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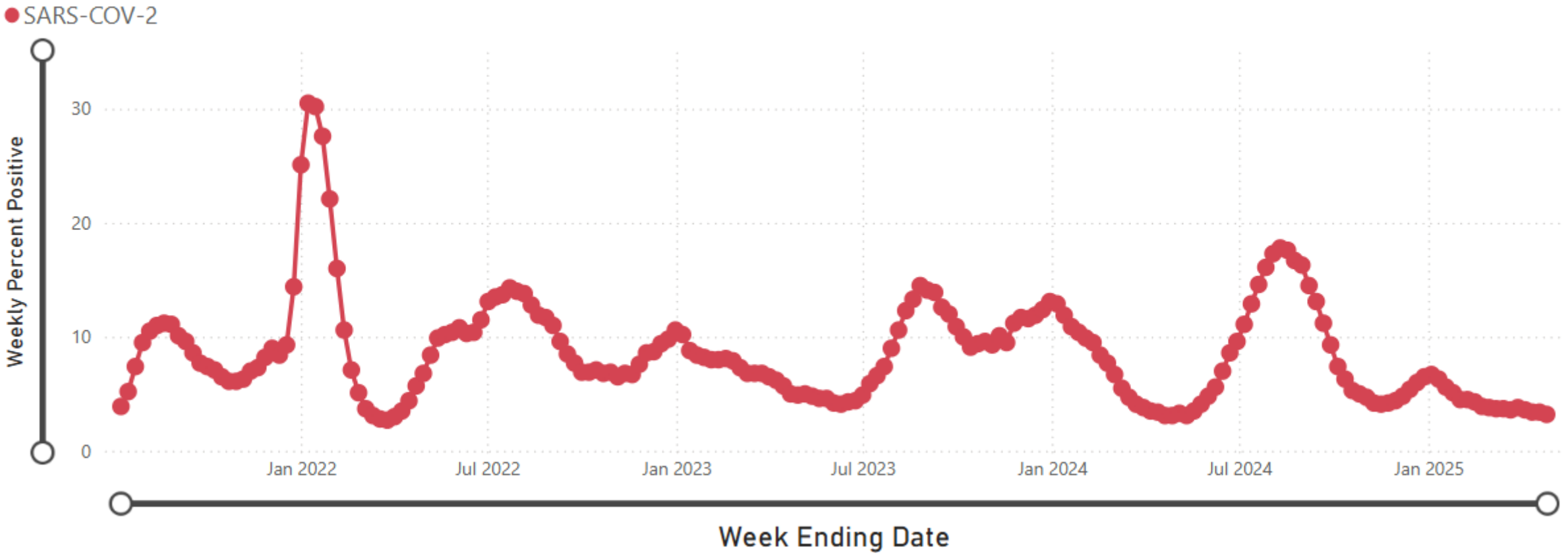
2024-2025 Update on Current Epidemiology of COVID-19 and SARS-CoV-2 Genomics

Natalie J. Thornburg, PhD

May 2025

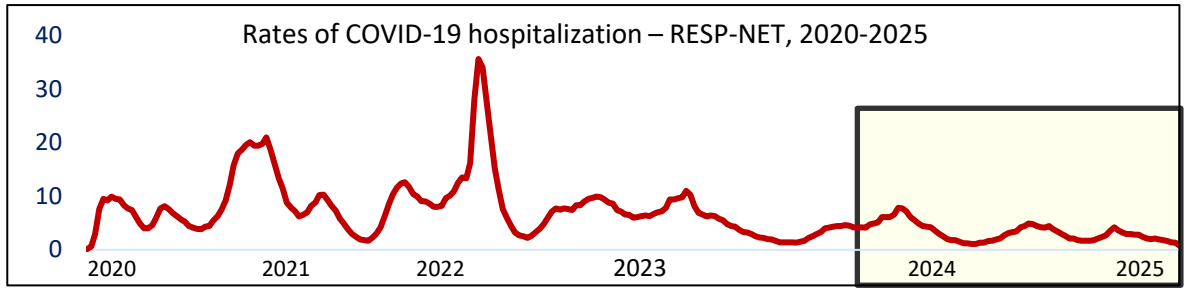
Chief, Respiratory Viruses Laboratory Branch
Coronavirus and Other Respiratory Viruses Division

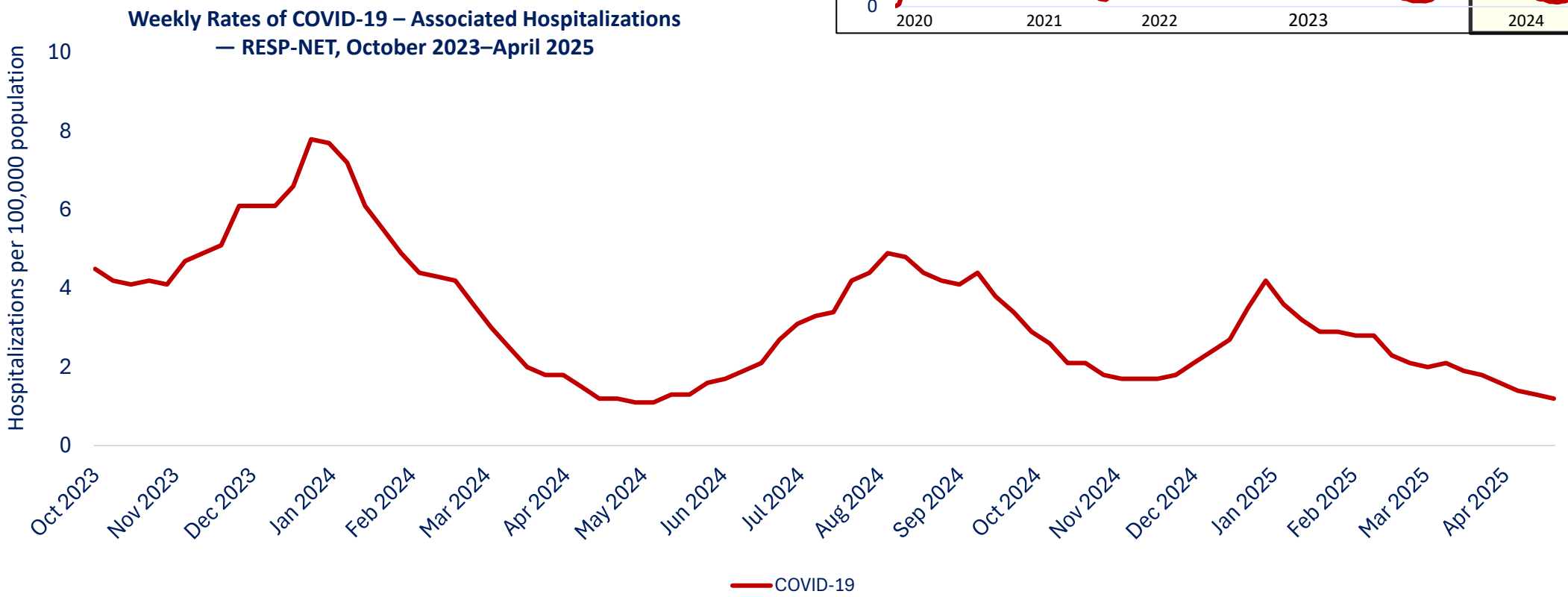
National SARS-CoV-2 weekly % positivity: 2021-2025



Source: Interactive Dashboard | The National Respiratory and Enteric Virus Surveillance system (NREVSS) | CDC
As of May 7, 2025

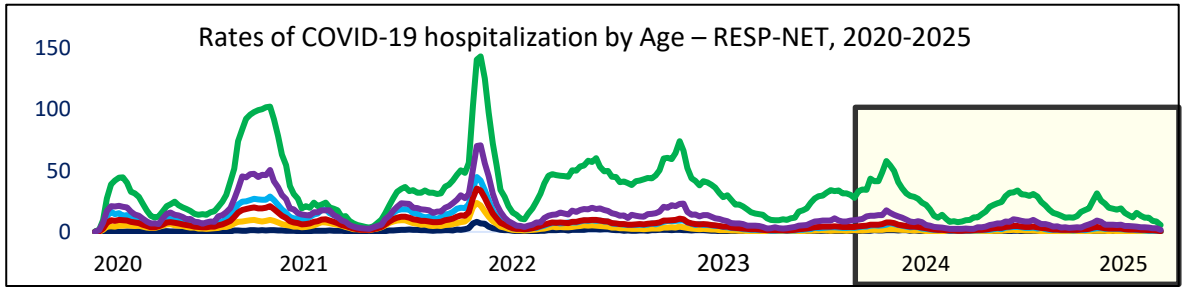
COVID-19 hospitalization rates have had both winter and summer peaks.

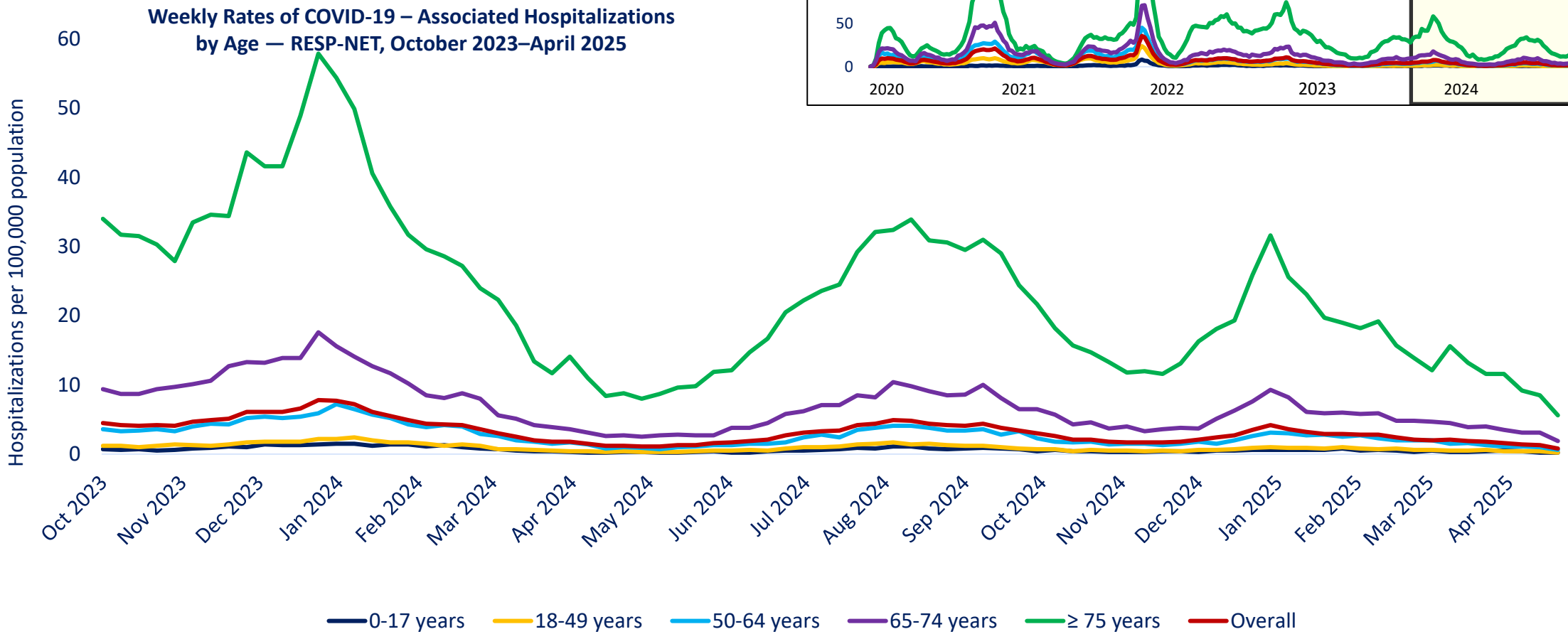




Rates for all three pathogens (COVID-19, influenza, and respiratory syncytial virus [RSV]) are laboratory-confirmed. Data source: https://www.cdc.gov/resp-net/dashboard/
Note that rates are not adjusted for testing or limited to admissions where the respiratory infection is the likely primary reason for admission.

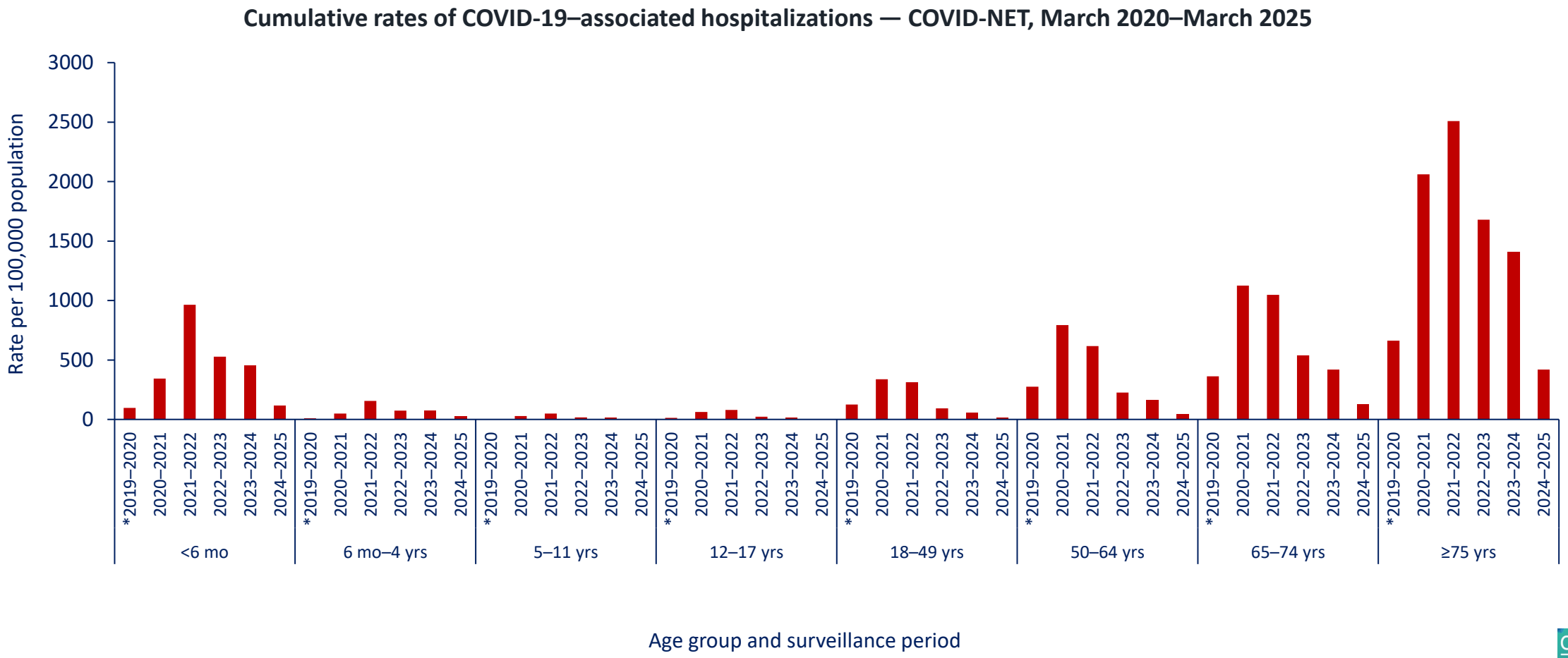
COVID-19 hospitalization rates are highest in older adults.





