			S
EG.5-like (EG.5, EG.6.1, FD.1.1, FE.1.1, XBB.1.5.10, XBB.1.5.59, XBB.1.5.72)										L									
FL.1.5.1-like (FL.1.5.1, XBB.1.16.6)										L		R							
HV.1								R		L									
HK.3-like (EG.5.1.8, GK.1.1, HK.3, JG.3, XBB.1.5.70)									F	L									
JD.1.1									F	L	V								
JN.1-like (JN.1, JN.1.13, JN.1.32, JN.1.7, JN.1.8.1, KV.2, XDP)	V	R	T	L	K	H	D	W	S				K	-	K		F		
JN.1.16-like (JN.1.11.1, JN.1.16, KW.1.1)	V	R	T	L	K	H	D	W	S	L			K	-	K		F		
KQ.1-like (JN.1.13.1, JN.1.18, KQ.1)	V		T	L	K	H	D	W	S				K	-	K		F		
KP.2-like (JN.1.16.1, KP.1.1, KP.2, KS.1)	V		T	L	K	H	D	W	S	L			K	-	K		F		
KP.3	V	R	T	L	K	H	D	W	S	L			K	-	K		F	E	

* Lineages with identical spike RBD (residues 332 to 527) amino acid sequences were grouped with a representative lineage and denoted as "representative lineage-like." Lineages or lineage groups with ≥5% prevalence in at least one 2-week period and substitutions present in ≥50% of sequences belonging to a lineage were included.

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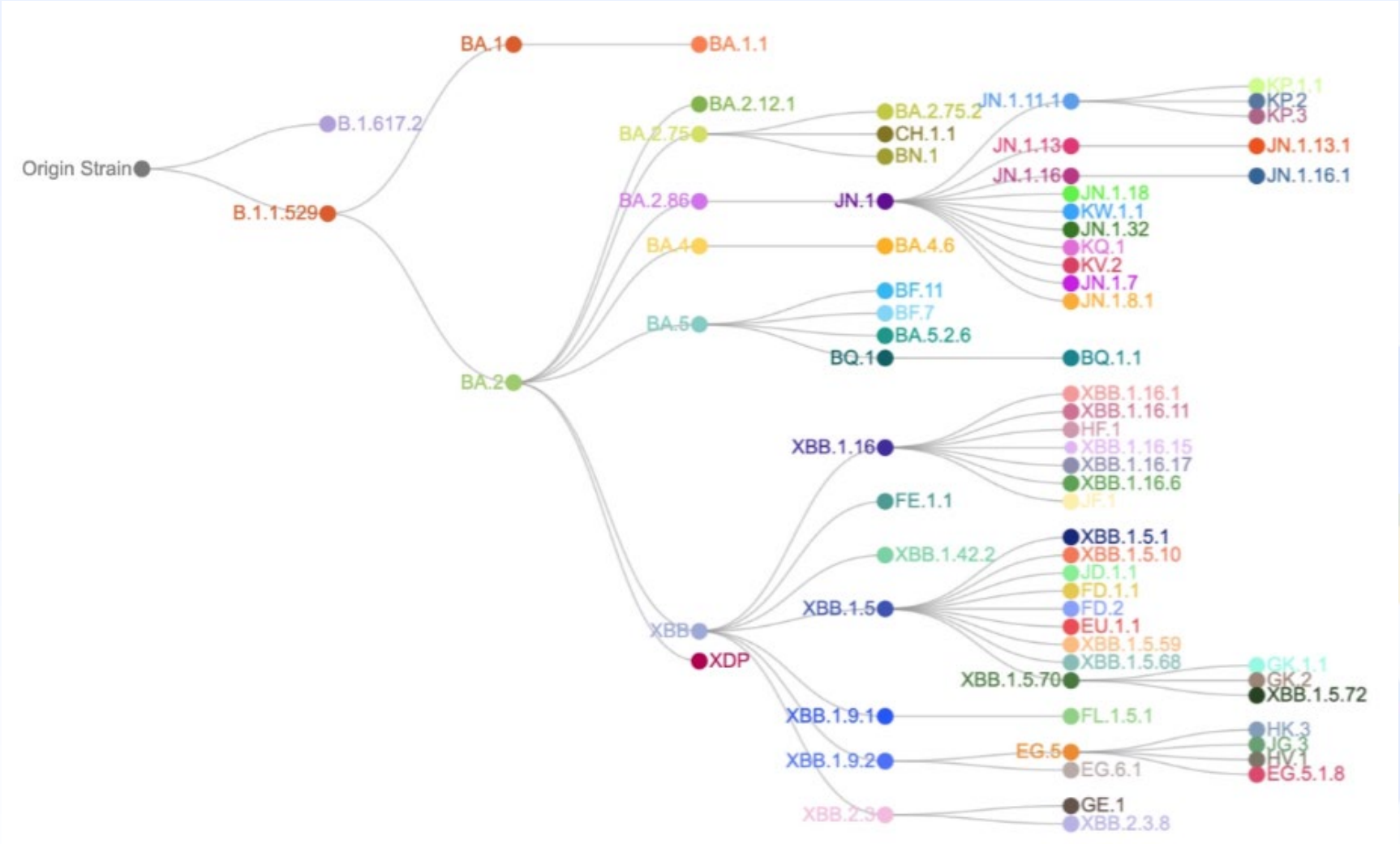
Bolded sub-lineages are expanding in the United States as of May 28, 2024.

