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Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC)

World Health Organization

Prof. Kanta Subbarao, TAG-CO-VAC Chair
Vaccines and Related Biological Products Advisory Committee
22 May 2025

WHO Technical Advisory Group on COVID-19 Vaccine Composition

Functions of the TAG-CO-VAC:

- Make recommendations to WHO on the **methods to assess the impact of SARS-CoV-2 variants** on COVID-19 vaccines;
- Provide **interpretation of available evidence on the effect of SARS-CoV-2 variants on COVID-19 vaccines**, including but not limited to vaccine effectiveness;
- **Recommend to WHO, for each COVID-19 vaccine platform, adaptations (if any) needed** so that vaccines continue to safely provide protection against SARS-CoV-2 variants.

Meeting frequency:

- The TAG-CO-VAC continues to convene closed, decision-making meetings approximately every six months. After each meeting, recommendations to either maintain current vaccine composition or to consider updates are issued.
- The twice-yearly evidence review by the TAG-CO-VAC is based on the need for continued monitoring of the evolution of SARS-CoV-2 and the kinetics of vaccine-derived immunity, as well as the time needed by manufacturers to update the antigen composition of approved COVID-19 vaccines. The TAG-CO-VAC will meet more frequently if necessary.

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TAG-CO-VAC: https://www.who.int/groups/technical-advisory-group-on-covid-19-vaccine-composition-(tag-co-vac)
Also described in: Grant R, et al. Nat Med 2023

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TAG-CO-VAC Members

Chair

Professor Kanta Subbarao

Director of the WHO Collaborating Centre for Reference and Research on Influenza and Professor, Department of Microbiology and Immunology

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Vice-Chair

Professor Cheryl Cohen

Professor in epidemiology at the University of the Witwatersrand and Head of the Centre for Respiratory Disease and Meningitis at the National Institute for Communicable Diseases

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Members

Dr Svein Rune Andersen >
Scientific Director for Vaccines at the Norwegian Institute of Public Health, Norway

Prof Narendra Kumar Arora >
Executive Director of The INCLEN Trust International, India

Professor Laith Abu-Raddad >

Associate Professor Deborah Cromer >
Lead of the Infection, Epidemiology and Policy Analytics Group at the Kirby Institute, University of New South Wales

Dr Irene Owusu Donkor >
Fellow in the Epidemiology Department of the Noguchi Memorial Institute for Medical Research (NMIMR)

Dr Bart Haagmans >
Associate professor at the Department of Viroscience of Erasmus MC, Rotterdam, the Netherlands

Dr Hideki Hasegawa >
Director of the WHO Collaborating Centre for Reference and Research on Influenza, Japan

Dr Janine Kimpel >
Group leader and deputy Director at the Institute of Virology at the Medical University of Innsbruck, Austria

Prof Bette Liu >
Professor at the Population Health Group at the National Centre for Immunisation Research and Surveillance (NCIRS) in Australia

Professor Elizabeth Miller >
Professor in Infectious Disease Epidemiology at the London School of Hygiene and a visiting professor at the Sackler School of Public Health at Tel Aviv University

Dr Sergio Nishioka >
Technical Adviser for Capacity Building and Clinical Evaluation of COVID-19 vaccines

Dr Stanley Perlman >
Professor of Microbiology and Immunology, and of Pediatrics at the University of Iowa

Prof Derek Smith >
Director of the Center for Pathogen Evolution, and Professor of Infectious Disease Informatics at the University of Cambridge in the United Kingdom

Dr Pragya Yadav >

Contact: tagcovac@who.int

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TAG-CO-VAC Deliberations: May 2025

Objective:

Achieve broadly cross-reactive vaccine-elicited immune responses in the context of continued SARS-CoV-2 evolution

Major questions:

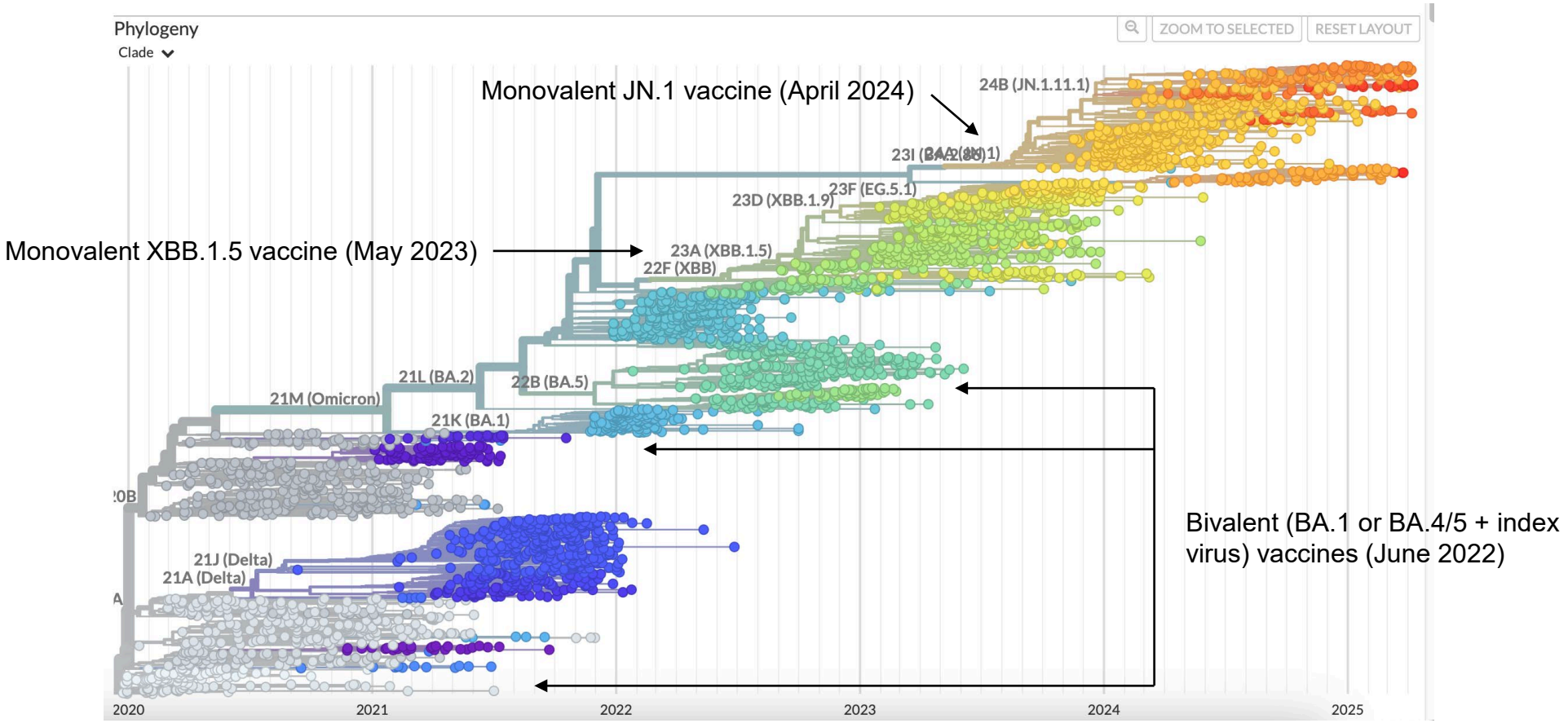
1. Are the current monovalent JN.1 lineage vaccines (e.g. JN.1 or KP.2) eliciting broadly cross-reactive immune responses to circulating SARS-CoV-2 variants?

2. Is there sufficient antigenic change in circulating variants to consider an update in the vaccine antigen? If so, to which antigen?

TAG-CO-VAC Evidence review: May 2025

1. SARS-CoV-2 **genetic evolution** with support from the WHO Technical Advisory Group on SARS-CoV-2 Virus Evolution (TAG-VE);
2. **Antigenic characterization** of previous and emerging SARS-CoV-2 variants using virus neutralization tests with animal antisera and further analysis of antigenic relationships using antigenic cartography;
3. **Immunogenicity data on the breadth of neutralizing antibody responses** elicited by currently approved vaccine antigens against circulating SARS-CoV-2 variants using animal and human sera;
4. Preliminary immunogenicity data on **immune responses following infection with circulating SARS-CoV-2 variants**;
5. Available **vaccine effectiveness (VE) estimates** of currently approved vaccines during periods of circulation of JN.1 variants; and
6. Preliminary preclinical and clinical immunogenicity data on the **performance of approved or candidate vaccines with updated antigens** shared confidentially by vaccine manufacturers with TAG-CO-VAC (data not shown).

1. SARS-CoV-2 evolution and COVID-19 vaccine composition



Phylogeny of SARS-CoV-2 variants since its introduction in humans illustrated using Nextstrain.

Time is shown on the x axis and selected named variants are labeled with their Nextstrain clade (Pango lineage) at their root nodes. Clades included as vaccine antigens are indicated with the date of the TAG-CO-VAC recommendation for this vaccine antigen composition.

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NextStrain: https://nextstrain.org/ncov 28 April 2025