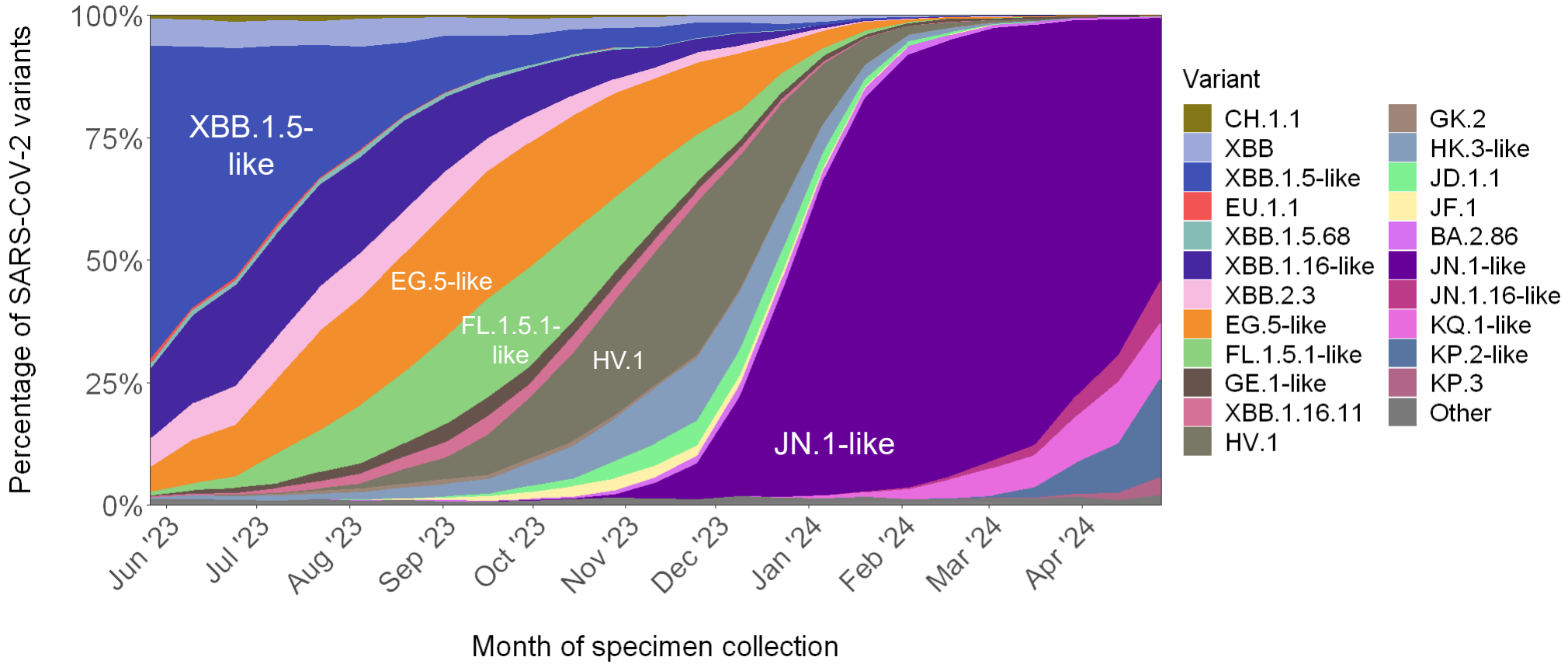
Rates for all three pathogens (COVID-19, influenza, and respiratory syncytial virus [RSV]) are laboratory-confirmed. Data source: https://www.cdc.gov/resp-net/dashboard/
Note that rates are not adjusted for testing or limited to admissions where the respiratory infection is the likely primary reason for admission.

Among all age groups, rates of COVID-19–associated hospitalizations have declined since the 2021–2022 season.



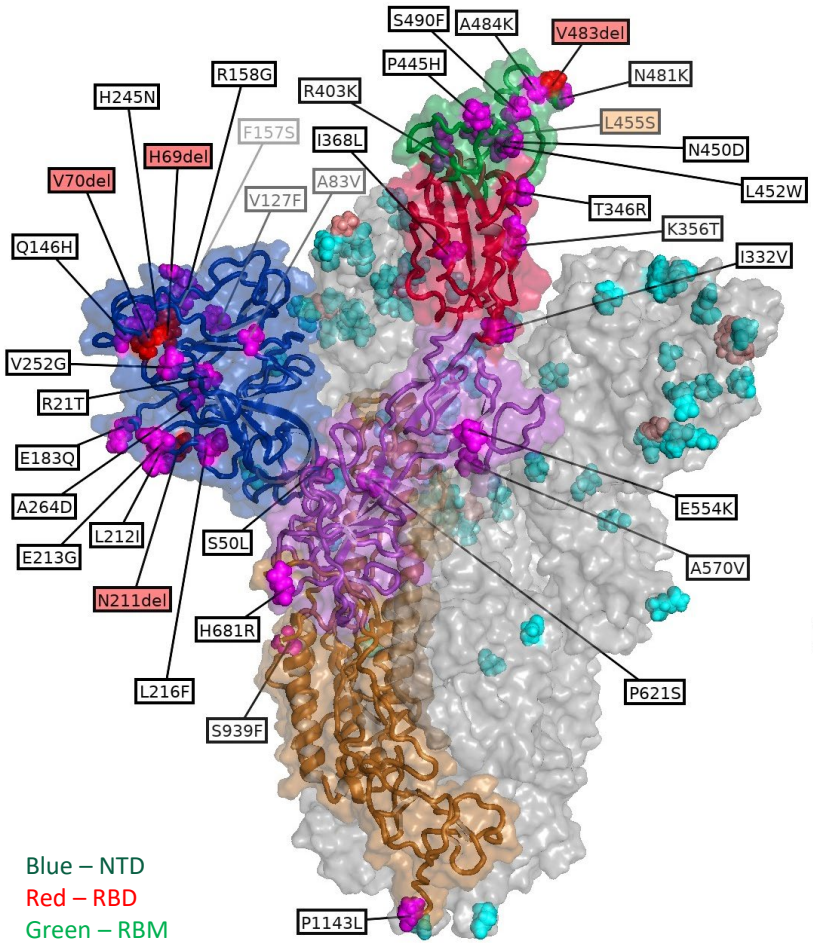
* The 2019–2020 surveillance period includes March–September 2020; other seasons are defined as October through September. The 2024–2025 season shows data from October 2024–March 2025 and is ongoing.

In winter 2023-2024, we observed a strain replacement of XBB.1.5-like viruses to JN.1-like viruses



[Genomic Surveillance for SARS-CoV-2 Variants: Circulation of Omicron XBB and JN.1 Lineages — United States, May 2023–September 2024 | MMWR]

Structure of XBB.1.5 vs. JN.1 spike



Blue – NTD
Red – RBD
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Purple – S1
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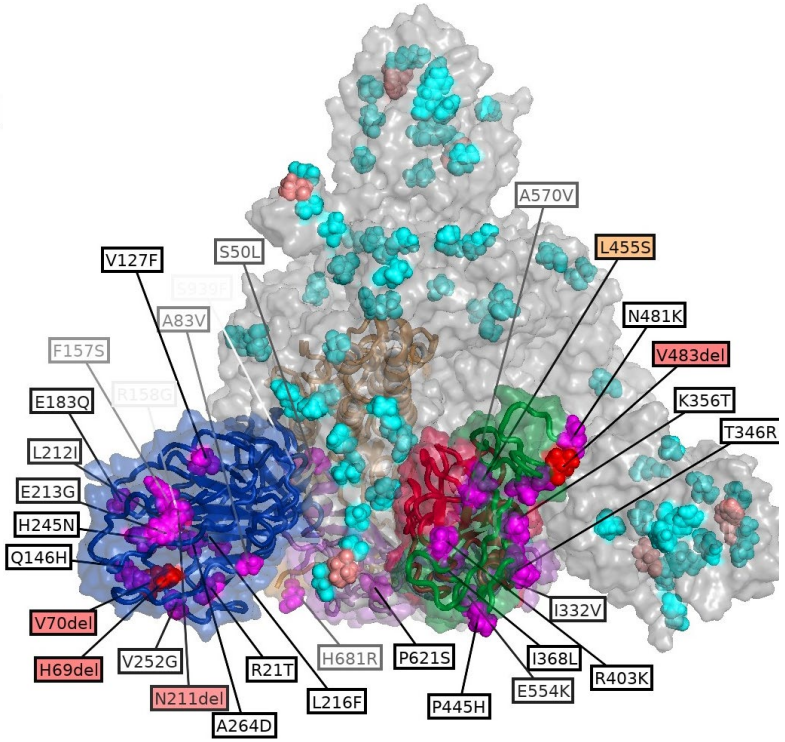
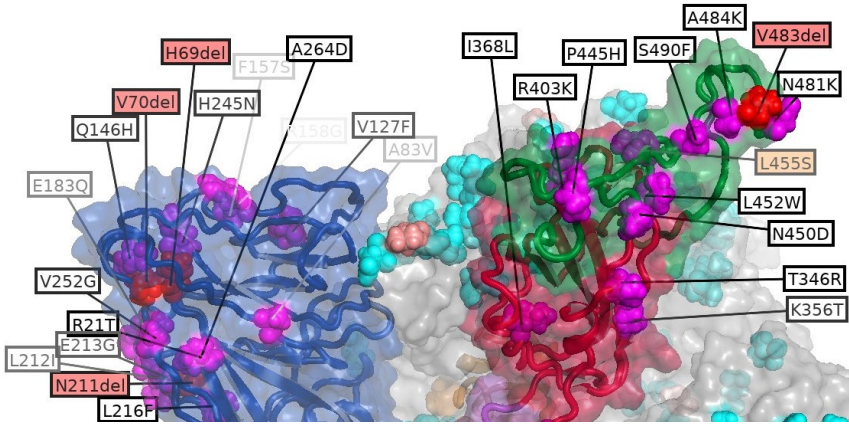
Brown – S2



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



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

Convergent evolution of XBB and JN.1 lineages

Key changes in the spike receptor binding domain (RBD)* May 2023 – May 2024

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.

† The XBB.1.5 spike protein sequence was used as a reference because of its inclusion in updated 2023–2024 COVID-19 vaccines. Substitutions compared to Wuhan-Hu-1 are underlined.

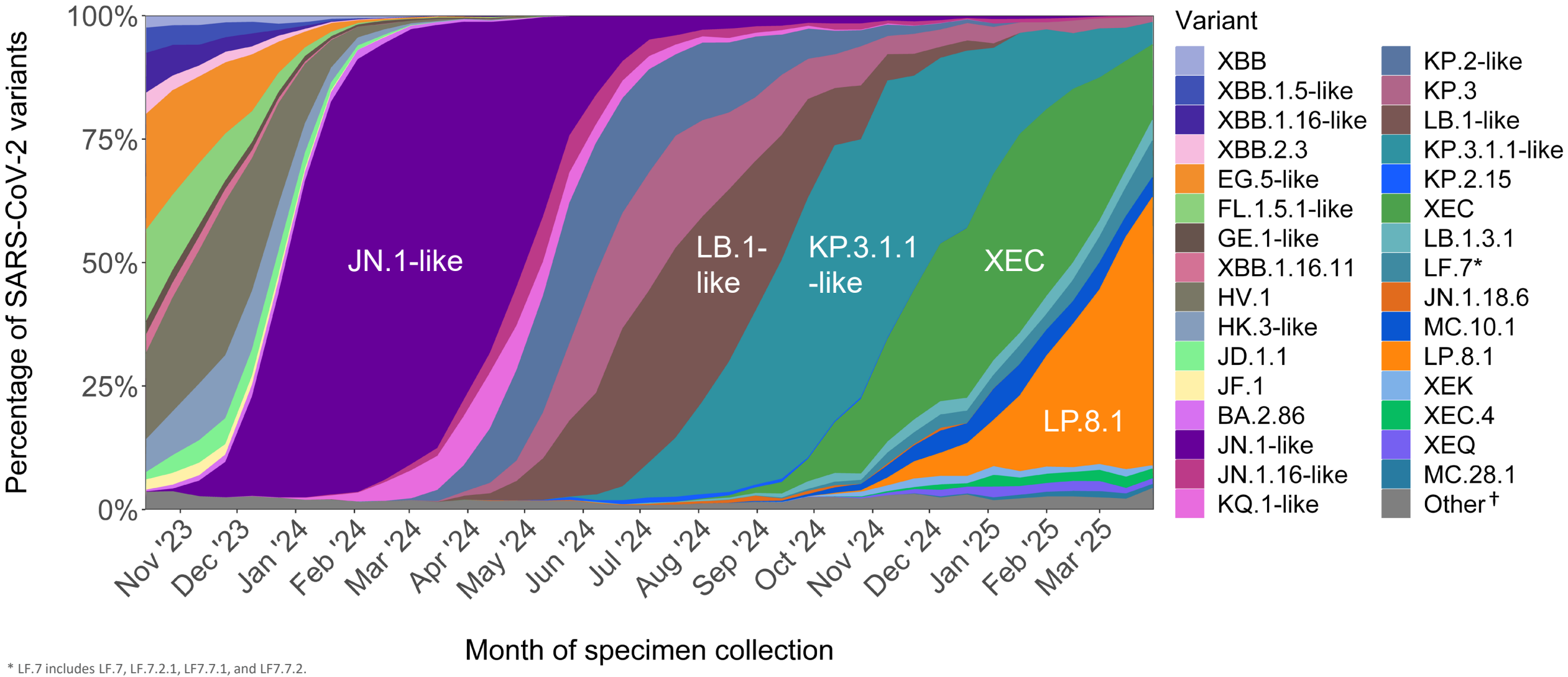
§ Indicates sites of independent substitutions in at least two different evolutionary lineages.

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

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

Weighted SARS-CoV-2 Variant Proportion Estimates: XBB and JN.1 Lineages

United States, October 1, 2023–March 29, 2025

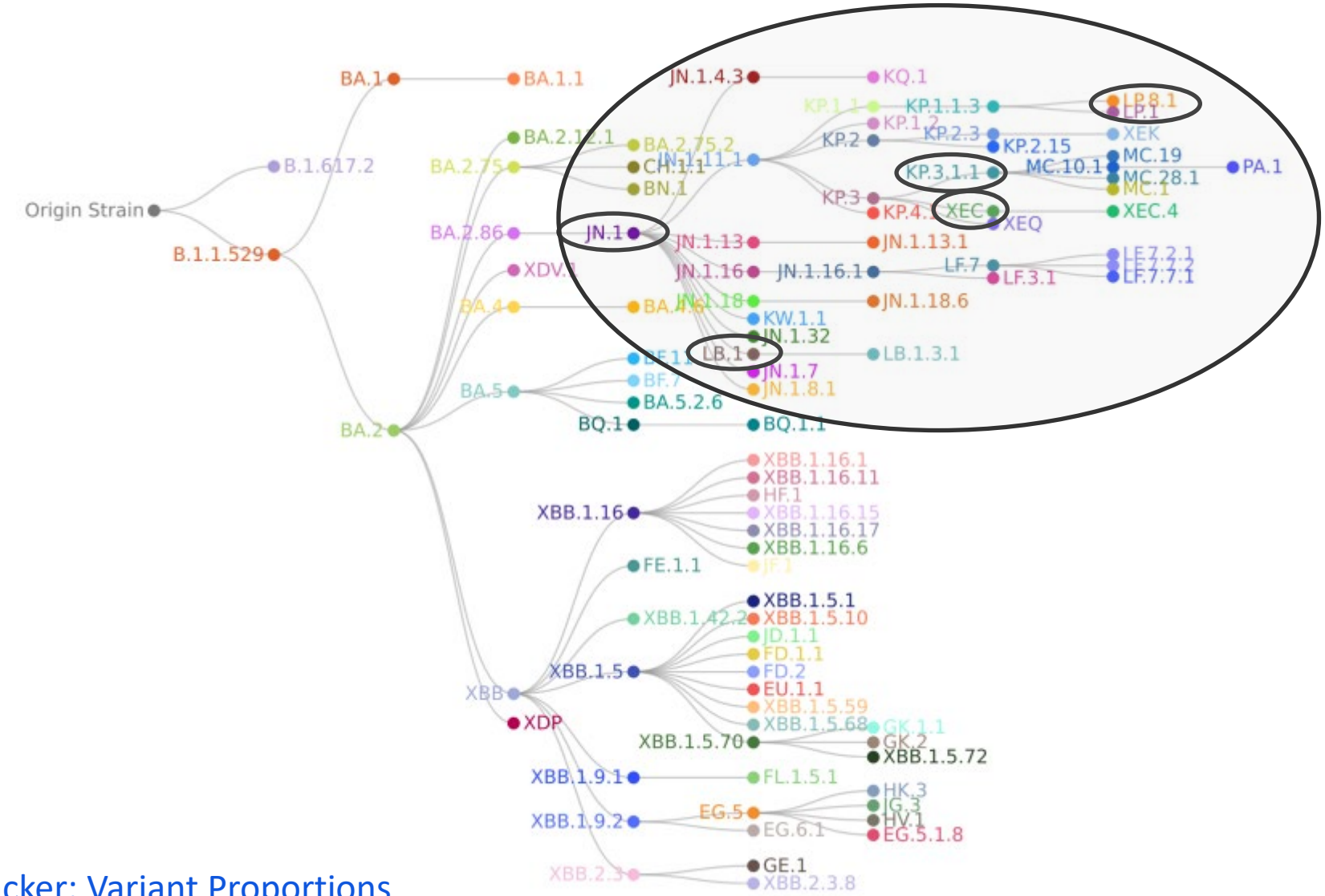


* LF.7 includes LF.7, LF.7.2.1, LF7.7.1, and LF7.7.2.