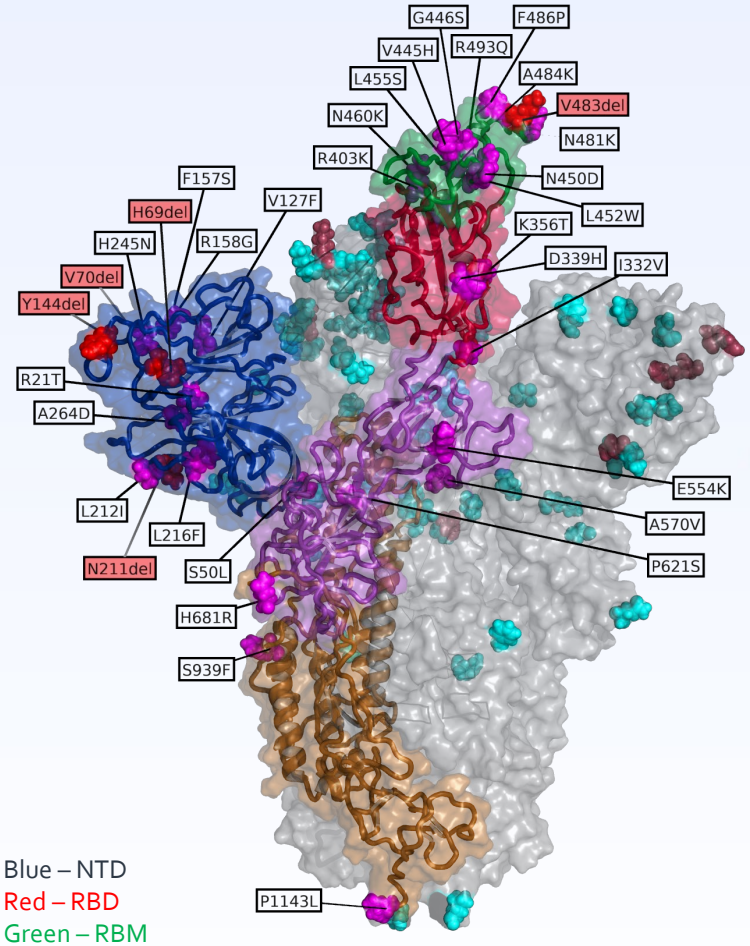
Relationship of recent SARS-CoV-2 lineages