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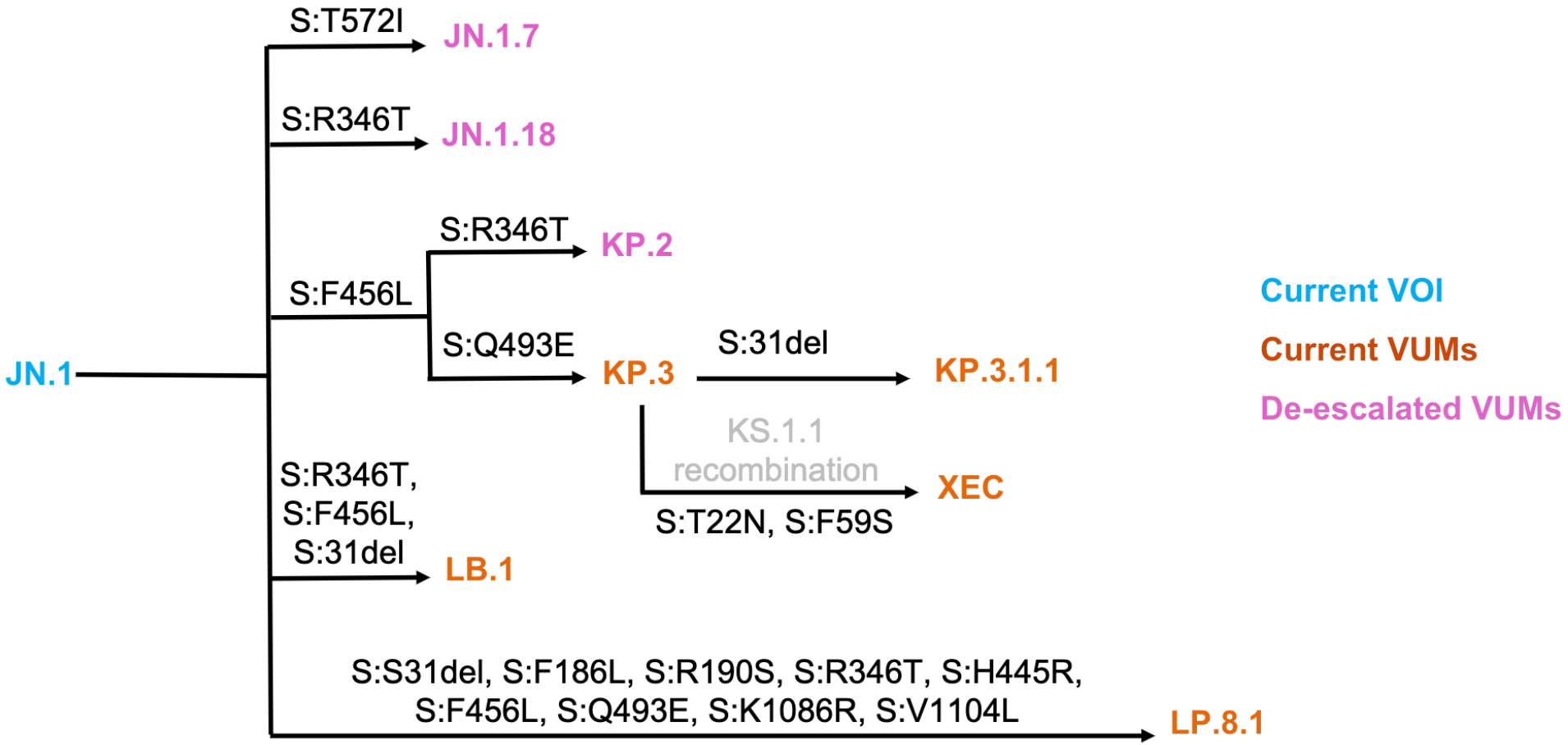
1. Variants of Interest (VOI) and Variants Under Monitoring (VUM)



Current SARS-CoV-2 Variants of Interest (VOI) and Variants Under Monitoring (VUM), with amino acid mutations relative to JN.1 indicated above each branch.

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List of VOI and VUM: https://www.who.int/activities/tracking-SARS-CoV-2-variants

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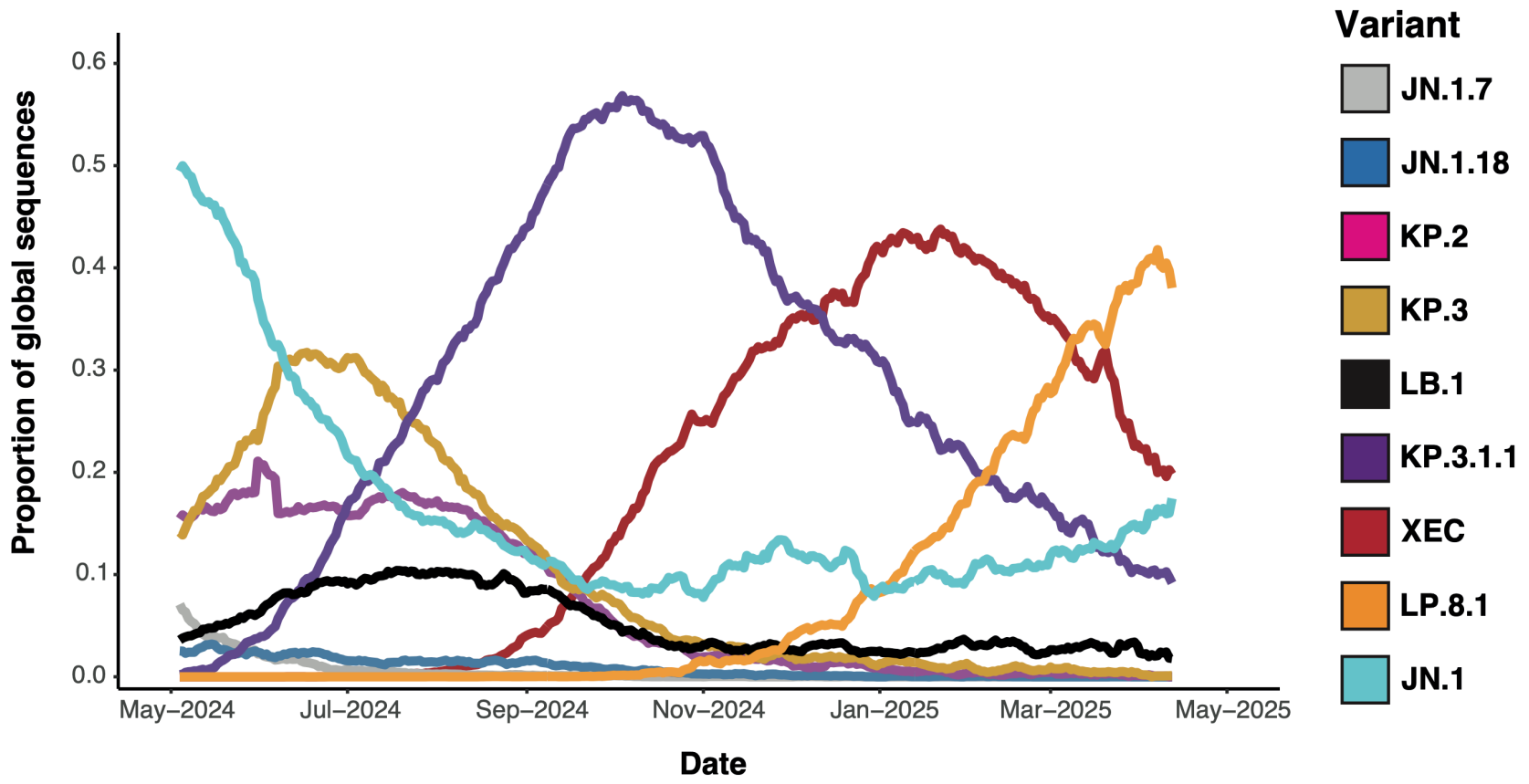
1. VOI and VUMs: Global data