† "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."

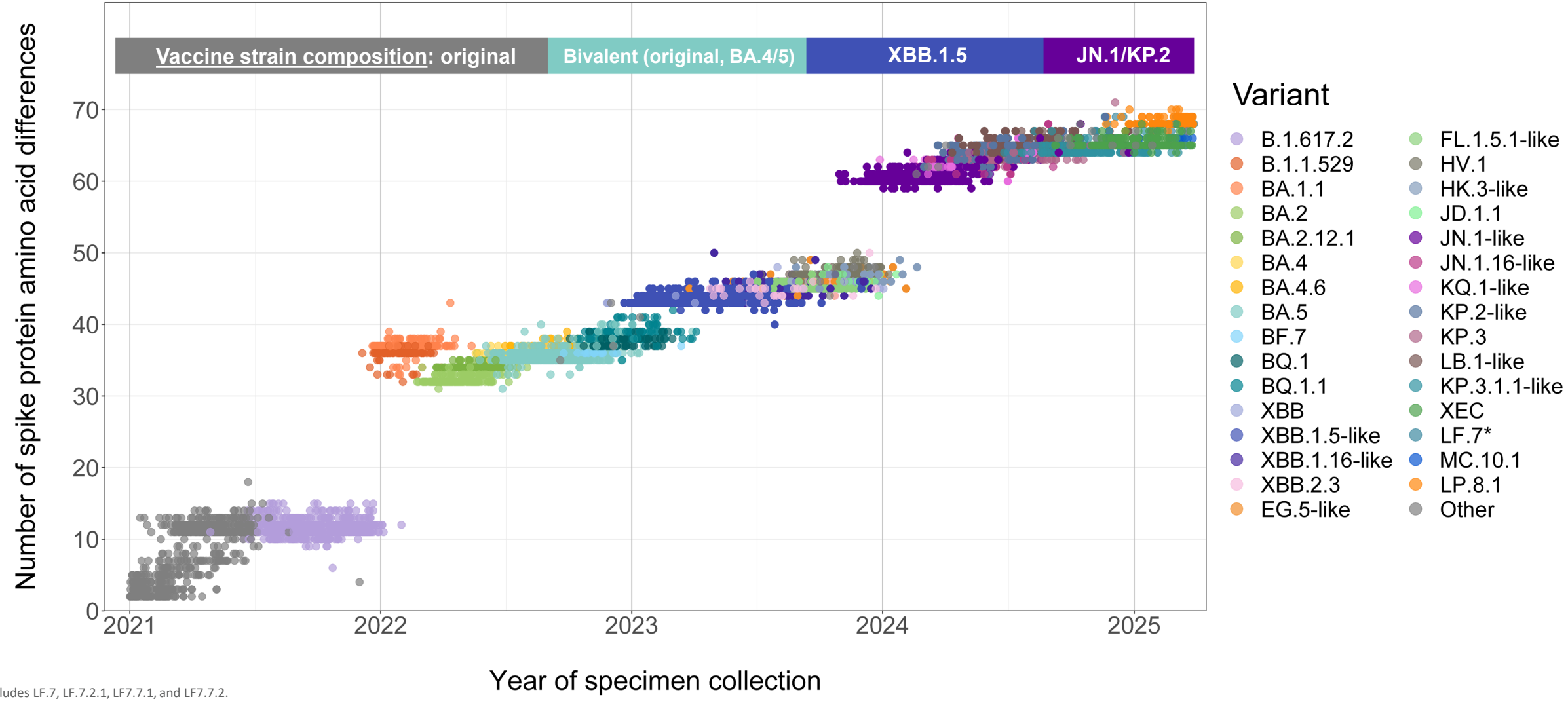
Viruses that have predominated since January 2025 are all JN.1 descendants



CDC COVID Data Tracker: Variant Proportions

Subsampled SARS-CoV-2 sequences by lineage group, date of specimen collection, and number of spike protein amino acid differences relative to Wuhan-Hu-1 reference

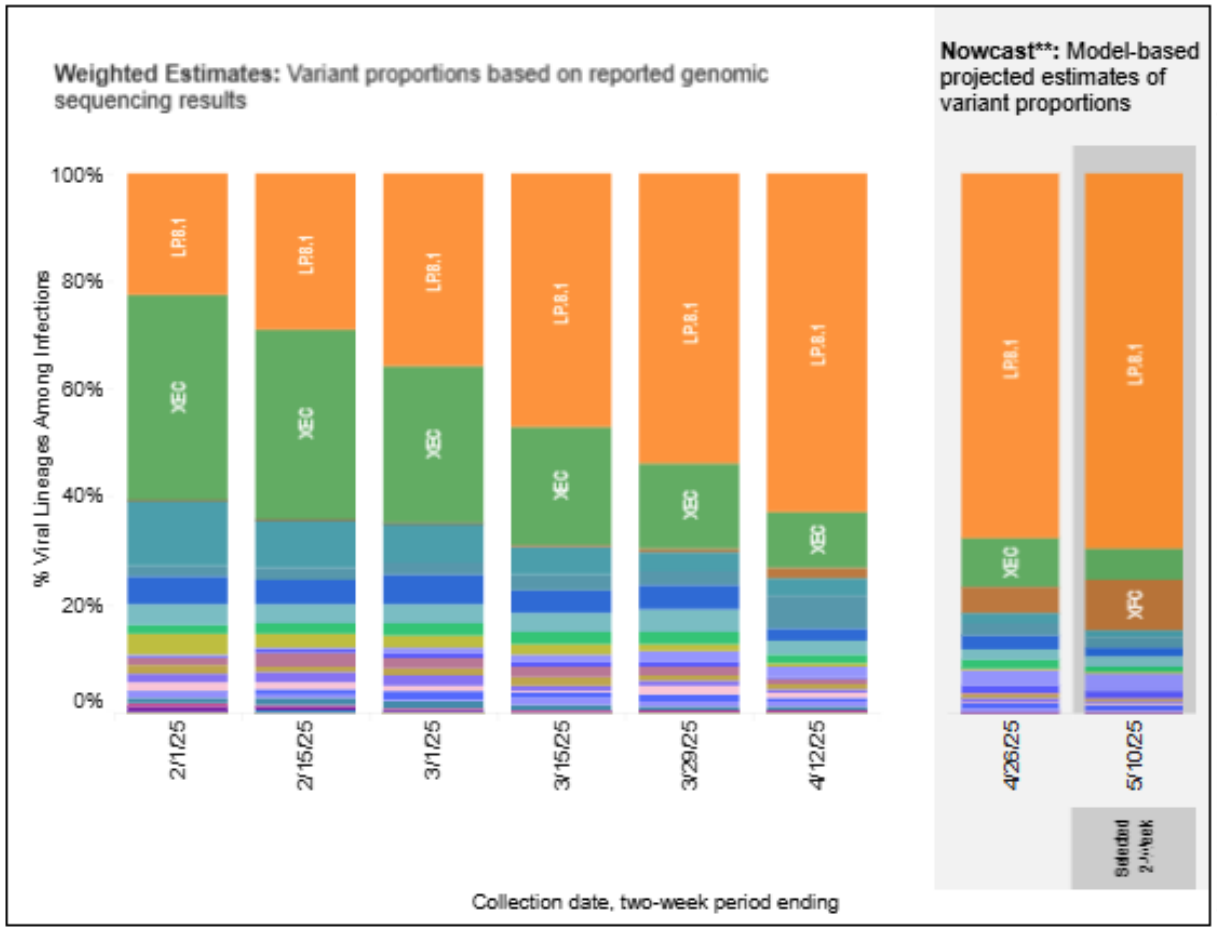
United States, January 1, 2021–March 29, 2025



* LF.7 includes LF.7, LF.7.2.1, LF7.7.1, and LF7.7.2.

Sequences were subsampled (100 per month) for analysis from an initial dataset of >1 million sequences spanning January 1, 2021–March 29, 2025. **Only lineages circulating at >5% prevalence nationally during at least one 2-week period are displayed.** Sequences are reported to CDC through the National SARS-CoV-2 Strain Surveillance program, contract laboratories, public health laboratories, and other U.S. institutions. 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." Vaccine availability for a given composition was defined by the estimated date of earliest possible administration.

Weighted and Nowcast Estimates in the United States for 2-week Periods, 1/19/2025 – 5/10/2025



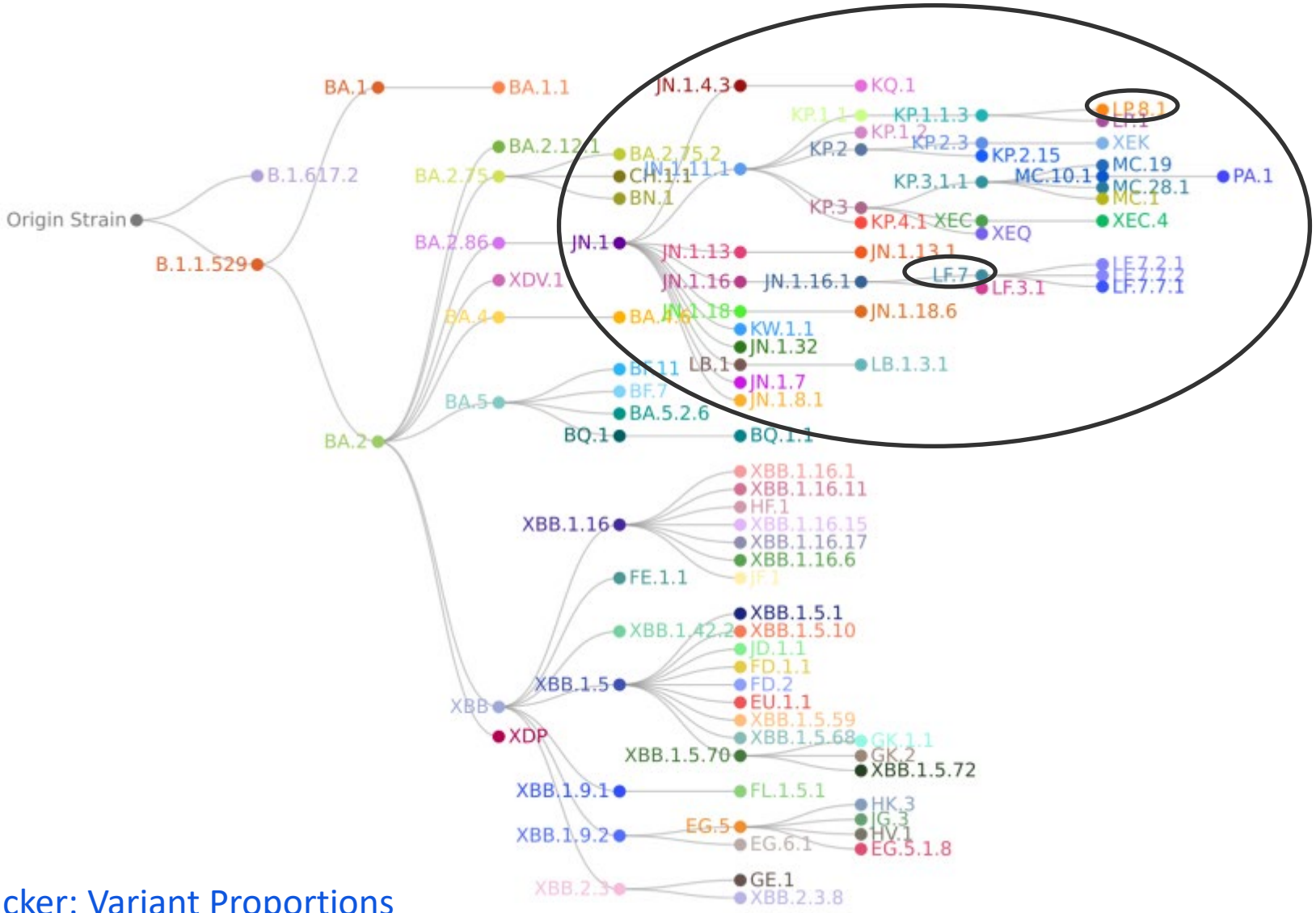
USA

WHO label	Lineage #	%Total	95%PI
Omicron	LP.8.1	70%	64–75%
	XFC	9%	4–19%
	XEC	6%	4–8%
	LF.7.7.2	3%	0–16%
	LF.7	2%	1–3%
	MC.10.1	2%	1–3%
	LB.1.3.1	2%	1–3%
	KP.3.1.1	1%	1–2%
	XEC.4	1%	1–2%
	PA.1	1%	0–3%
	LF.7.7.1	1%	1–2%
	XEQ	0%	0–1%
	LF.7.2.1	0%	0–1%
	KP.3	0%	0–1%
	XEK	0%	0–1%
	MC.1	0%	NA
	JN.1.16	0%	NA
	MC.19	0%	NA
	JN.1	0%	NA

** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
# 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% nationally during all 2-week periods displayed. While all lineages are tracke by CDC, those named lineages not enumerated in this graphic are aggregated with their parent lineages, based on Pango lineage definitions, described in more detail here: https://web.archive.org/web/20240116214031/https://www.pango.network/the-pango-nomenclature-system/statement-of-nomenclature-rules.