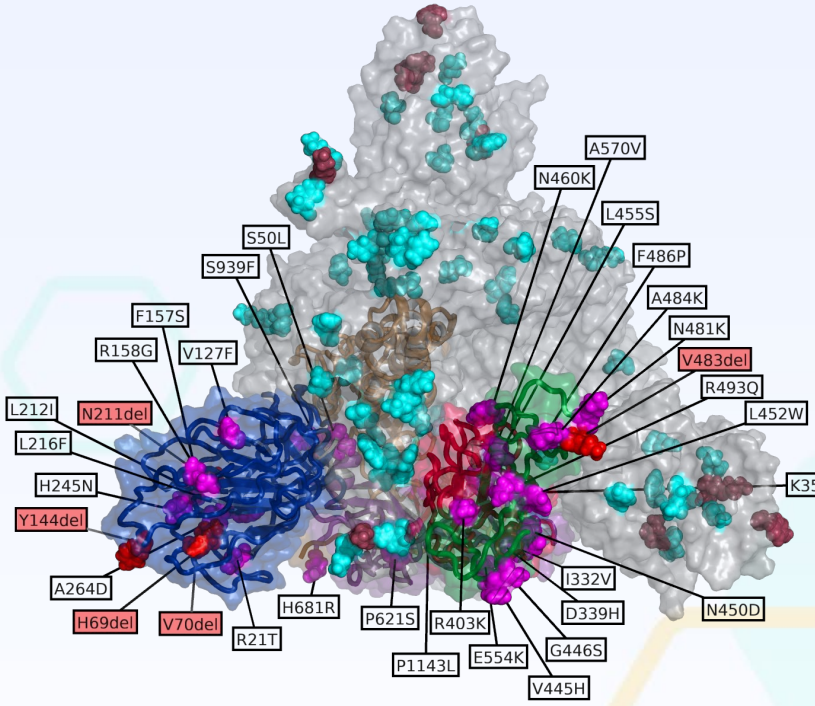


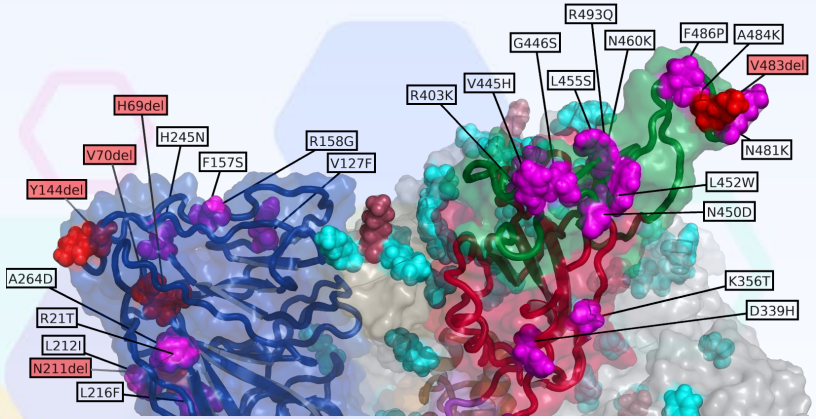
Covid data tracker: CDC COVID Data Tracker: Variant Proportions updated 5/24/2024

Structure of BA.2 vs JN.1

Red sphere – deletions in one chain (labeled)
Magenta sphere – substitutions in one chain (labeled)
Raspberry sphere – deletions in rest 2 chains
Cyan sphere – substitutions in rest 2 chains



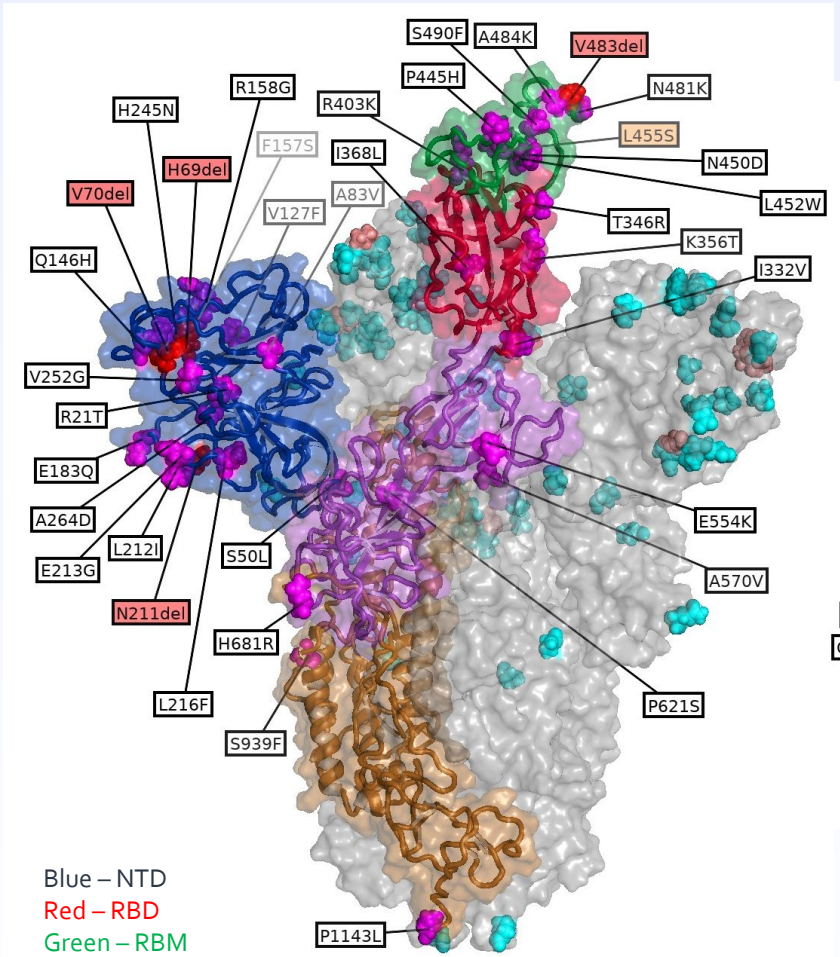




Blue – NTD
Red – RBD
Green – RBM
Purple – S1
Gold – FCS
Brown – S2

Schrodinger homology model of JN.1, starting with 7YR2 (BA.2.75)
Prepared by CDC: Megha Aggarwal, PhD