Proportion of SARS-CoV-2 sequences from May 2024 – May 2025.

Figure produced by WHO based on SARS-CoV-2 sequence and metadata from cov-spectrum.org on 9 May 2025, based on sequences and metadata from GISAID as of 6 May 2025. SARS-CoV-2 variants shown are VUMs with the exception of JN.1 which is a VOI and includes all descendent sublineages that are not part of one of the other labelled VUMs.

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JN.1 includes LF.7.2 which has not yet met the criteria for VUM
List of VOI and VUM: https://www.who.int/activities/tracking-SARS-CoV-2-variants

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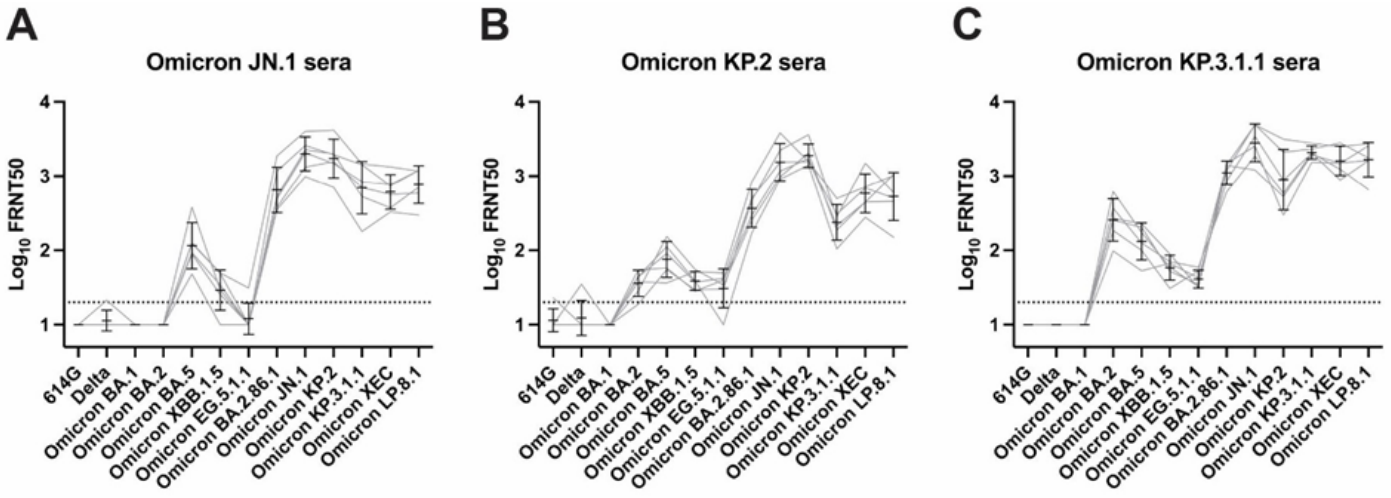
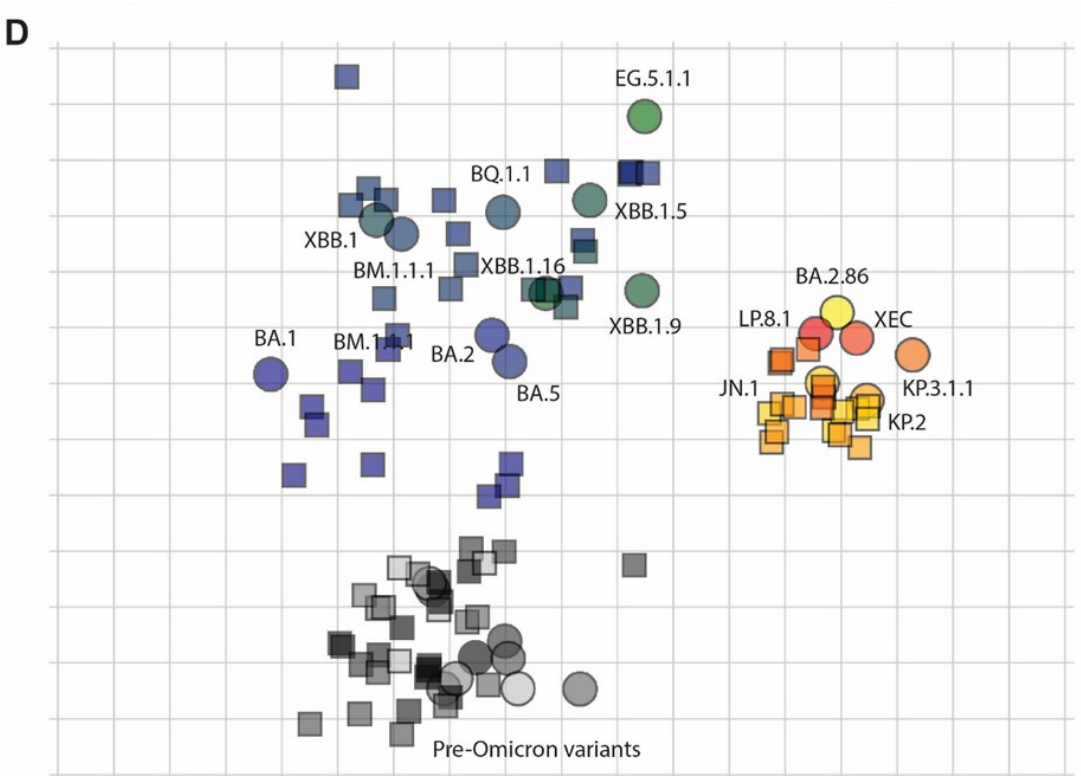
2. Antigenic characterization of SARS-CoV-2 variants