CDC COVID Data Tracker: Variant Proportions: Updated 5/12/2025

All currently circulating viruses are JN.1 descendants



[CDC COVID Data Tracker: Variant Proportions]

Convergent Evolution of Different Omicron JN.1 Lineages

Key changes in the spike receptor binding domain (RBD)* detected relative to KP.2

Lineage	*N-terminal domain*								*Receptor binding domain*								*S2*				
	22	31	59	146	182	183	186	190	346	435	444	445	456	493	572	679	748	929	1086	1104	1235
KP.2 Reference†	**T**	**S**	**F**	**H**	**K**	**Q**	**F**	**R**	**T**	**A**	**K**	**H**	**L**	**Q**	**T**	**K**	**E**	**S**	**K**	**L**	**C**
KP.3									R					E							
KP.3.1.1		Δ							R					E							
KP.3.3									R					E							
KP.2.3		Δ		Q														I			
JN.1									R				F							V	
JN.1.16				Q					R											V	
JN.1.18.6	N		S																		
KP.2.15		Δ																			
LB.1		Δ				H														V	
LF.7	N	P			R			S			R				I					V	
LP.8.1		Δ					L	S				R		E					R		
MC.10.1		Δ							R	S				E							
MC.28.1		Δ								S				E							F
XEC	N		S						R					E							
XEC.4	N		S						R					E	I						
XEK	N		S						R					E			Q				
XFC	N	P			R			S				R		E		R			R		

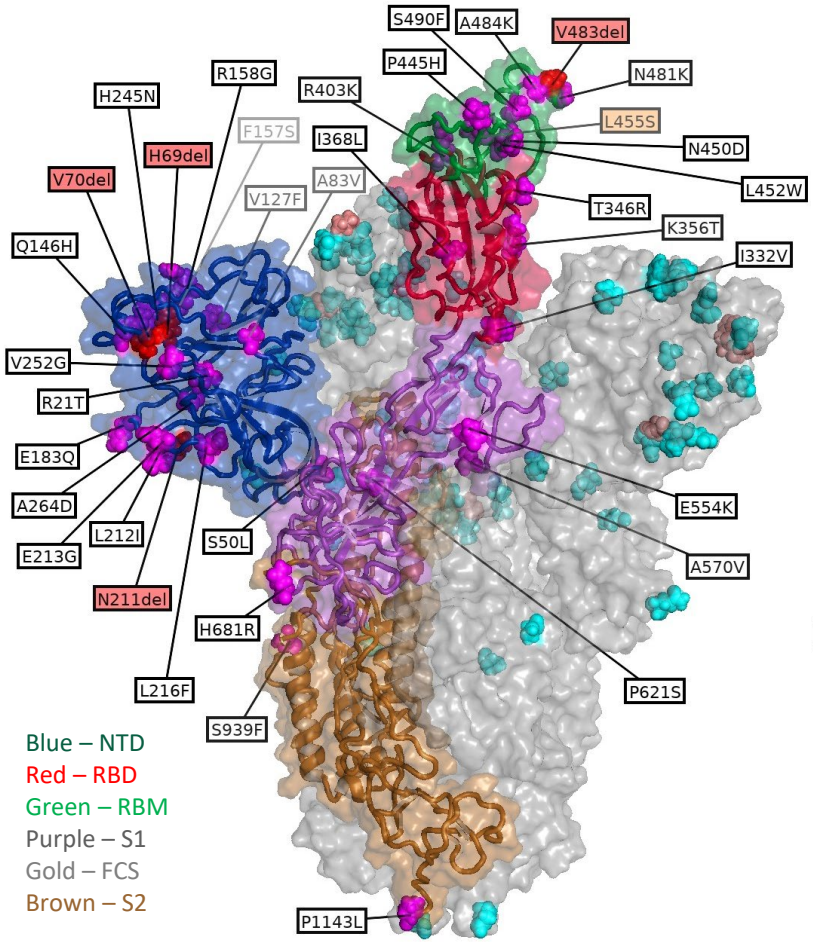
* Lineages or lineage groups with ≥1% prevalence in at least one 2-week period and substitutions present in ≥50% of sequences belonging to a lineage were included.

† The KP.2 spike protein sequence was used as a reference because of its inclusion in updated mRNA-based 2024–2025 COVID-19 vaccines. Substitutions compared to Wuhan-Hu-1 are underlined.

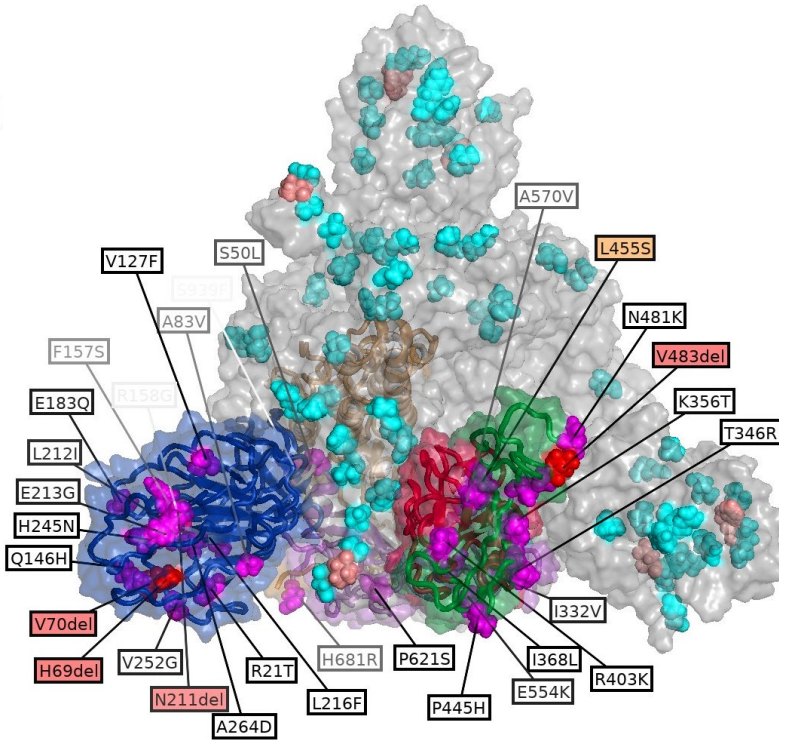
§ Indicates sites of independent substitution or deletion in at least two different evolutionary lineages.

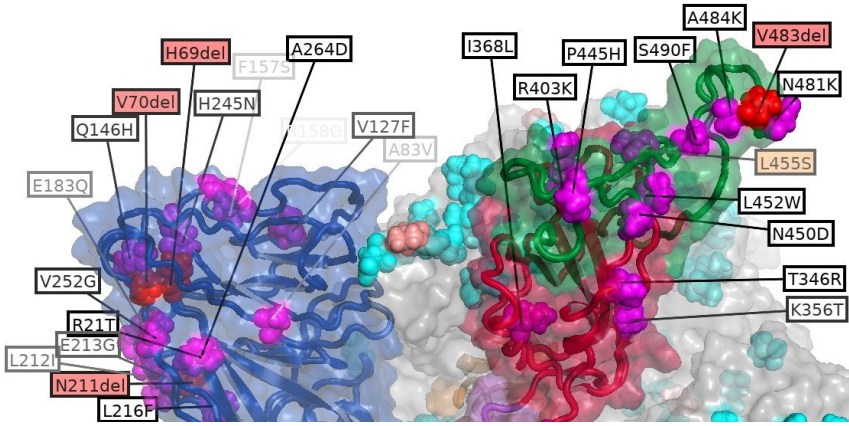
Bolded sub-lineages are expanding in the United States as of May 10, 2025.

In June 2024, JN.1-viruses were predominate: JN.1 vs. 2023-2024 vaccine (XBB.1.5) had numerous spike substitutions



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

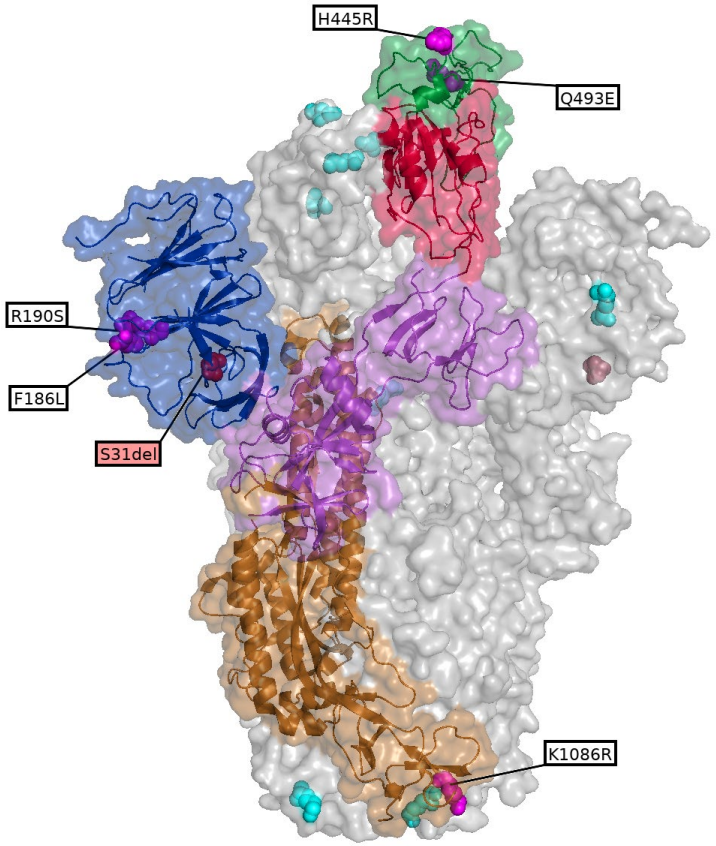


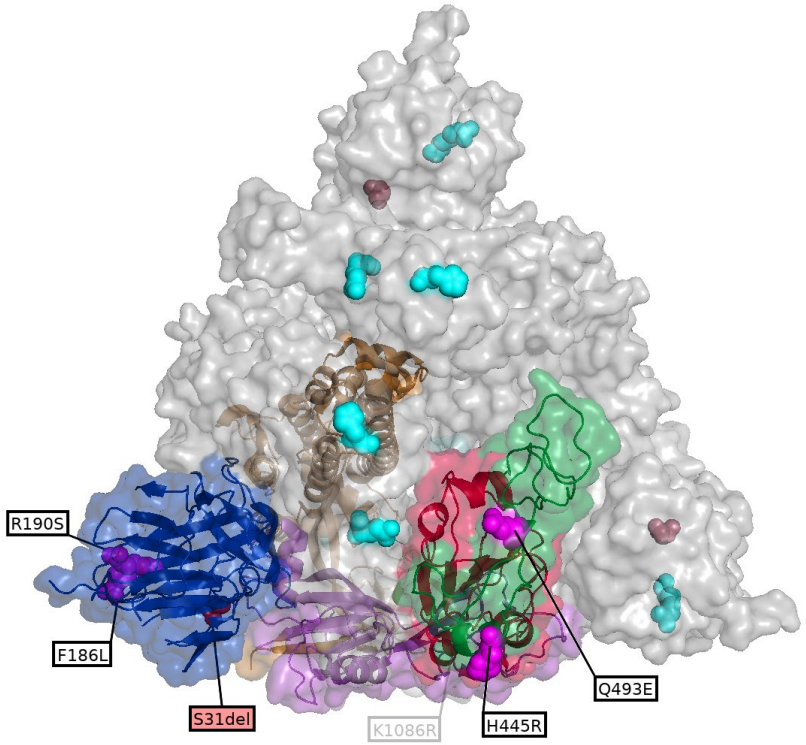


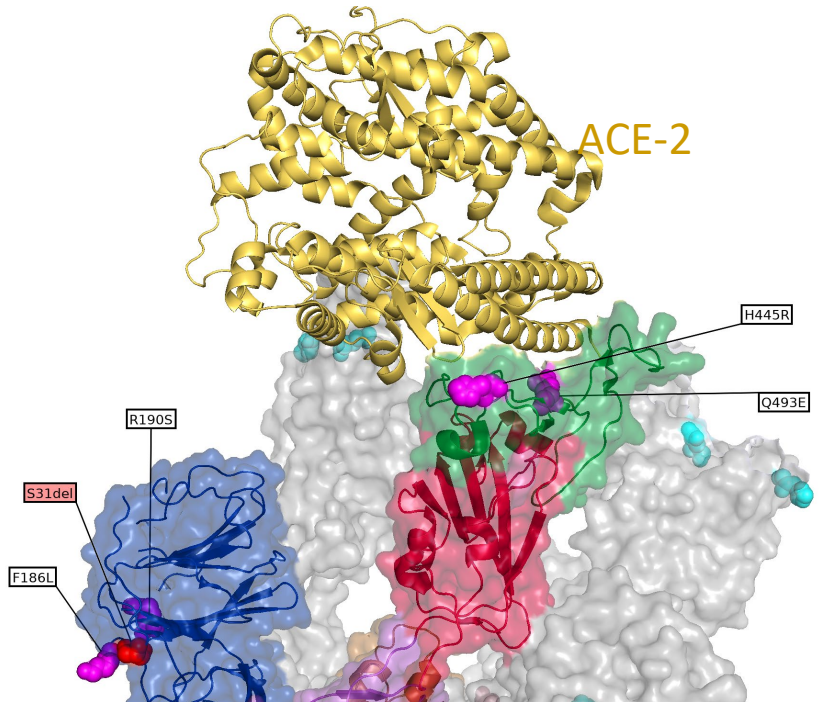
Red sphere – deletions in one chain (labeled)
Magenta sphere – substitutions in one chain (labeled)
Raspberry sphere – deletions in rest 2 chains
Cyan sphere – substitutions in rest 2 chains

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

LP.8.1, the current most prevalent lineage, has limited spike substitutions in comparison to KP.2







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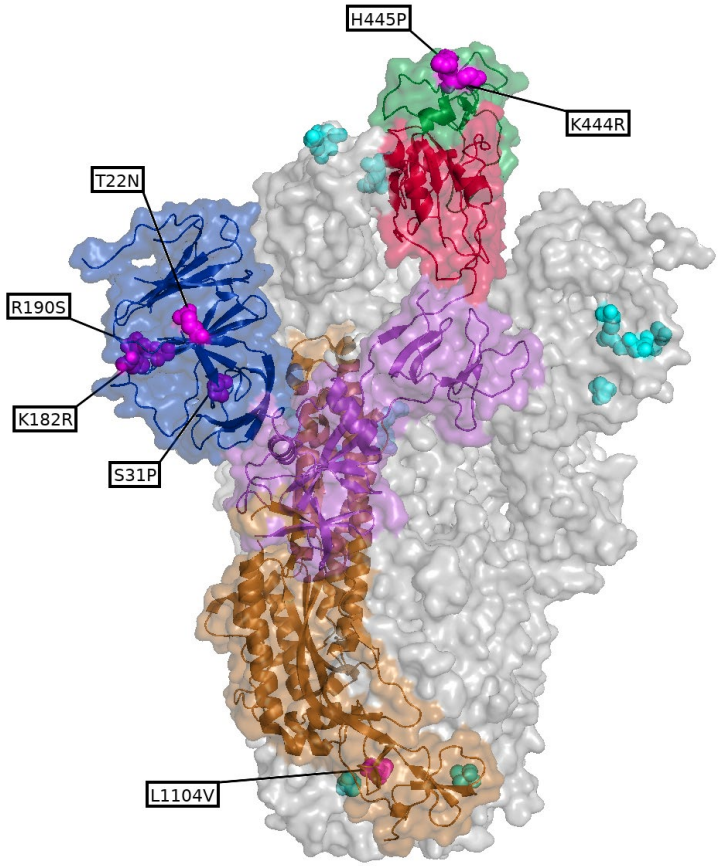
Brown – S2

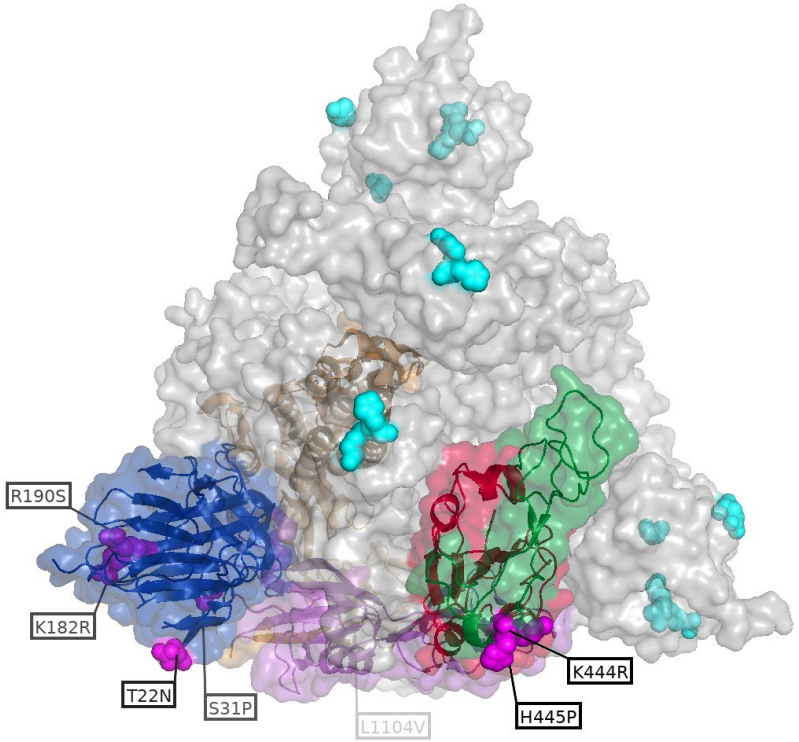
Structure of JN.1 (PDB ID: 8Y5J)