Structure of XBB.1.5 vs JN.1



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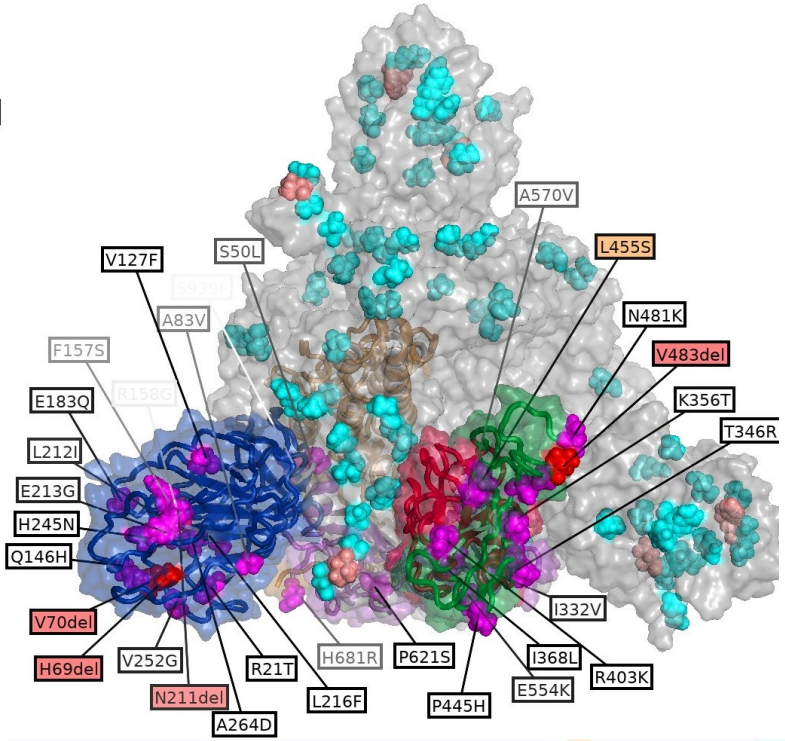

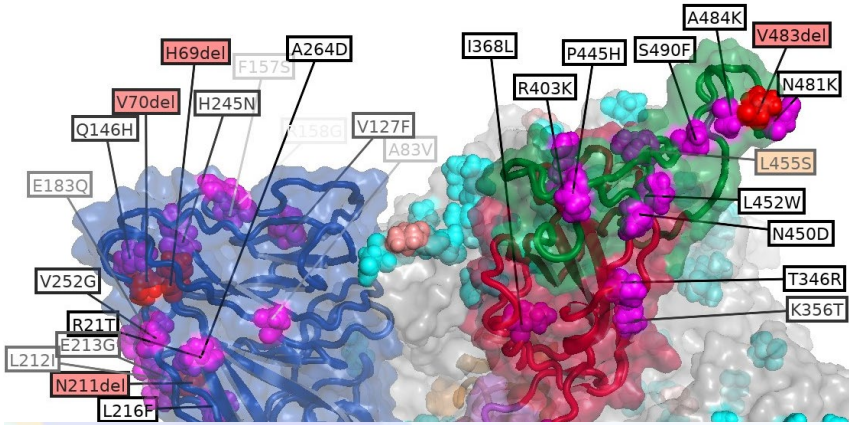

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HV.1								R		L									
HK.3-like (EG.5.1.8, GK.1.1, HK.3, JG.3, XBB.1.5.70)									F	L									
JD.1.1									F	L	V								
JN.1-like (JN.1, JN.1.13, JN.1.32, JN.1.7, JN.1.8.1, KV.2, XDP)	V	R	T	L	K	H	D	W	S				K	-	K		F		
JN.1.16-like (JN.1.11.1, JN.1.16, KW.1.1)	V	R	T	L	K	H	D	W	S	L			K	-	K		F		
KQ.1-like (JN.1.13.1, JN.1.18, KQ.1)	V		T	L	K	H	D	W	S				K	-	K		F		
KP.2-like (JN.1.16.1, KP.1.1, KP.2, KS.1)	V		T	L	K	H	D	W	S	L			K	-	K		F		
KP.3	V	R	T	L	K	H	D	W	S	L			K	-	K		F	E	