Hamster sera following primary infection



Neutralizing antibody titers (FRNT50) of sera from naïve hamsters infected with either JN.1 (A), KP.2 (B) or KP.3.1.1 (C) against 614G, Delta, BA.1, BA.2, BA.5, XBB.1.5, EG.5.1.1, BA.2.86.1, JN.1, KP.2, KP.3.1.1, XEC or LP.8.1.



Antigenic cartography of hamster sera following primary infection

Each square indicates a plasma sample and each circle indicates a SARS-CoV-2 variant.

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Unpublished data shared with permission from Dr. Bart Haagmans, Erasmus MC.
Methodology previously described in Mykytyn AZ, et al. Sci Immunol. 2022;
doi:10.1126/sciimmunol.abq4450

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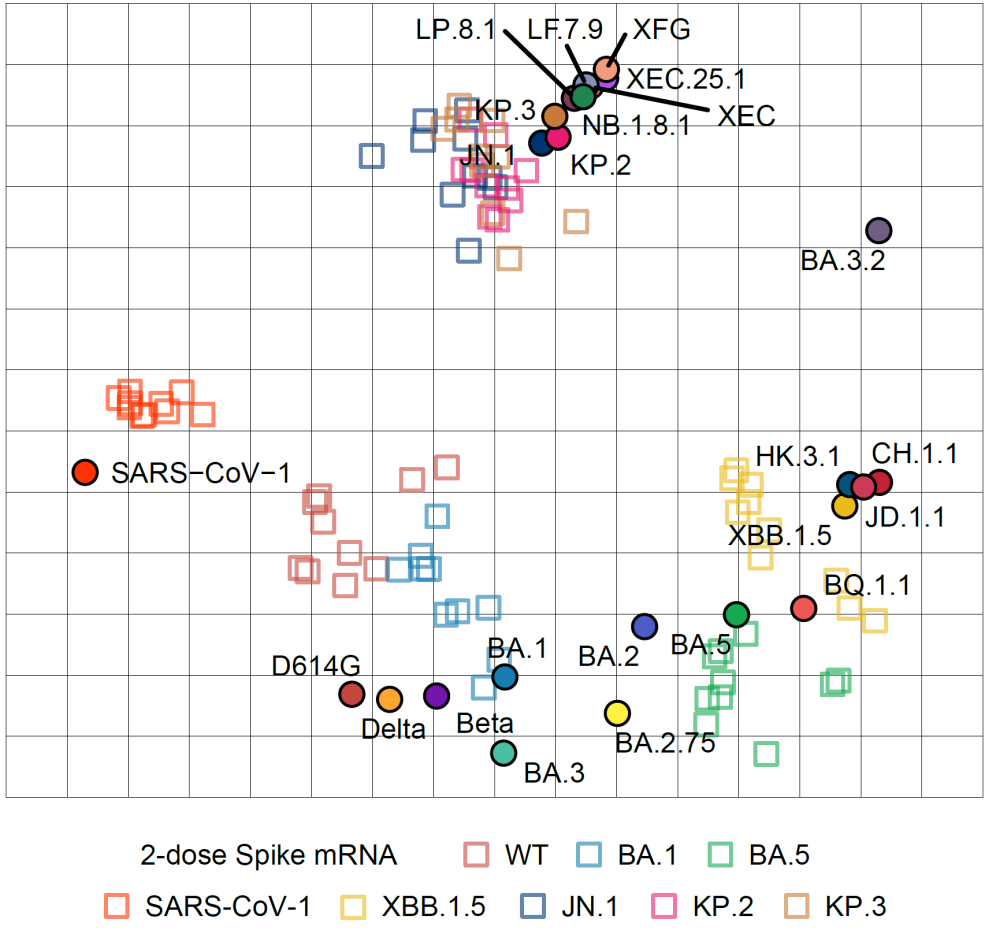
2. Antigenic characterization of SARS-CoV-2 variants (cont.)