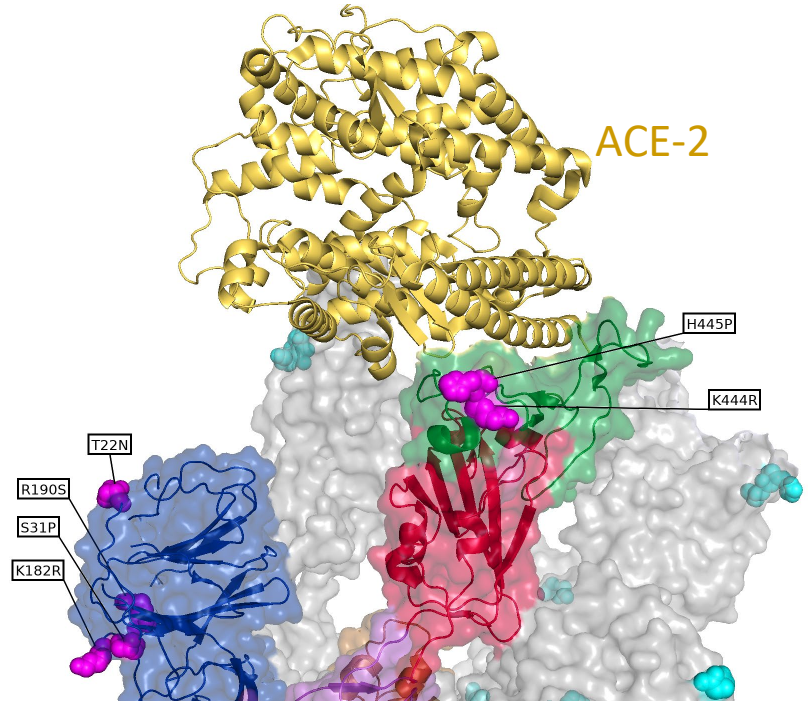
Structure of JN.1 in complex with ACE-2 (PDB ID: 8YZE)

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

LF.7.7.2 also has limited spike substitutions in comparison to KP.2 spike







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

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

Structure of JN.1 (PDB ID: 8Y5J)

Structure of JN.1 in complex with ACE-2 (PDB ID: 8YZE)

Situational report BA.3.2

- A new lineage that would represent a potential shift has been detected – BA.3.2
  - 4 sequences worldwide as of 5/12/25
    - 3 in South Africa (11/22/24 – 1/10/25)
    - 1 in Netherlands (4/2/25)
  - Has only been detected in South Africa through waste water surveillance
  - 54-56 aa substitutions compared to KP.2

Recommended sample sizes for detecting rare variants

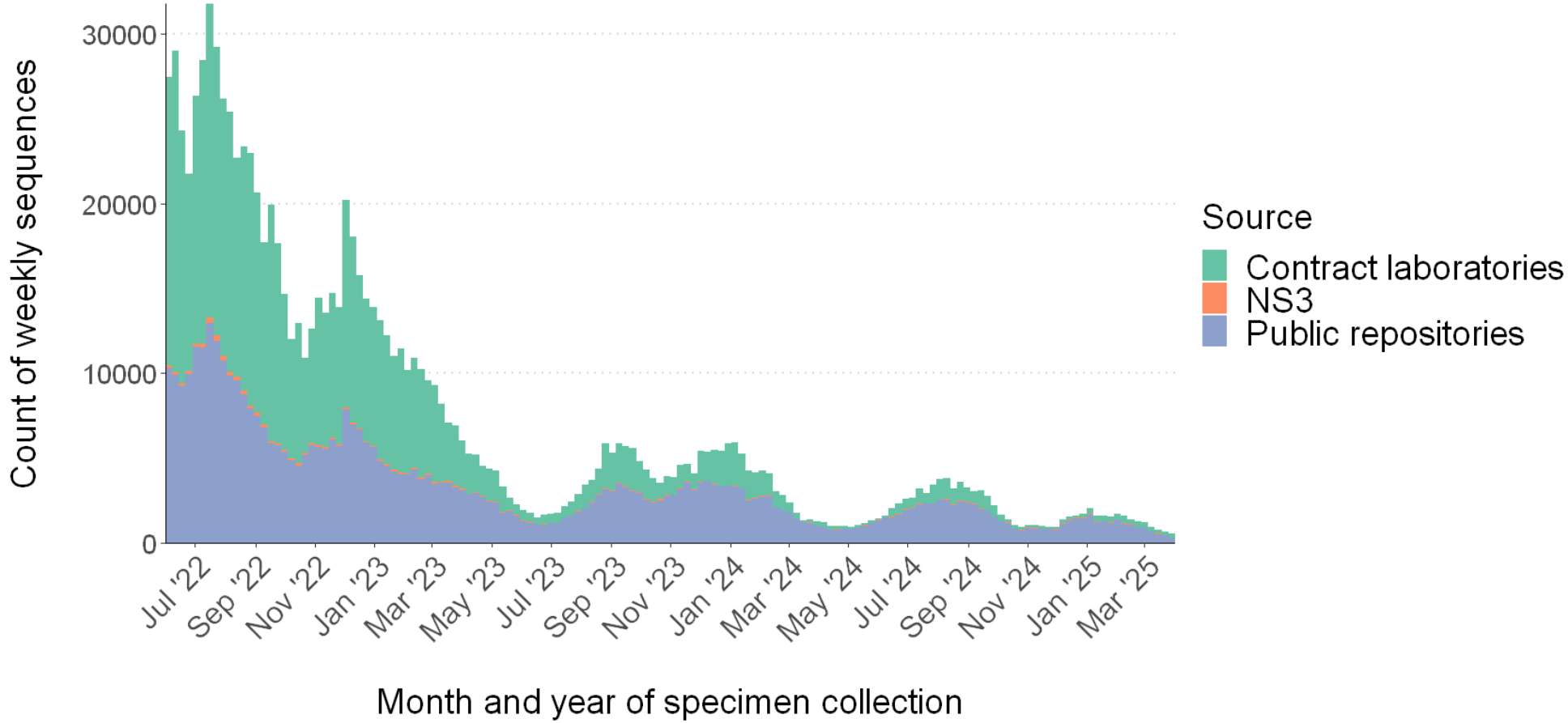
	Minimum COVID+ Sequences		
Detection Threshold	99% Confidence	95% Confidence	90% Confidence
1/1000 (0.10%)	4603	2995	2302
1/400 (0.25%)	1840	1197	920
1/200 (0.50%)	919	598	460
1/100 (1.00%)	459	299	230
1/50 (2.00%)	228	149	114
1/25 (4.00%)	113	74	57

- With current sequencing numbers, we have about 0.25% detection threshold for weighted estimates

Variant Detection Calculator

Weekly counts of sequences generated by or submitted to CDC* from the National SARS-CoV-2 Strain Surveillance program,† contract commercial laboratories, and public repositories§

United States, June 1, 2022–March 29, 2025

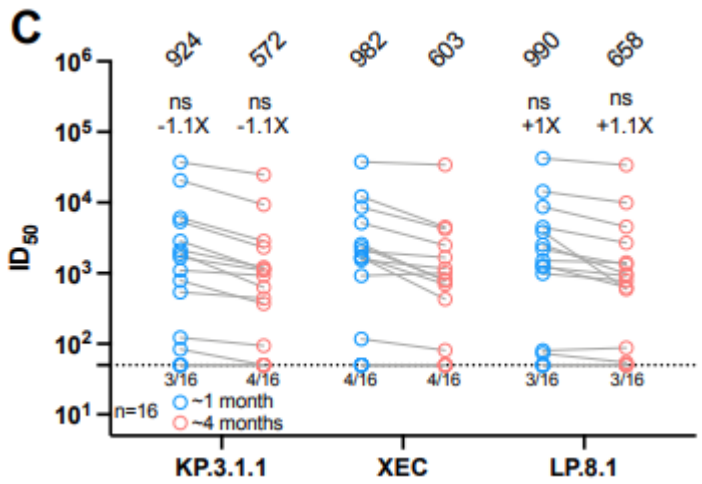


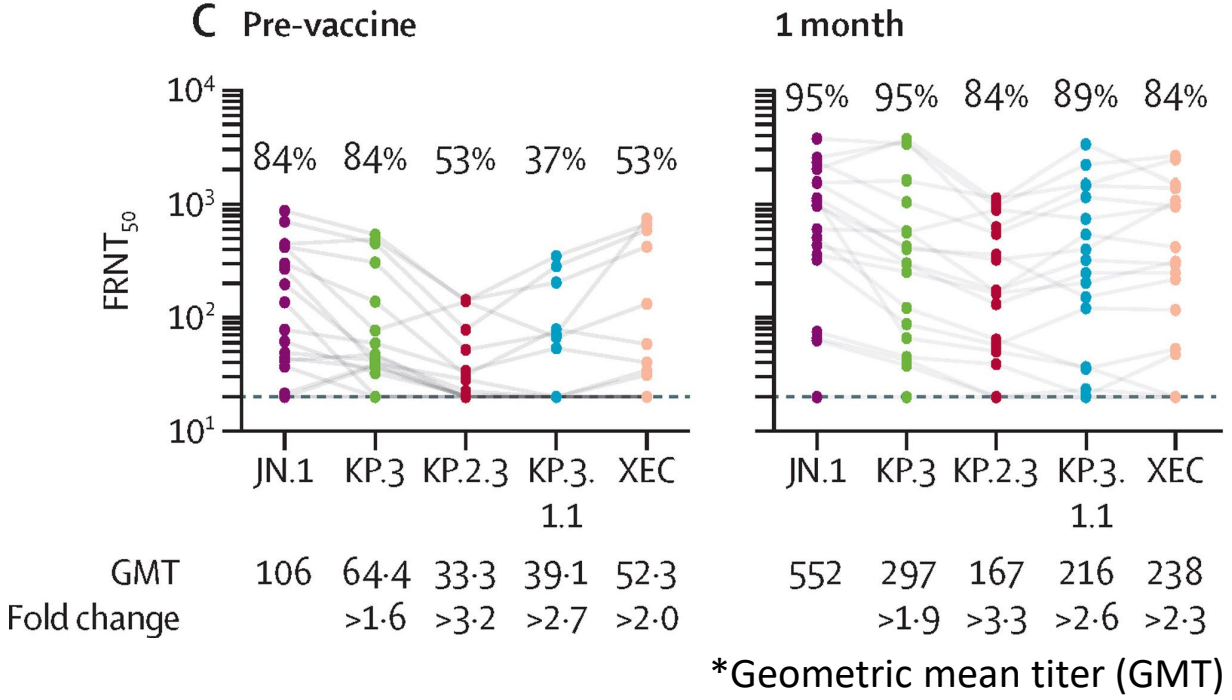
* https://covid.cdc.gov/covid-data-tracker/#published-sars-cov-2-sequences

† https://www.cdc.gov/covid/php/variants/

§ Sequences with metadata labelled as baseline surveillance were obtained from repositories including the Global Initiative on Sharing All Influenza Data repository and National Center for Biotechnology Information GenBank. Data were quality-filtered by only including human-derived sources and United States–specific sequences and screened for valid state names and laboratory sources.

Human sera collected after 2024-2025 COVID-19 vaccination neutralizes LP.8.1 pseudoviruses and XEC virus

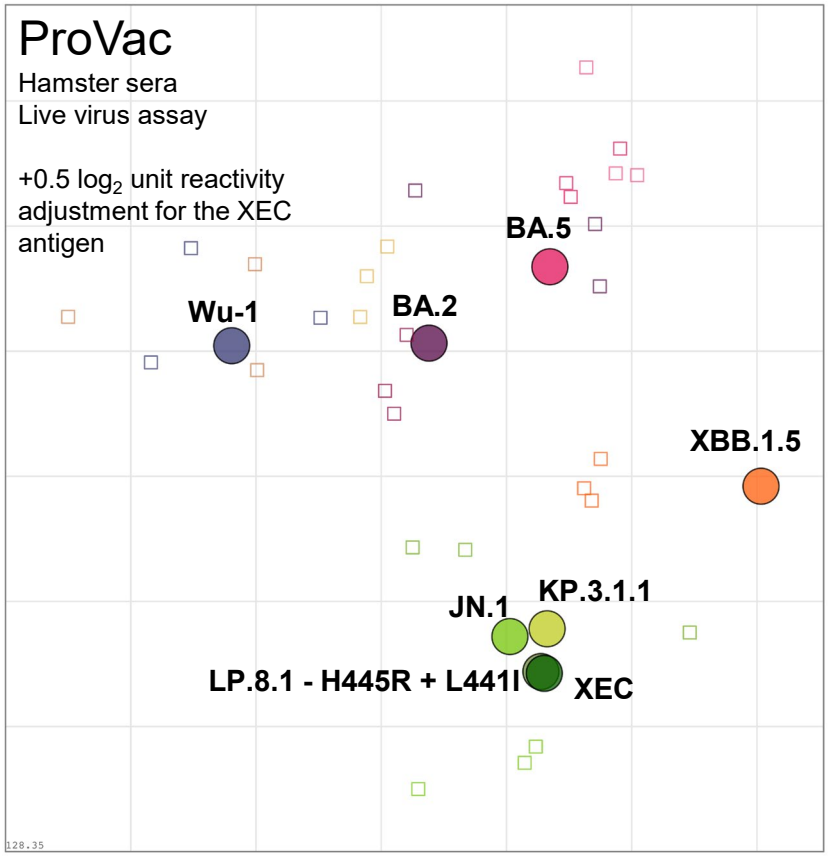




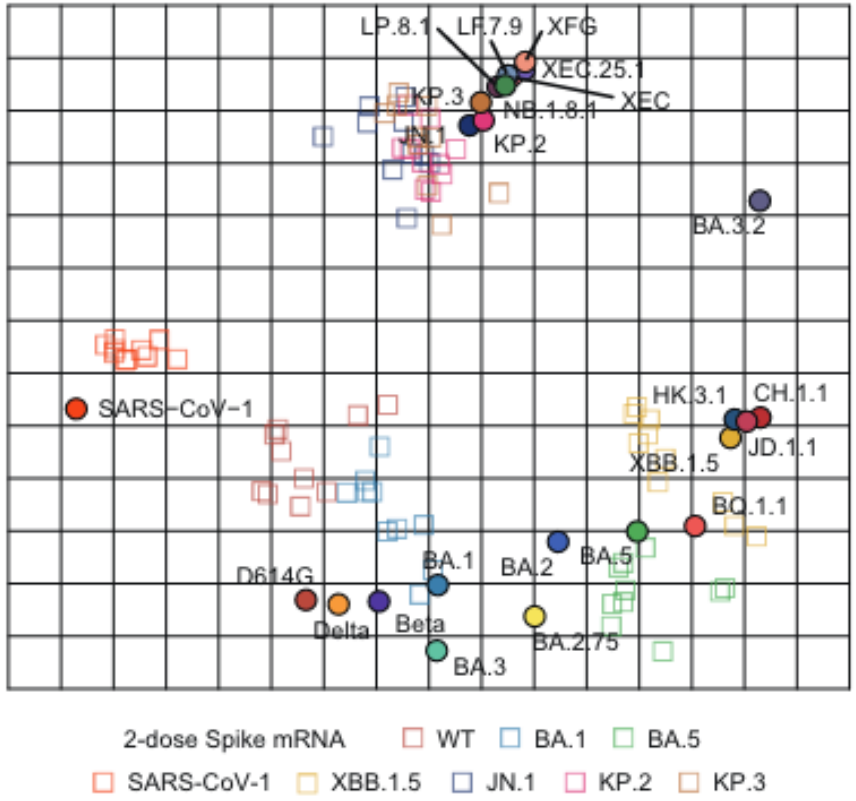
[Mellis et al. bioRxiv: Do Existing COVID-19 Vaccines Need to Be Updated in 2025?]