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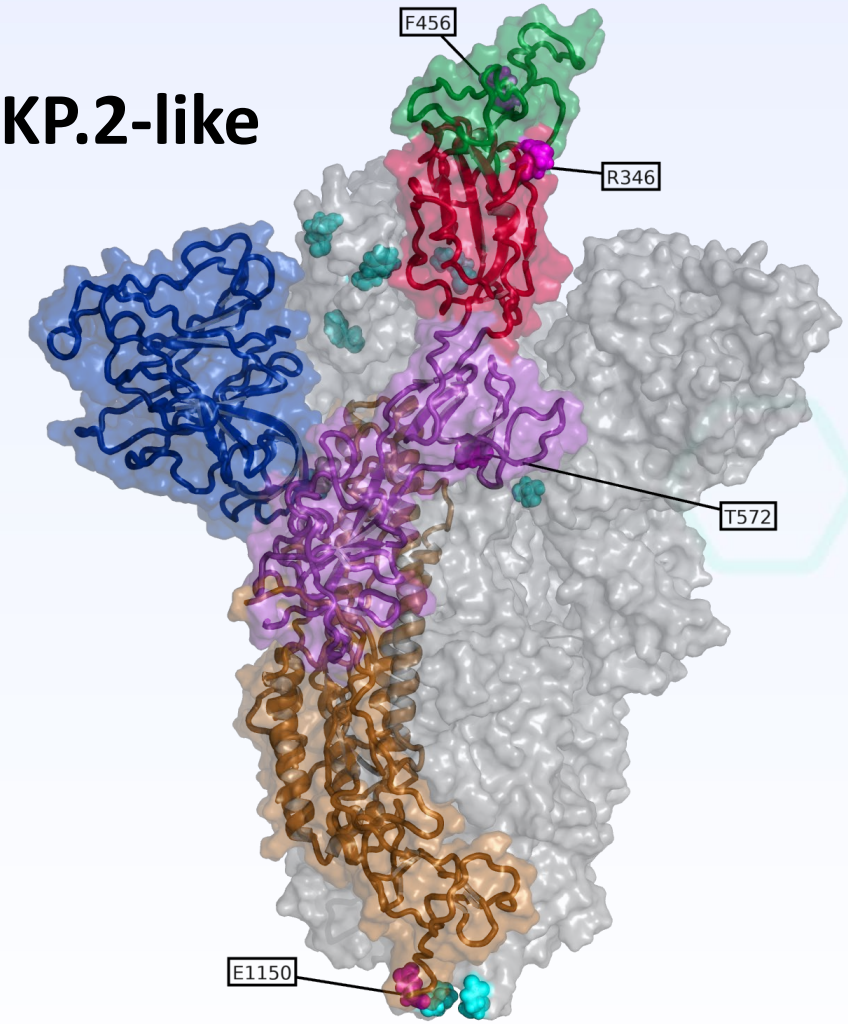
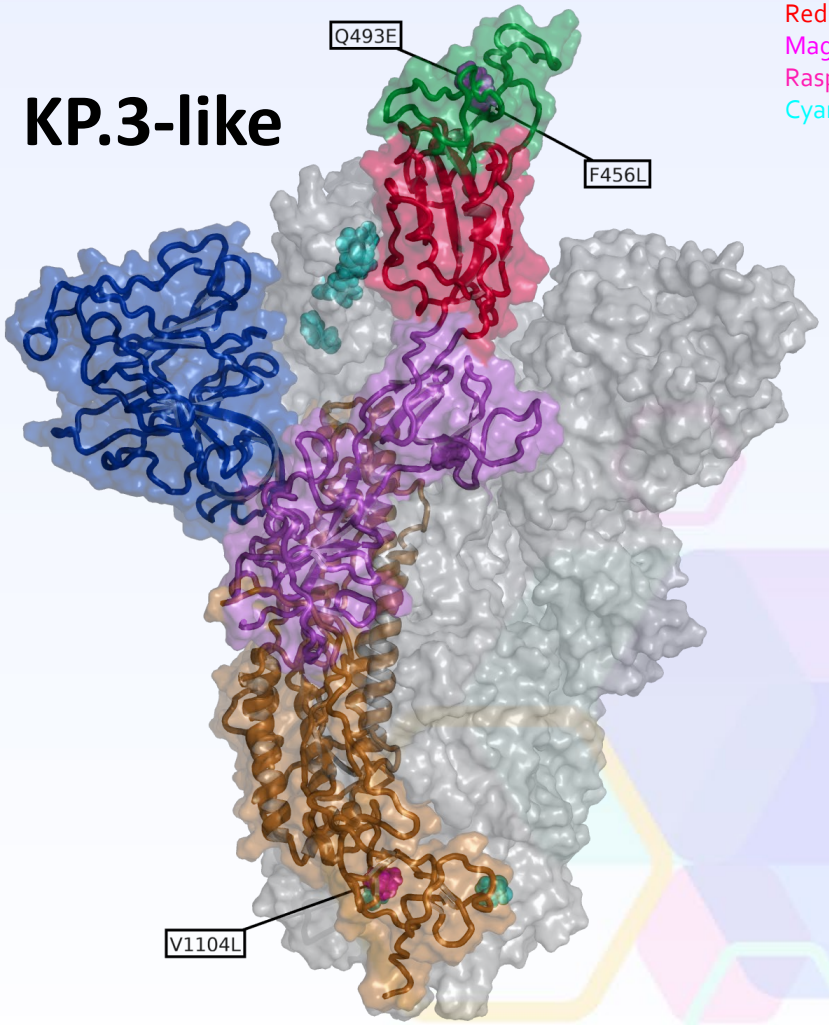
Structure of JN.1 vs. KP.2-like and KP.3 lineage spike