Mice sera following primary vaccination



Antigenic cartography of naïve mice immunized with 2-doses of 10μg spike mRNA vaccine.
Each square indicates a plasma sample and each circle indicates a SARS-CoV-2 variant.

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Guo C, et al. bioRxiv (preprint). 2025; doi: 10.1101/2025.04.30.651462

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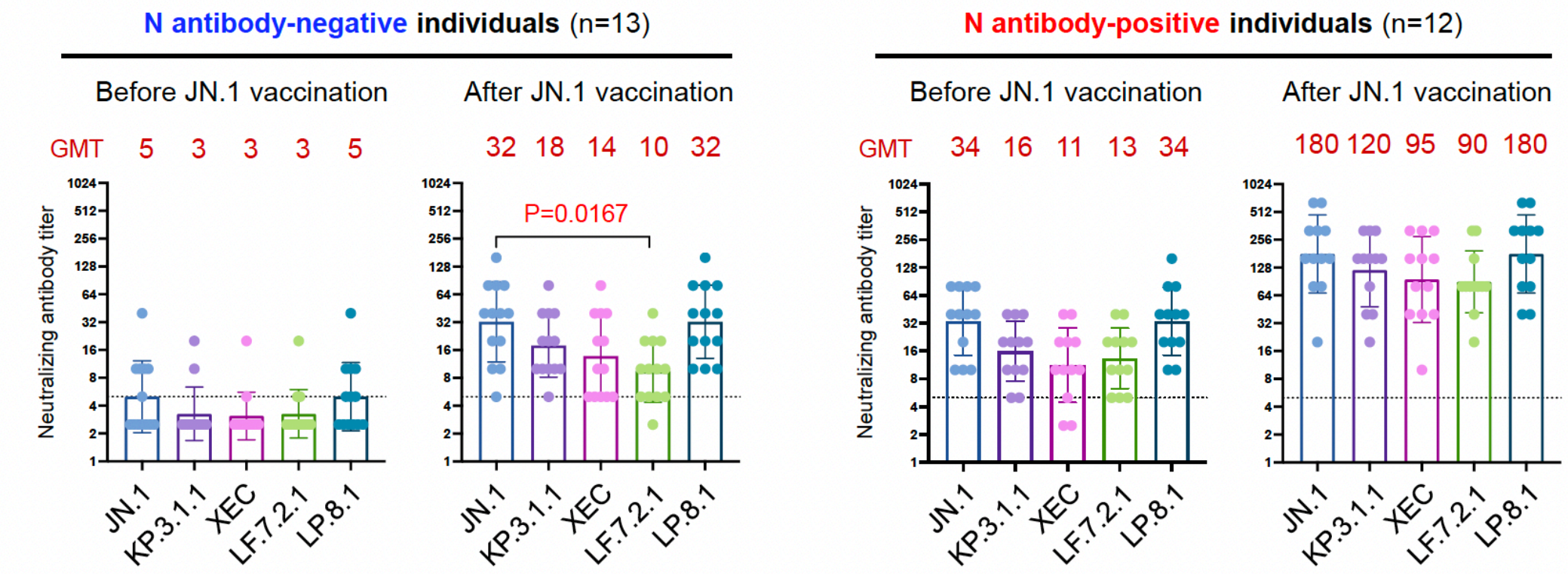
3. Breadth of neutralizing antibody responses