[Suthar et al. The Lancet Infectious Diseases: The KP.2-adapted COVID-19 vaccine improves neutralising activity against the XEC variant - ScienceDirect]

Antigenic cartography with hamster and human sera indicate that JN.1 lineage viruses group together



Francis Crick Institute
MRC University of Glasgow Centre for Virus Research
Center for Pathogen Evolution, University of Cambridge



[Antigenic and Virological Characteristics of SARS-CoV-2 Variant BA.3.2, XFG, and NB.1.8.1]

Conclusions

- Since June 2024, the 2024 summer COVID-19 wave was larger than the 2024-2025 winter wave
- Hospitalization rates have declined since 2021-2022 among all age groups, but are highest among the older adults and infants <6 months of age.

- Current viruses are JN.1 descendants with 2-3 substitutions in the spike receptor binding domain in comparison to KP.2 spike
- Current viruses are neutralized with sera from participants who received the 2024-2025 COVID-19 vaccine
- Antigenic cartography indicates JN.1 viruses are antigenically similar

- A new lineage, BA.3.2, has been identified that could indicate a shift, however very few sequences have been detected world-wide

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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 U.S. Centers for Disease Control and Prevention.

Updates to COVID-19 Vaccine Effectiveness

Ruth Link-Gelles, PhD, MPH

CDR, US Public Health Service

Centers for Disease Control and Prevention

May 2025

Agenda – COVID-19 vaccine effectiveness (VE)

- **Vaccine effectiveness methods & context**
- **Estimates of *2023-2024* (monovalent XBB.1.5) COVID-19 Vaccine Effectiveness in *Children****
- **Interim Estimates of *2024-2025* (monovalent KP.2 or JN.1) COVID-19 Vaccine Effectiveness in *Adults***
  - Strain-specific vaccine effectiveness
- **Conclusions**

Note that due to both low COVID-19 vaccine coverage in children, as well as relatively lower baseline rates of disease compared to earlier seasons, VE could not yet be estimated for children in the 2024-2025 season

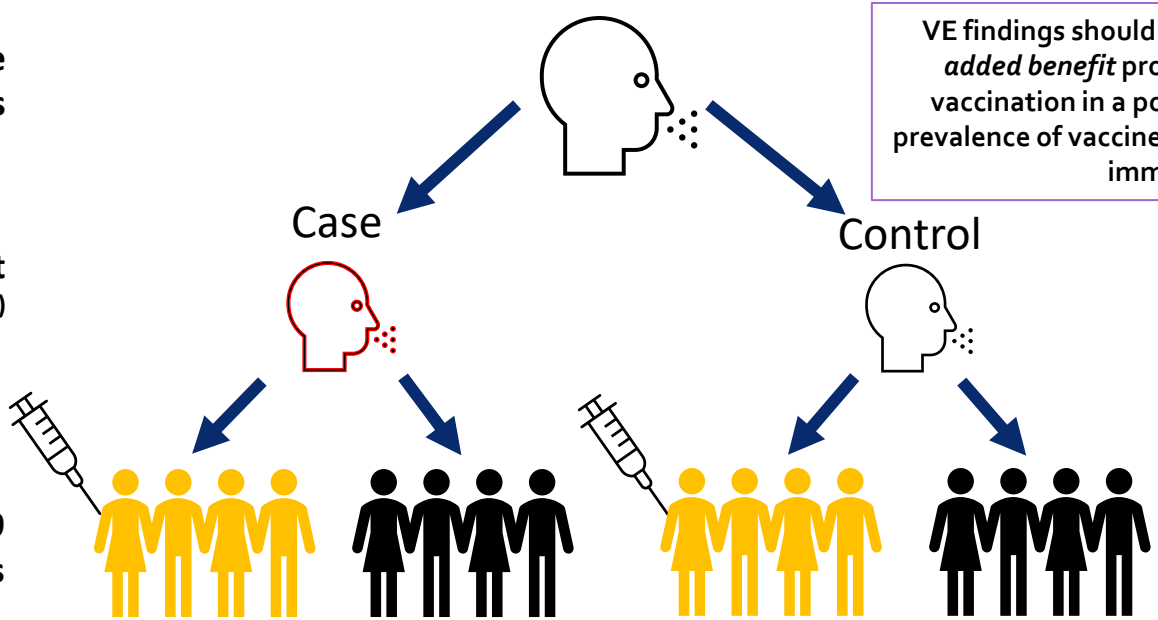
Methods & Context

For respiratory viruses, CDC primarily uses test-negative design (TND) studies to measure vaccine effectiveness (VE)

Person with acute respiratory illness

Pathogen test
(e.g., SARS-CoV-2, RSV, flu, etc.)

COVID-19 vaccination status



VE findings should be interpreted as the *added benefit* provided by COVID-19 vaccination in a population with a high prevalence of vaccine- and infection-induced immunity.

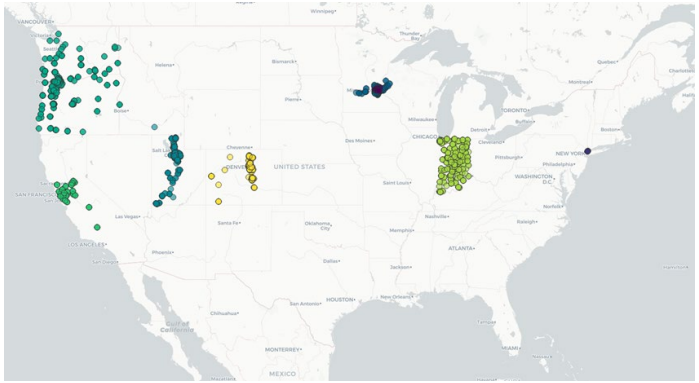
Effectiveness = 1 – (odds ratio) x 100% Odds ratio = $\frac{Odds\ of\ immunization_{cases}}{Odds\ of\ immunization_{controls}}$

VISION Multi-Site Network of Electronic Health Records

>300 emergency departments and urgent cares clinics and >200 hospitals

- **Design:** Test-negative design

- **Population:** Persons visiting a participating emergency department or urgent care (ED/UC) or hospitalized with COVID-19-like illness (CLI) with a SARS-CoV-2 NAAT test result within 10 days before or 72 hours after encounter
  - **Cases**: CLI with *positive* NAAT or antigen for SARS-CoV-2 and no positive NAAT for RSV or influenza
  - **Controls**: CLI with *negative* NAAT for SARS-CoV-2 and no positive NAAT for influenza (≥18 years) or RSV (≥60 years)



- **Vaccination data:** Documented by electronic health records and state and city registries

CLI = COVID-19-like illness; ED/UC = emergency department/urgent care; RSV = respiratory syncytial virus; NAAT = nucleic acid amplification test
CLI is defined based on the presence of specific discharge diagnosis codes. Additional methods available: Link-Gelles, et al. MMWR. https://www.cdc.gov/mmwr/volumes/74/wr/mm7406a1.htm

IVY Network — 26 hospitals, 20 U.S. States

- **Design**: Test-negative, case-control design
- **Population**: 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
  - **Cases:** CLI and test *positive* for SARS-CoV-2 by NAAT or antigen
  - **Controls**: CLI and test *negative* for SARS-CoV-2, influenza and RSV by RT-PCR
- **Vaccination data:** Electronic medical records (EMR), state and city registries, and plausible self-report
- **Specimens:** Nasal swabs obtained on all patients for central RT-PCR testing and whole genome sequencing

IVY

INVESTIGATING RESPIRATORY VIRUSES IN THE ACUTELY ILL

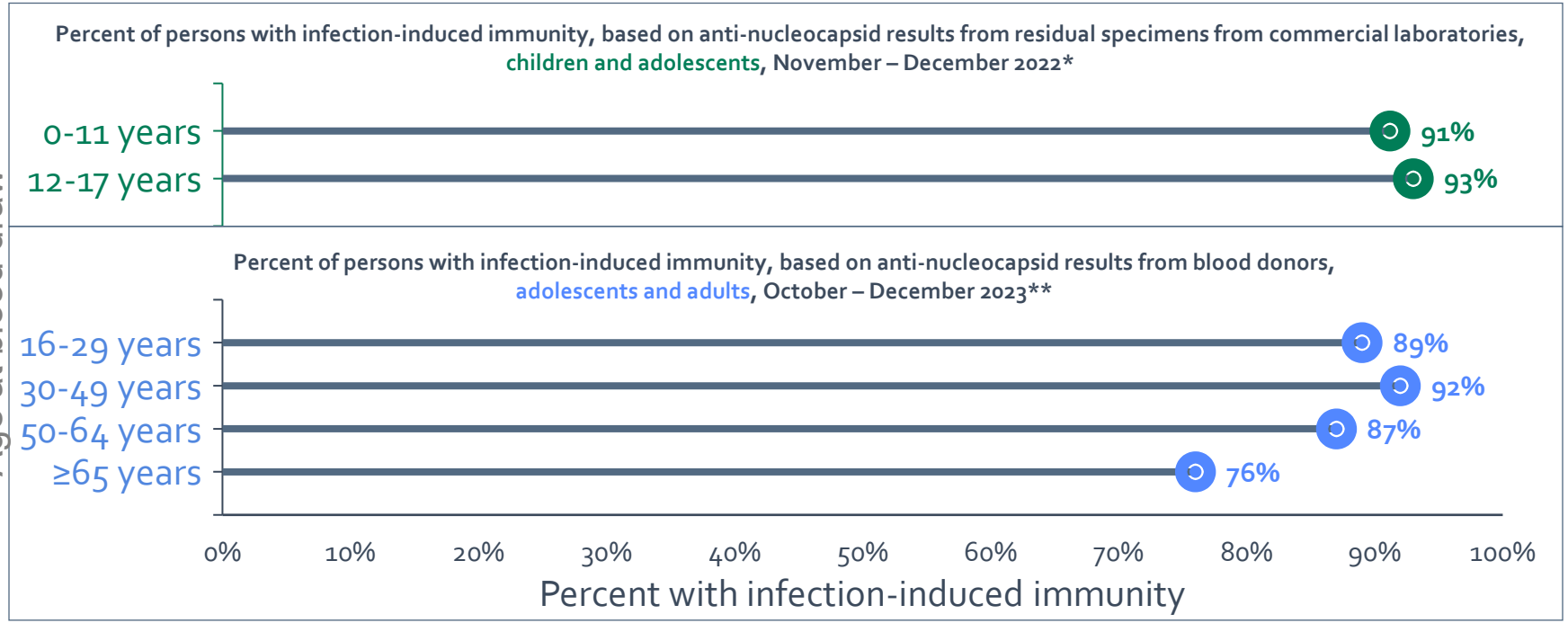
*CLI is defined as presence of any one of the following: fever, cough, shortness of breath, chest imaging consistent with pneumonia, or hypoxemia
NAAT = nucleic acid amplification test

Measuring COVID-19 vaccine effectiveness

Measure	Definition*	Example vaccinated group	Example comparison group
Absolute VE	Compares frequency of health outcomes in vaccinated and unvaccinated people	Received original monovalent dose	Received no COVID-19 vaccines ever
Relative VE	Compares frequency of health outcomes in people who received one type of vaccine to people who received a different vaccine	Received bivalent dose	Eligible for, but did not receive, bivalent COVID-19 vaccine, but received original monovalent dose
VE of 2023-2024 COVID-19 vaccines	Compares people who received 2023-2024 COVID-19 vaccine to people who did not, regardless of past COVID-19 vaccination	Received 2023-2024 dose	Eligible for, but did not receive, an 2023-2024 dose, regardless of past COVID-19 vaccination history
VE of 2024-2025 COVID-19 vaccines	Compares people who received 2024-2025 COVID-19 vaccine to people who did not, regardless of past COVID-19 vaccination	Received 2024-25 dose	Eligible for, but did not receive, an 2024-25 dose, regardless of past COVID-19 vaccination history

* Prior SARS-CoV-2 infection is not generally considered as it is documented inconsistently in medical records.

Context for interpreting COVID-19 VE across age groups: high infection-induced seroprevalence in children and adults



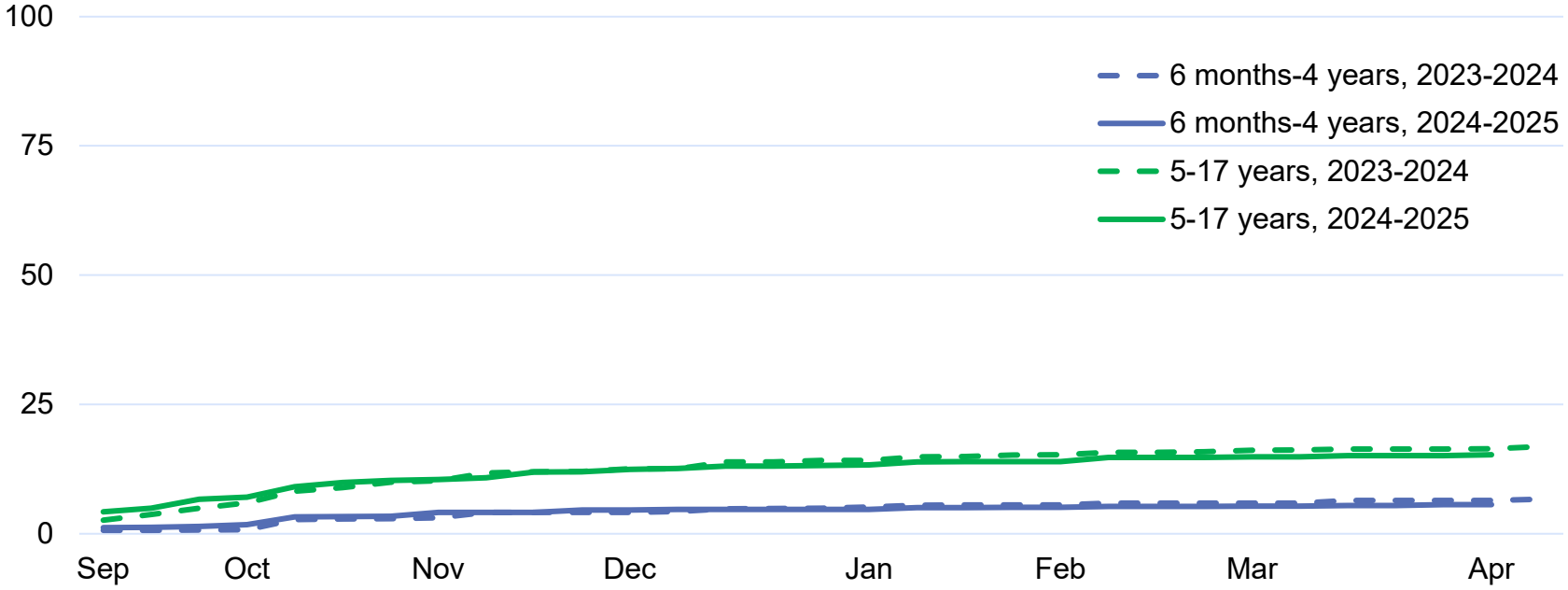
VE findings should be interpreted as the *added benefit* provided by COVID-19 vaccination in a population with a high prevalence of vaccine- and infection-induced immunity.