KP.2-like



KP.3-like



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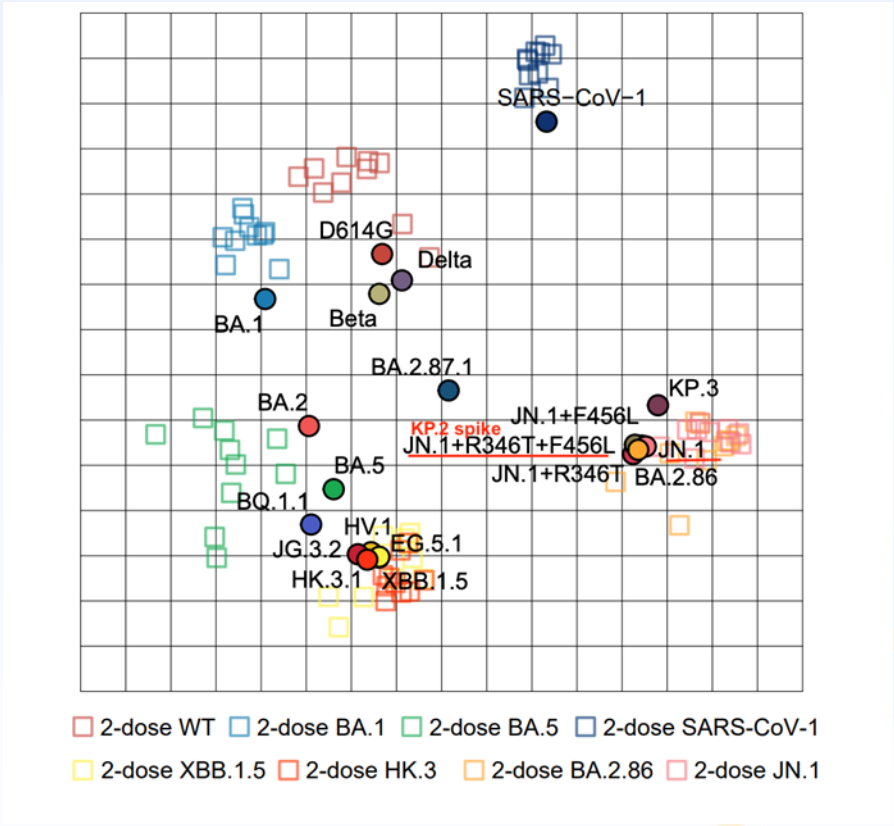
Schrodinger homology model of JN.1, starting with 7YR2 (BA.2.75)

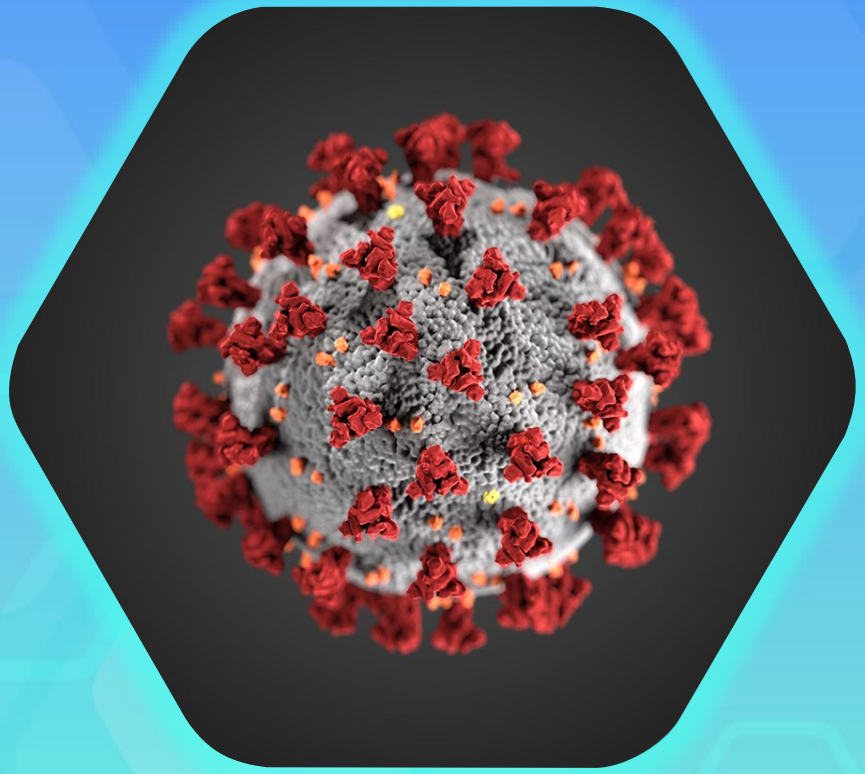
Prepared by CDC: Megha Aggarwal, PhD

Using mouse sera, JN.1 descendent viruses, including KP.2 and KP.3, are antigenically similar



Jian et al Source: Jian et. al. bioRxiv. httpd://dx.doi.org/10.1101/2024.04.19.590276

COVID-19 severity by lineage
2023-2024



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IVY: *Clinical severity* of *COVID-19–associated hospitalization* among adults with sequence-confirmed *JN.1 versus XBB lineage infection*