Human sera pre- and post-**JN.1** vaccination

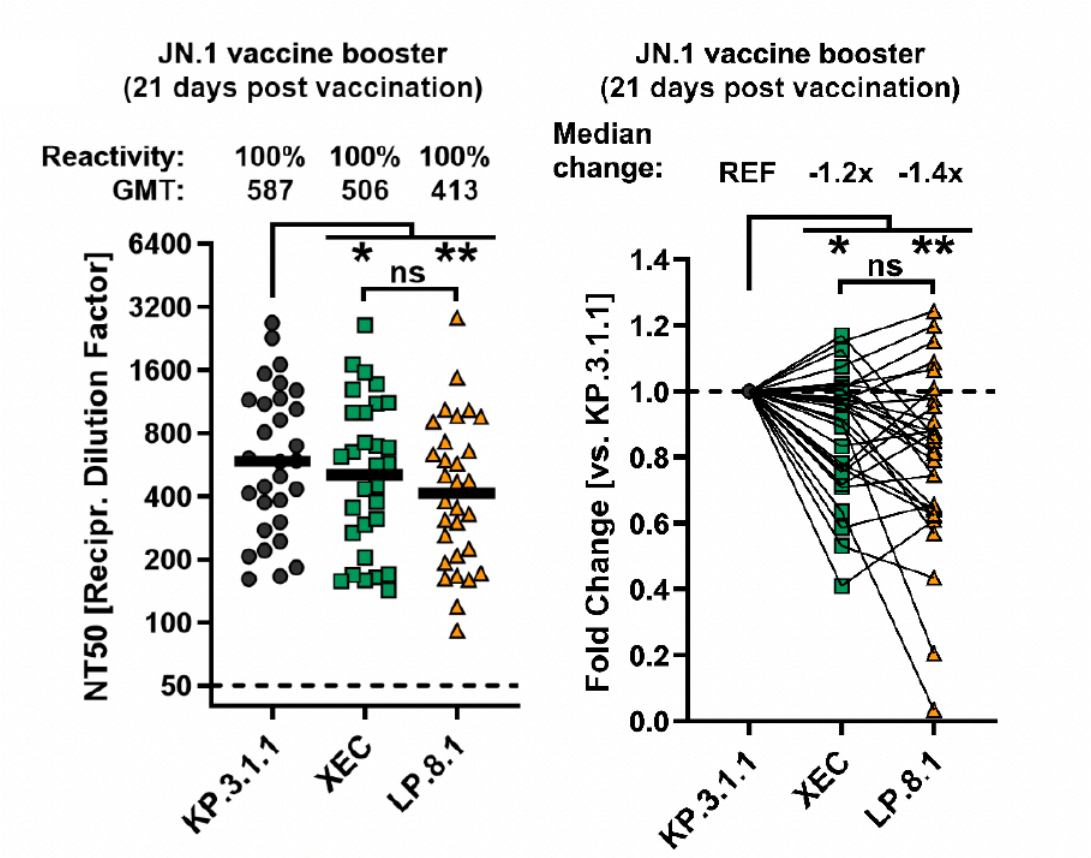


Neutralization titers against JN.1, KP.3.1.1, XEC, LF.7.2.1 or LP.8.1 pre- and post-monovalent JN.1 vaccination

Information on GMT (also indicated by horizontal lines) response rates are indicated above the graphs.

3. Breadth of neutralizing antibody responses (cont.)

Human sera post-**JN.1** vaccination



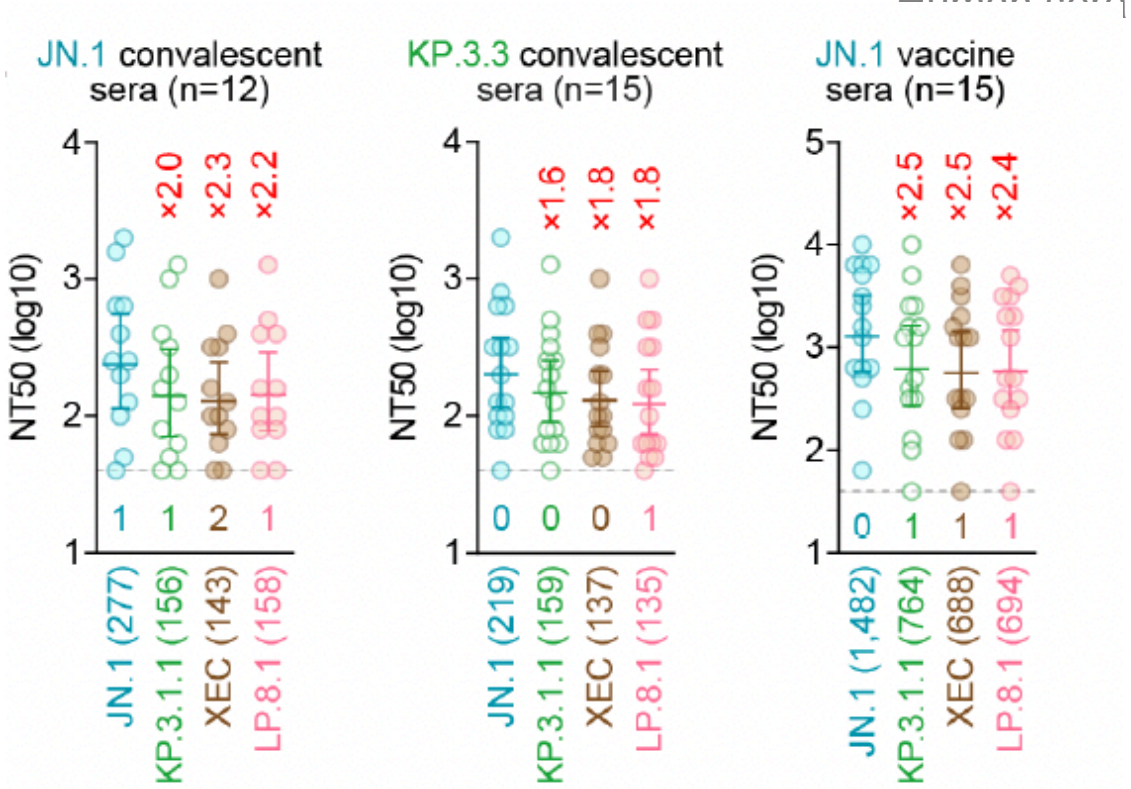
Neutralization titers (NT50) (L) and fold changes in neutralization relative to KP.3.1.1 pseudovirus particles (R) of sera from individuals 21 days post monovalent JN.1 vaccination (n = 30) against SARS-CoV-2 variants KP.3.1.1, XEC or LP.8.1