* Data on persons 0-17 years from nationwide commercial laboratory testing of residual serum specimens from ~27,000 children and adolescents originally submitted for routine screening or clinical management, https://covid.cdc.gov/covid-data-tracker/#pediatric-seroprevalence

** Data on persons aged ≥16 years from a longitudinal, national cohort of ~35,000 blood donors, https://covid.cdc.gov/covid-data-tracker/#nationwide-blood-donor-seroprevalence-2022

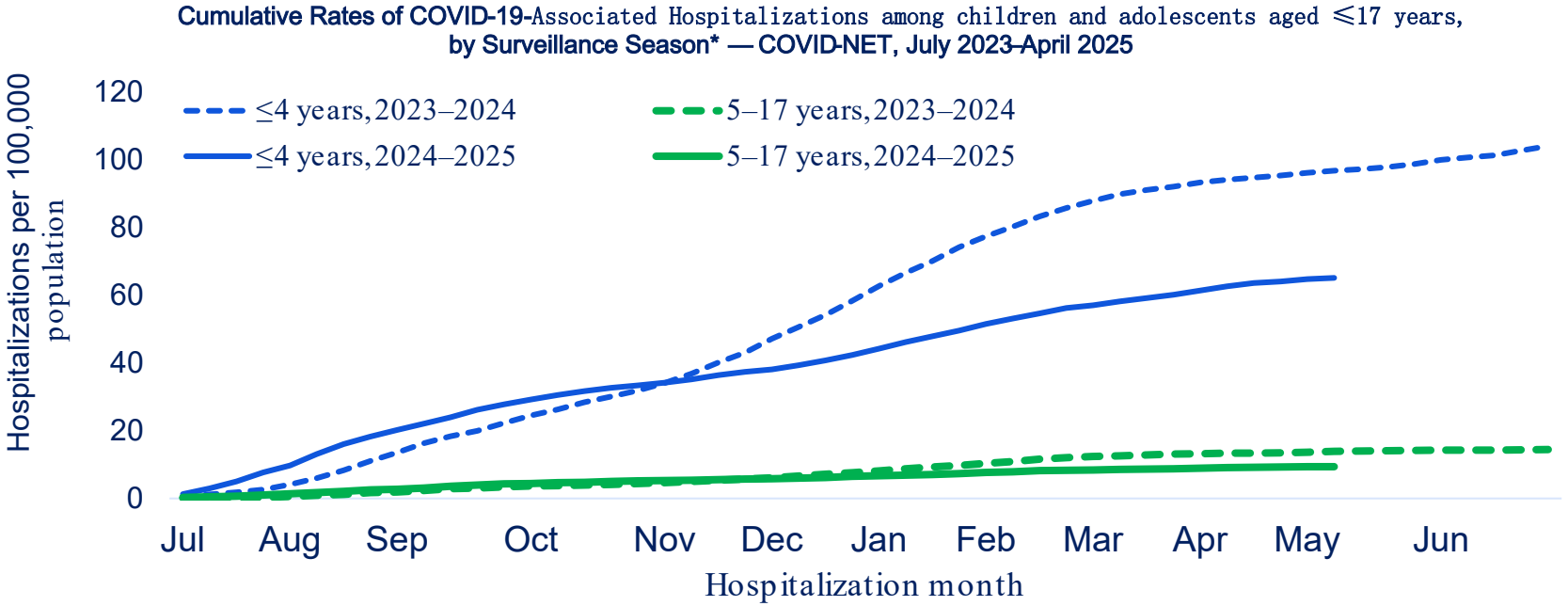
Estimates of *2023-2024* COVID-19 Vaccine Effectiveness in Children

COVID-19 Vaccination Coverage Among Children and Adolescents 6 Months-17 Years, by Season and Age Group, National Immunization Survey, 2023-2025



Weekly estimates of COVID-19 vaccination coverage and parental intent for vaccination among children through December 31, 2023, were calculated using data from the National Immunization Survey–Child COVID Module (NIS–CCM). The NIS–CCM was discontinued at the end of 2023 and questions regarding COVID-19 vaccination status and intent were added to the National Immunization Survey–Flu (NIS–Flu). NIS–CCM and NIS–Flu are national random-digit dial cellular telephone surveys of households with children ages 6 months through 17 years; NIS–Flu is conducted during October-June. The respondent to a NIS–Flu survey is a parent or guardian who said they were knowledgeable about the child's vaccination history. All estimates are based upon parental report of receipt of vaccination and month of that vaccination.
More information: https://www.cdc.gov/covidvaxview/weekly -dashboard/child-coverage-vaccination.html

Cumulative rates of COVID-19 hospitalizations for the 2024–2025 season are lower compared to 2023-2024 season.



* Seasons are defined as July through June. The 2024–2025 season shows data from July 2024–April 2025 and is ongoing.

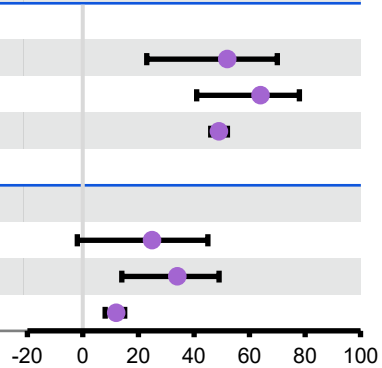
Data source: https://www.cdc.gov/resp-net/dashboard/

Note that rates are not adjusted for testing or limited to admissions where the respiratory infection is the likely primary reason for admission.

VISION: VE of *2023–2024 COVID-19 vaccine doses* against *emergency department/urgent care encounters* was similar across age groups

September 2023 – August 2024

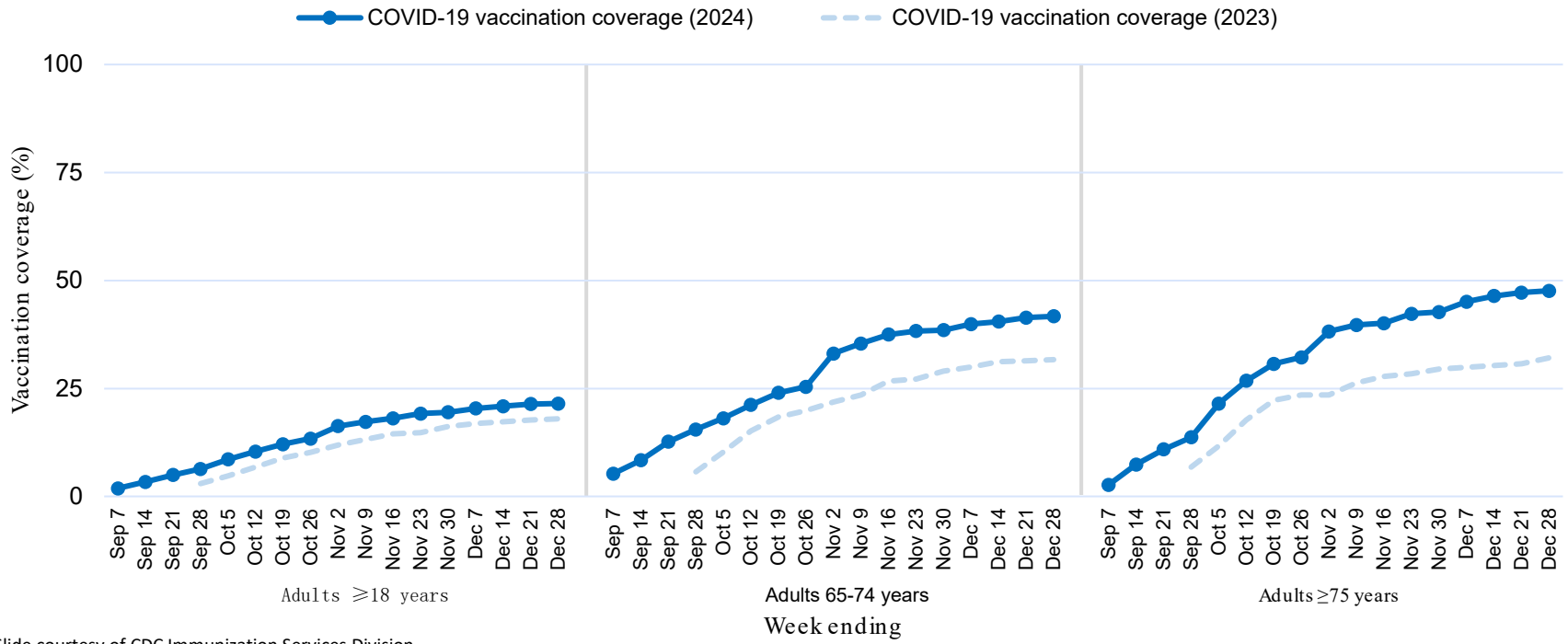
Age group | COVID-19 vaccination status	Total encounters	SARSCoV-2-test-positive, N (%)	Median interval since last dose among those vaccinated, days (IQR)	Adjusted vaccine effectiveness % (95% CI)
No updated 2023-2024 COVID-19 vaccine dose*				
9 months-4 years	44,978	1,946 (4)	368 (251-471)	**Ref**
5-17 years	54,320	2,071 (4)	679 (491-810)	**Ref**
⩾18 years	279,733	31,167 (11)	756 (61-189)	**Ref**
2023-2024 COVID-19 dose received 7-59 days earlier				
9 months-4 years	724	18 (2)	32 (20-46)	**52 (23 to 70)**
5-17 years	952	16 (2)	34 (19-47)	**64 (41 to 78)**
≥18 years	16,082	1,228 (8)	34 (21-47)	**49 (46 to 52)**
2023-2024 COVID-19 dose received 60-299 days earlier				
9 months-4 years	1,340	47 (4)	129 (91-177)	**25 (-2 to 45)**
5-17 years	2,511	63 (3)	138 (100-185)	**34 (14 to 49)**
≥18 years	49,824	4,701 (9)	149 (100-211)	**12 (8 to 15)**



* Includes all individuals who did not receive a 2023-2024 COVID-19 vaccine. For those aged ≥5 years, this includes unvaccinated persons and persons who were vaccinated with ≥1 original monovalent or bivalent COVID-19 doses. For those aged <5 years, both those in the referent group and those in the vaccinated group were required to have completed an initial series. The 2023-2024 dose could have been part of the initial series or in addition to the initial series.

Interim Estimates of *2024-2025* COVID-19 Vaccine Effectiveness in Adults

COVID-19 Vaccination Coverage Among Adults ≥18 Years, 65-74 Years, and ≥75 Years, 2023 and 2024, NIS-ACM



Slide courtesy of CDC Immunization Services Division.

National Immunization Survey-Adult COVID Module: Data from adults age ≥18 years are collected by telephone interview using a random-digit-dialed sample of cell telephone numbers stratified by state, the District of Columbia, five local jurisdictions (Bexar County TX, Chicago IL, Houston TX, New York City NY, and Philadelphia County PA), and Puerto Rico and the U.S. Virgin Islands. Data are weighted to represent the non-institutionalized U.S. population and mitigate possible bias that can result from an incomplete sample frame (exclusion of households with no phone service or only landline telephones) or non-response. All responses are self-reported. For more information about the survey, see https://www.cdc.gov/nis/about/index.html.

Characteristics of emergency department and urgent care encounters and hospitalizations among adults aged ≥18 years with COVID-19-like illness, by COVID-19 case status and CDC vaccine effectiveness network — VISION and IVY Networks

September 2024–April 2025

Characteristic	Vaccine effectiveness network and setting, no. (column %)								
	VISION ED/UC encounters, all adults aged ≥18 years			VISION hospitalizations, all adults aged ≥65 years			IVY hospitalizations, all adults aged ≥65 years		
	Total	COVID-19 case-patients	COVID-19 control-patients	Total	COVID-19 case-patients	COVID-19 control-patients	Total	COVID-19 case-patients	COVID-19 control-patients
Total	**208,552**	**13,643**	**194,909**	**54,520**	**4,076**	**50,444**	**4,287**	**1,170**	**3,117**
Median age	52 [34, 71]	57 [36, 74]	52 [34, 71]	78 [72, 85]	80 [74, 87]	78 [72, 85]	75 [70, 82]	77 [71, 84]	75 [69, 81]
Age group									
18-64 years	136,685 (66)	8,110 (59)	128,575 (66)	--	--	--	--	--	--
≥65 years	71,867 (34)	5,533 (41)	66,334 (34)	54,520 (100)	4,076 (100)	50,444 (100)	4,287 (100)	1,170 (100)	3,117 (100)
Immunocompromised*	--	--	--	12,909 (24)	840 (21)	12,069 (24)	1,101 (26)	252 (22)	849 (27)

Updated from Link-Gelles, et al. MMWR: https://www.cdc.gov/mmwr/volumes/74/wr/mm7406a1.htm

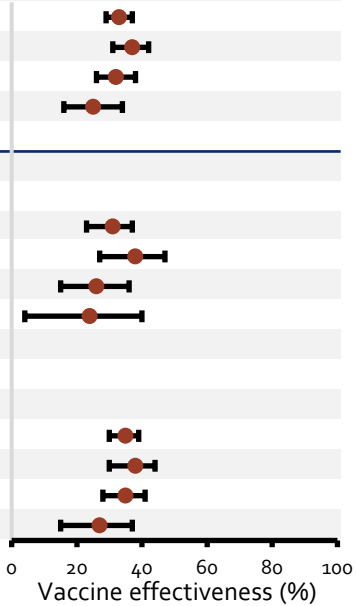
ED/UC = emergency department/urgent care; VISION data go through March 2025; IVY data go through April 2025

* Immunocompromised status is not evaluated for ED/UC encounters due to a higher likelihood of incomplete discharge diagnosis codes in this setting.

Effectiveness of *2024–2025 COVID-19* vaccination against COVID-19–associated *emergency department/urgent care* encounters by age group — VISION

September 2024 – March 2025

Age group/2024 -2025 COVID-19 vaccination status/days since dose	COVID-19 case-patients N (Col %)	COVID-19 control -patients N (Col %)	Median interval since last dose among vaccinated*, days (IQR)	Adjusted vaccine effectiveness % (95% CI)
≥18 years				
No 2024-2025 COVID-19 dose (Ref)	12,110 (89)(7)	161,640 (83)	1,043 (698-1,195)	**Ref**
Received 2024-2025 COVID-19 dose 7–179 days earlier	1,533 (11)(4)	33,269 (17)	83 (47-120)	**33 (29-37)**
2024-2025 COVID-19 dose, 7–59 days earlier	550 (4)(5)	11,021 (6)	34 (21-47)	**37 (31-42)**
2024-2025 COVID-19 dose, 60–119 days earlier	680 (5)(5)	13,777 (7)	89 (74-104)	**32 (26-38)**
2024-2025 COVID-19 dose, 120–179 days earlier	303 (2)(3)	8,471 (4)	142 (130-157)	**25 (16-34)**
18-64 years				
No 2024-2025 COVID-19 dose (Ref)	7,673 (95)	117,047 (91)	1,084 (825-1,221)	**Ref**
Received 2024-2025 COVID-19 dose 7–179 days earlier	437 (5)	11,528 (9)	79 (44-115)	**31 (23-37)**
2024-2025 COVID-19 dose, 7–59 days earlier	159 (2)	4,085 (3)	33 (20-46)	**38 (27-47)**
2024-2025 COVID-19 dose, 60–119 days earlier	203 (2)	4,808 (4)	88 (74-103)	**26 (15-36)**
2024-2025 COVID-19 dose, 120–179 days earlier	75 (1)	2,635 (2)	141 (129-156)	**24 (4-40)**
≥65 years				
No 2024-2025 COVID-19 dose (Ref)	4,437 (80)	44,593 (67)	845 (394-1,131)	**Ref**
Received 2024-2025 COVID-19 dose 7–179 days earlier	1,096 (20)	21,741 (33)	86 (49-122)	**35 (30-39)**
2024-2025 COVID-19 dose, 7–59 days earlier	391 (7)	6,936 (10)	35 (21-47)	**38 (30-44)**
2024-2025 COVID-19 dose, 60–119 days earlier	477 (9)	8,969 (14)	89 (75-104)	**35 (28-41)**
2024-2025 COVID-19 dose, 120–179 days earlier	228 (4)	5,836 (9)	143 (130-157)	**27 (15-37)**

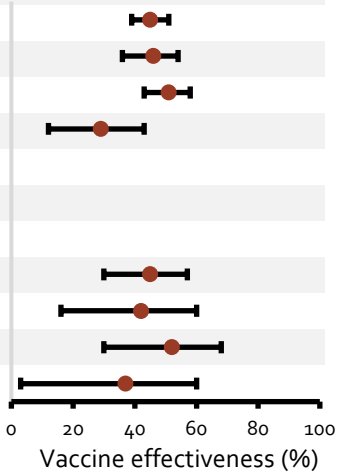


Updated from: Link-Gelles, et al. MMWR: https://www.cdc.gov/mmwr/volumes/74/wr/mm7406a1.htm. Vaccine effectiveness was calculated by comparing the odds of 2024–2025 COVID-19 vaccination in case-patients and control-patients using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multivariable logistic regression. The odds ratio was adjusted for age, sex, race and ethnicity, calendar day, and geographic region. The "no 2024–2025 dose" group included all eligible persons who did not receive a 2024–2025 COVID-19 vaccine dose, regardless of number of previous COVID-19 vaccine doses (if any) received. * Time since vaccination is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, or 2024-2025 COVID-19 vaccine.