- **Population (IVY Network — 26 hospitals, 20 U.S. States)**
  - Adults aged ≥18 years hospitalized with COVID-like illness (CLI)* and SARS-CoV-2 test results within 10 days of illness onset and 3 days of admission
  - **Restricted to patients who tested positive for SARS-CoV-2 and had sequence-confirmed† JN.1 lineage (BA.2.86 and its descendants) infection or XBB lineage (all other co-circulating lineages) infection**

- **Period for analysis**: October 18, 2023–March 9, 2024
  - First date on which a patient was admitted with sequence-confirmed JN.1 lineage infection
  - Last week during which a patient was admitted with sequence-confirmed XBB lineage infection

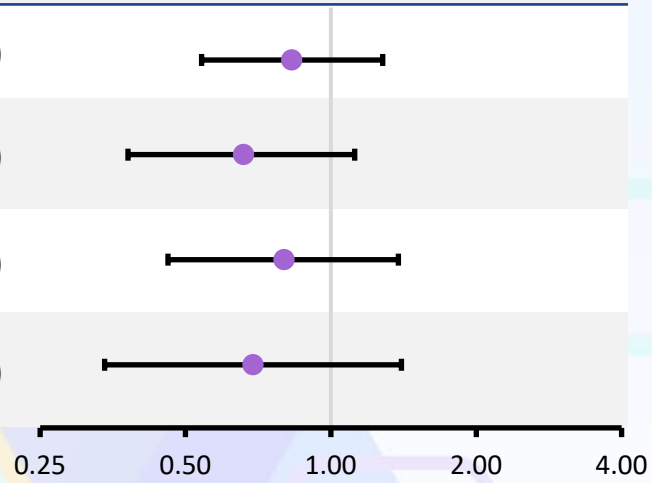
- Multivariable logistic regression was used to estimate the odds of four adverse in-hospital outcomes§ among patients with JN.1 versus XBB lineage infection adjusting for confounders¶

*CLI is defined as presence of any one of the following: fever, cough, shortness of breath, chest imaging consistent with pneumonia, or hypoxemia. Patients who tested positive for influenza or RSV were excluded.
† Identification of a SARS-CoV-2 lineage through viral whole-genome sequencing was successful for 63% of COVID-19 patients during the analysis period.
§ Severe in-hospital outcomes included 1) supplemental oxygen therapy (defined as supplemental oxygen at any flow rate and by any device for those not on chronic oxygen therapy, or with escalation of oxygen therapy for patients receiving chronic oxygen therapy); 2) advanced respiratory support (defined as new receipt of high-flow nasal cannula, non-invasive ventilation, or invasive mechanical ventilation [IMV]); 3) intensive care unit (ICU) admission; or 4) a composite of IMV or death.
¶ Odds ratios were adjusted for age, sex, race and ethnicity, geographic region, calendar time, Charlson comorbidity index, and receipt of an updated 2023–2024 COVID-19 vaccine.

IVY: Adjusted odds ratios of severe in-hospital outcomes among adults aged ≥18 years hospitalized with COVID-19 by SARS-CoV-2 lineage*

October 18, 2023 – March 9, 2024

In-hospital severe outcome**	No. of JN lineage patients with outcome (% among 397 total patients)	No. of XBB lineage patients with outcome (% among 585 total patients)	*P*-value	Adjusted odds ratio† (95% CI)
Supplemental oxygen therapy§	245 (62)	366 (63)	0.40	0.83 (0.54–1.28)
Advanced respiratory support¶	76 (19)	99 (17)	0.12	0.66 (0.38–1.12)
Intensive care unit admission	61 (15)	87 (15)	0.42	0.80 (0.46–1.38)
Invasive mechanical ventilation or death	32 (8)	44 (8)	0.30	0.69 (0.34–1.40)



* JN lineages comprised BA.2.86 and its descendants. XBB lineages comprised all other co-circulating lineages.

† Odds ratios were adjusted for age, sex, race and ethnicity, geographic region, calendar time, Charlson comorbidity index, and receipt of an updated 2023–2024 COVID-19 vaccine.

§ Supplemental oxygen therapy was defined as supplemental oxygen at any flow rate and by any device for those not on chronic oxygen therapy, or with escalation of oxygen therapy for patients receiving chronic oxygen therapy.

¶ Advanced respiratory support was defined as new receipt of high-flow nasal cannula, non-invasive ventilation, or invasive mechanical ventilation.

** Outcomes are not mutually exclusive.

CDC unpublished data.