Effectiveness of *2024–2025 COVID-19 vaccination* against COVID-19–associated *hospitalization* among *immunocompetent* adults aged ≥65 years — VISION and IVY Networks

September 2024 – March 2025

Network/2024 -2025 COVID-19 vaccination status/days since dose	COVID-19 case-patients N (Col %)	COVID-19 control - patients N (Col %)	Median interval since last dose among vaccinated*, days (IQR)	Adjusted vaccine effectiveness % (95% CI)
VISION				
No 2024-2025 COVID-19 dose (Ref)	2,787 (86)	28,696 (75)	875 (424-1,143)	**Ref**
Received 2024-2025 COVID-19 dose 7–179 days earlier	449 (14)	9,679 (25)	82 (47-118)	**45 (39-51)**
2024-2025 COVID-19 dose, 7–59 days earlier	153 (5)	3,280 (9)	34 (21-47)	**46 (36-54)**
2024-2025 COVID-19 dose, 60–119 days earlier	189 (6)	4,055 (11)	89 (74-104)	**51 (43-58)**
2024-2025 COVID-19 dose, 120–179 days earlier	107 (3)	2,344 (6)	140 (129-154)	**29 (12-43)**
IVY				
No 2024-2025 COVID-19 dose (Ref)	811 (88)	1,792 (79)	Not available	**Ref**
Received 2024-2025 COVID-19 dose 7–179 days earlier	107 (12)	476 (21)	89 (54–127)	**45 (30-57)**
2024-2025 COVID-19 dose, 7–59 days earlier	43 (5)	124 (5)	32 (20–46)	**42 (16-60)**
2024-2025 COVID-19 dose, 60–119 days earlier	36 (4)	196 (9)	88 (73–103)	**52 (30-68)**
2024-2025 COVID-19 dose, 120–179 days earlier	28 (3)	156 (7)	147 (130–161)	**37 (3-60)**



Updated from: Link-Gelles, et al. MMWR: https://www.cdc.gov/mmwr/volumes/74/wr/mm7406a1.htm

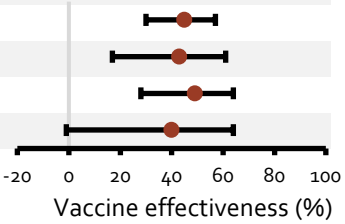
Vaccine effectiveness was calculated by comparing the odds of 2024–2025 COVID-19 vaccination in case-patients and control-patients using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multivariable logistic regression. For VISION, the odds ratio was adjusted for age, sex, race and ethnicity, calendar day, and geographic region. For IVY, the odds ratio was adjusted for age, sex, race and ethnicity, geographic region (U.S. Department of Health and Human Services Region) and calendar time (biweekly intervals). The "no 2024–2025 dose" group included all eligible persons who did not receive a 2024–2025 COVID-19 vaccine dose, regardless of number of previous COVID-19 vaccine doses.

*Time since vaccination is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, or 2024-2025 COVID-19 vaccine.

Effectiveness of *2024–2025 COVID-19 vaccination* against COVID-19–associated *critical illness* among *immunocompetent* adults aged ≥65 years — VISION

September 2024 – March 2025

2024-2025 COVID-19 vaccination status/days since dose	COVID-19 case-patients N (Col %)	COVID-19 control-patients N (Col %)	Median interval since last dose among vaccinated*, days (IQR)	Adjusted vaccine effectiveness % (95% CI)
VISION				
No 2024-2025 COVID-19 dose (Ref)	513 (86)	28,696 (75)	879 (426-1,144)	**Ref**
Received 2024-2025 COVID-19 dose 7–179 days earlier	84 (14)	9,679 (25)	82 (47-118)	**45 (30-57)**
2024-2025 COVID-19 dose, 7–59 days earlier	30 (5)	3,280 (9)	34 (21-47)	**43 (17-61)**
2024-2025 COVID-19 dose, 60–119 days earlier	38 (6)	4,055 (11)	89 (74-104)	**49 (28-64)**
2024-2025 COVID-19 dose, 120–179 days earlier	16 (3)	2,344 (6)	140 (129-155)	**40 (-1-64)**



Based on methods in: Link-Gelles, et al. MMWR: https://www.cdc.gov/mmwr/volumes/74/wr/mm7406a1.htm

Vaccine effectiveness was calculated by comparing the odds of 2024–2025 COVID-19 vaccination in case-patients and control-patients using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multivariable logistic regression. For VISION, the odds ratio was adjusted for age, sex, race and ethnicity, calendar day, and geographic region. For IVY, the odds ratio was adjusted for age, sex, race and ethnicity, geographic region (U.S. Department of Health and Human Services Region) and calendar time (biweekly intervals). The "no 2024–2025 dose" group included all eligible persons who did not receive a 2024–2025 COVID-19 vaccine dose, regardless of number of previous COVID-19 vaccine doses.

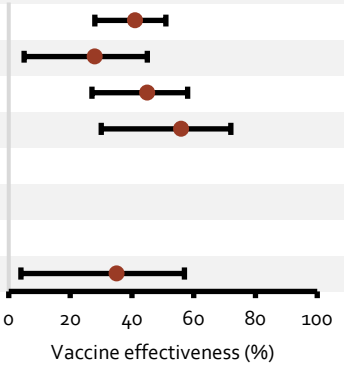
Critical illness is defined as admission to the intensive care unit or in-hospital death.

*Time since vaccination is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, or 2024-2025 COVID-19 vaccine.

Effectiveness of *2024–2025 COVID-19 vaccination* against COVID-19–associated *hospitalization* among *immunocompromised* adults aged ≥65 years — VISION and IVY Networks

September 2024 – April 2025

Network/2024 -2025 COVID-19 vaccination status/days since dose	COVID-19 case-patients N (Col %)	COVID-19 control - patients N (Col %)	Median interval since last dose among vaccinated, days (IQR)	Adjusted vaccine effectiveness % (95% CI)
VISION				
No 2024-2025 COVID-19 dose (Ref)	699 (83)	8,539 (71)	801 (379-1,117)	**Ref**
Received 2024-2025 COVID-19 dose 7–179 days earlier	141 (17)	3,530 (29)	83 (48-119)	**41 (28-51)**
2024-2025 COVID-19 dose, 7–59 days earlier	60 (7)	1,148 (10)	34 (20-47)	**28 (5-45)**
2024-2025 COVID-19 dose, 60–119 days earlier	60 (7)	1,502 (12)	89 (74-103)	**45 (27-58)**
2024-2025 COVID-19 dose, 120–179 days earlier	21 (2)	880 (7)	141 (130-154)	**56 (30-72)**
IVY				
No 2024-2025 COVID-19 dose (Ref)	211 (84)	651 (77)	Not available	**Ref**
Received 2024-2025 COVID-19 dose 7–179 days earlier	41 (16)	198 (23)	79 (46-128)	**35 (4-57)**



Updated from: Link-Gelles, et al. MMWR: https://www.cdc.gov/mmwr/volumes/74/wr/mm7406a1.htm

Vaccine effectiveness was calculated by comparing the odds of 2024–2025 COVID-19 vaccination in case-patients and control-patients using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multivariable logistic regression. For VISION, the odds ratio was adjusted for age, sex, race and ethnicity, calendar day, and geographic region. The "no 2024–2025 dose" group included all eligible persons who did not receive a 2024–2025 COVID-19 vaccine dose, regardless of number of previous COVID-19 vaccine doses (if any) received.

* Time since vaccination is for most recent dose, which could have been an original monovalent, bivalent, 2023-2024, or 2024-2025 COVID-19 vaccine.

IVY*: VE of *2024–2025 COVID-19 vaccine* against *hospitalization* among adults aged ≥18 years *by SARS-CoV-2 lineage* using viral whole-genome sequencing

- **Population**
  - **Cases:** COVID-like illness (CLI) and test *positive* for SARS-CoV-2†; **restricted to patients with sequence-confirmed§ KP.3.1.1 lineage (Nextstrain clade 24E) or XEC lineage (Nextstrain clade 24F)**
  - **Controls:** CLI and test *negative* for SARS-CoV-2, influenza viruses, and RSV by RT-PCR

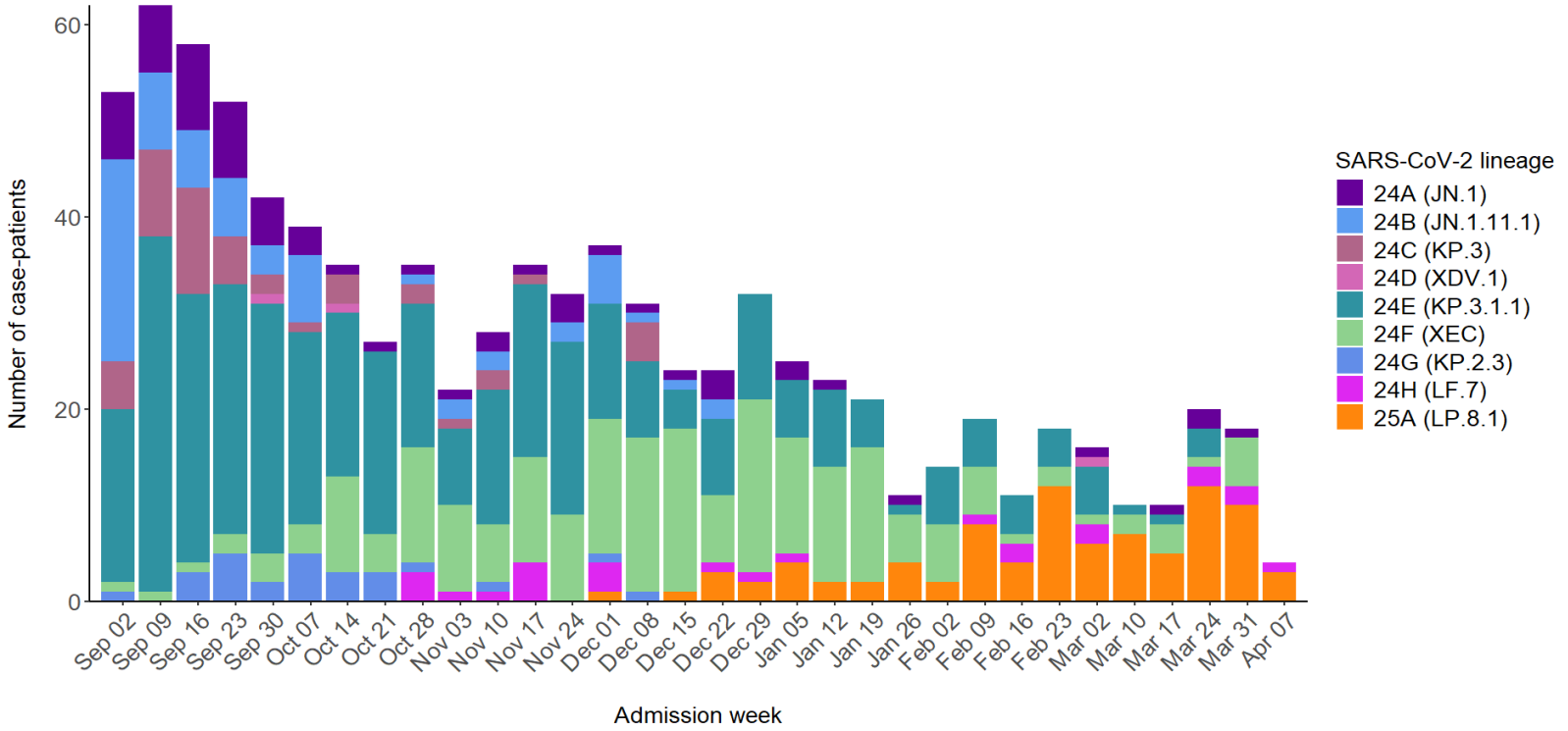
- **Analytic Period:** September 1, 2024–April 11, 2025

- VE¶ against hospitalization was calculated separately using case-patients with sequence-confirmed SARS-CoV-2 KP.3.1.1 and XEC lineage infections

* Investigating Respiratory Viruses in the Acutely Ill (IVY) Network. https://www.cdc.gov/flu/vaccines-work/ivy.htm
† Case patients who tested positive for influenza viruses or RSV were excluded.
§ Identification of a SARS-CoV-2 lineage through viral whole-genome sequencing was successful for 50% of case-patients during the analysis period.
¶ Logistic regression models were adjusted for age, sex, race and ethnicity, geographic region, and calendar time.

IVY: Number of COVID-19 case-patients by hospital admission week and SARS-CoV-2 lineage

September 1, 2024–April 11, 2025

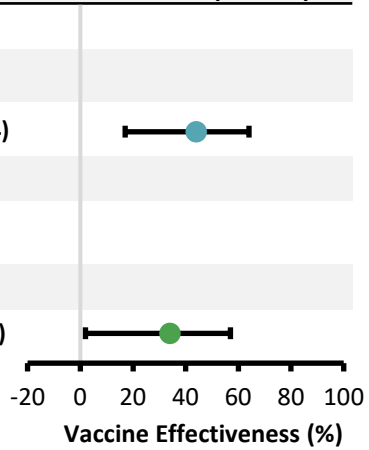


Dates are for the start of the admission week.

IVY: Effectiveness of *2024–2025 COVID-19 vaccine* against *hospitalization* among adults aged ≥18 years* *by SARS-CoV-2 lineage†*

September 1, 2024 – April 11, 2025

Lineage and 2024-2025 COVID-19 vaccination status	COVID-19 case-patients		COVID-19 control-patients		Vaccine Effectiveness§ % (95% CI)
	N (Col %)	Median interval since last dose among vaccinated, days (IQR)	N (Col %)	Median interval since last dose among vaccinated, days (IQR)	
KP.3.1.1					
No **2024-2025 COVID-19 dose** (Ref)	307 (91)	Not available	4,604 (83)	Not available	**Ref**
Received **2024-2025 COVID-19 dose** 7–179 days earlier	29 (9)	56 (33–75)	911 (17)	89 (53–127)	**44 (17–64)**
XEC					
No **2024-2025 COVID-19 dose** (Ref)	169 (84)	Not available	4,604 (83)	Not available	**Ref**
Received **2024-2025 COVID-19 dose** 7–179 days earlier	31 (16)	85 (50–111)	911 (17)	89 (53–127)	**34 (2–57)**



* These results include both immunocompetent and immunocompromised persons.
† KP.3.1.1 lineage was defined by Nextstrain clade 24E, and XEC lineage was defined by Nextstrain clade 24F.
§ Logistic regression models were adjusted for age, sex, race and ethnicity, geographic region, and calendar time.

Conclusions: effectiveness of COVID-19 vaccines

- **For the respective year, compared to no in-season dose, COVID-19 vaccination provided additional protection against:**
  - COVID-19-associated **emergency department and urgent care* visits among children**; protection was generally similar across age groups.
  - COVID-19-associated **emergency department and urgent care visits among adults**.
  - COVID-19-associated **hospitalizations among adults aged ≥65 years with and without immunocompromising conditions**.
  - COVID-19-associated **critical illness among adults aged ≥65 years**; protection appeared to be more durable against critical illness compared to less severe outcomes.

- **VE should be interpreted as the added benefit of 2023–2024 or 2024–2025 COVID-19 vaccination in a population with high levels of infection-induced immunity, vaccine-induced immunity, or both.**
  - Prior SARS-CoV-2 infection contributes protection against future disease, though protection wanes over time.
  - An increase in SARS-CoV-2 circulation in the United States during late summer 2024, just before the 2024–2025 COVID-19 vaccines were approved and authorized, may have resulted in higher population-level immunity against JN.1-lineage strains, which could have resulted in lower measured VE than in a population with less recent infection.

* Estimates for children are from 2023-2024. Additionally, due to lower baseline rates of severe disease, VE against hospitalization and critical illness in children could not be estimated.

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