Summary

- Current circulation of SARS-CoV-2 is relatively low
- JN.1 lineages replaced XBB.1.5 lineages during winter 2023-2024
- Severity of JN.1 infections did not appear to be worse than earlier lineages
- JN.1 lineages are undergoing phylogenetic diversification
  - Convergent evolution of spike is occurring
  - KP.2-like lineages and KP.3 are increasing
  - Both of these lineages have only 2 substitutions in spike RBD in comparison to JN.1

- Preliminary data indicate JN.1 lineages are antigenically similar

Acknowledgements

- Megha Aggarwal
- Juan Castro
- Fatimah Dawood
- Jennifer DeCuir
- Jefferson Jones
- Kevin Ma
- Clinton Paden
- Wesley Self
- Diya Surie

- IVY network

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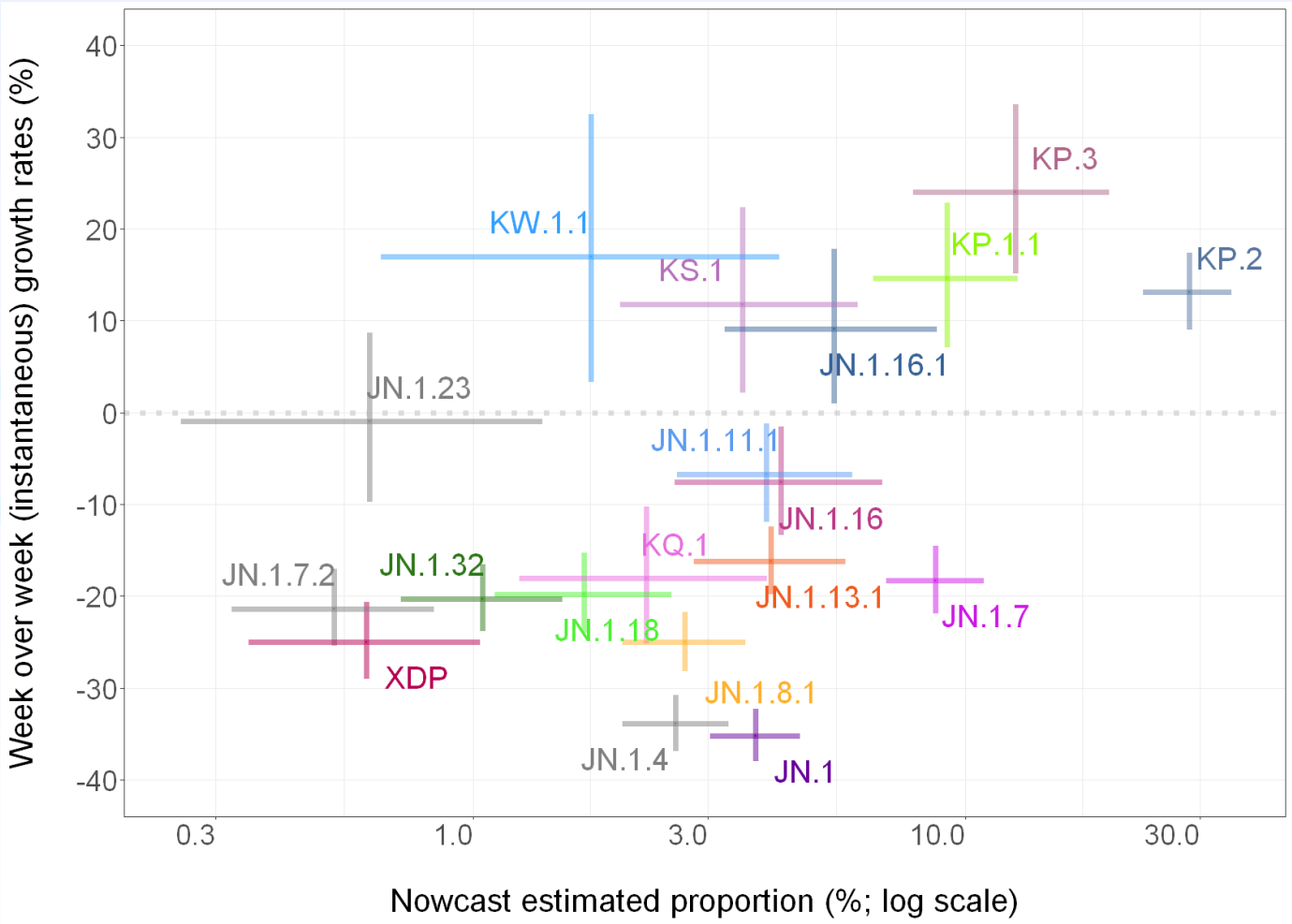
The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

SARS-CoV-2 Variant Growth Rates And Estimated Proportions Using Nowcast

United States, May 25, 2024

Lineages with positive growth rate point estimates grouped by spike receptor binding domain mutations compared to JN.1:

- **JN.1.16.1, KP.1.1, KP.2, KS.1**: R346T, F456L
- **KP.3**: F456L, Q493E
- **KW.1**: F456L, T572I



Nowcast predictions using multinomial regression fit on the previous26 weeks of data were used to produce estimates for the two most recent 2-week periods. Instantaneous growth rates of lineages with prevalence >0.5% were estimated from the coefficients of the multinomial nowcasting model. A growth rate of 100% corresponds to a doubling time of one week. Bars represent 95% confidence intervals for growth rates and estimated proportions, respectively.