Reactivity and geometric mean titers (GMT) are labeled above.

Zhang L, et al. Lancet Infect Dis; 2025. doi: 10.1016/S1473-3099(25)00113-6.

4. Breadth of neutralizing antibody responses

Human sera post-**JN.1** infection or vaccination



Neutralization titers (NT50) of human sera following JN.1 (L) or KP.3.3 infection (middle) or monovalent JN.1 vaccination (R) against SARS-CoV-2 variants JN.1, KP.3.1.1, XEC or LP.8.1

Assays were performed with pseudoviruses harboring the S proteins of JN.1, KP.3.1.1, XEC and LP.8.1. Assays for each serum sample were performed in quadruplicate to determine the 50% neutralization titer (NT50). Each dot represents one NT50 value, and the median and 95% confidence interval are shown. The number in parenthesis indicates the geometric mean of NT50 values. The horizontal dash line indicates a detection limit (40-fold) and the number of serum donors with the NT50 values below the detection limit is shown in the figure (under the bars and dots of each variant). The fold changes of NT50 versus JN.1 are calculated as the average ratio of inverted NT50 obtained from each individual. The fold changes versus JN.1 are indicated with “x.”

Chen L, et al. Lancet Infect Dis; 2025. doi: 10.1016/S1473-3099(25)00079-9

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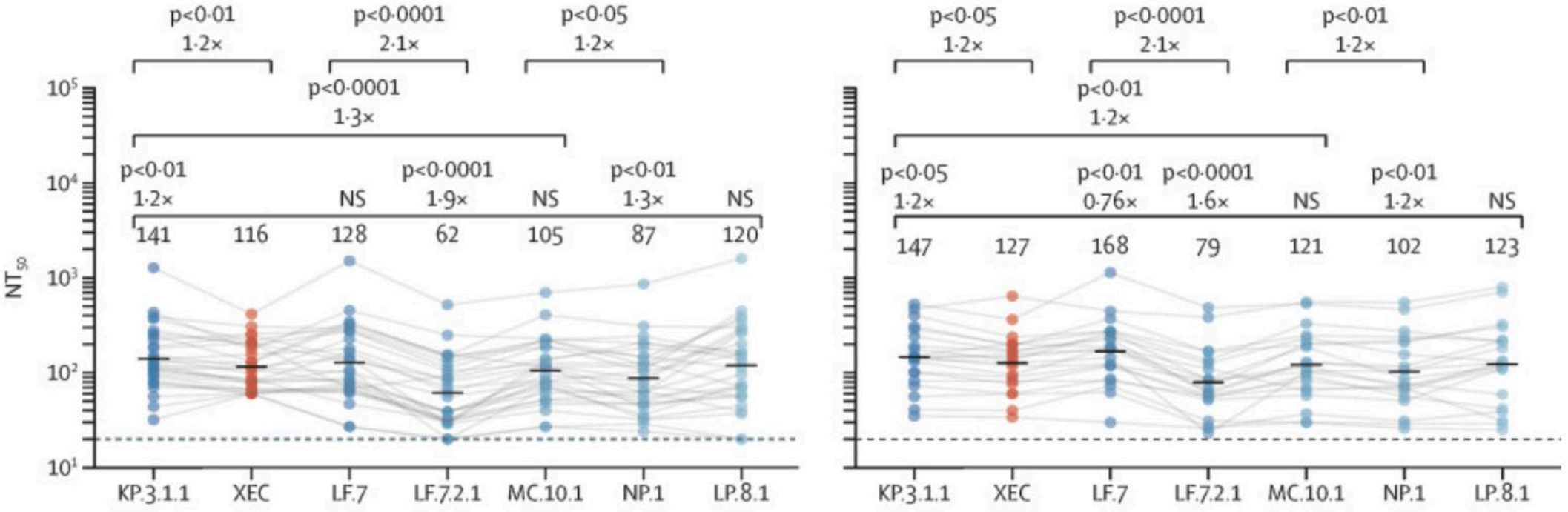
4. Breadth of neutralizing antibody responses (cont.)

Human sera post-**JN.1** infection

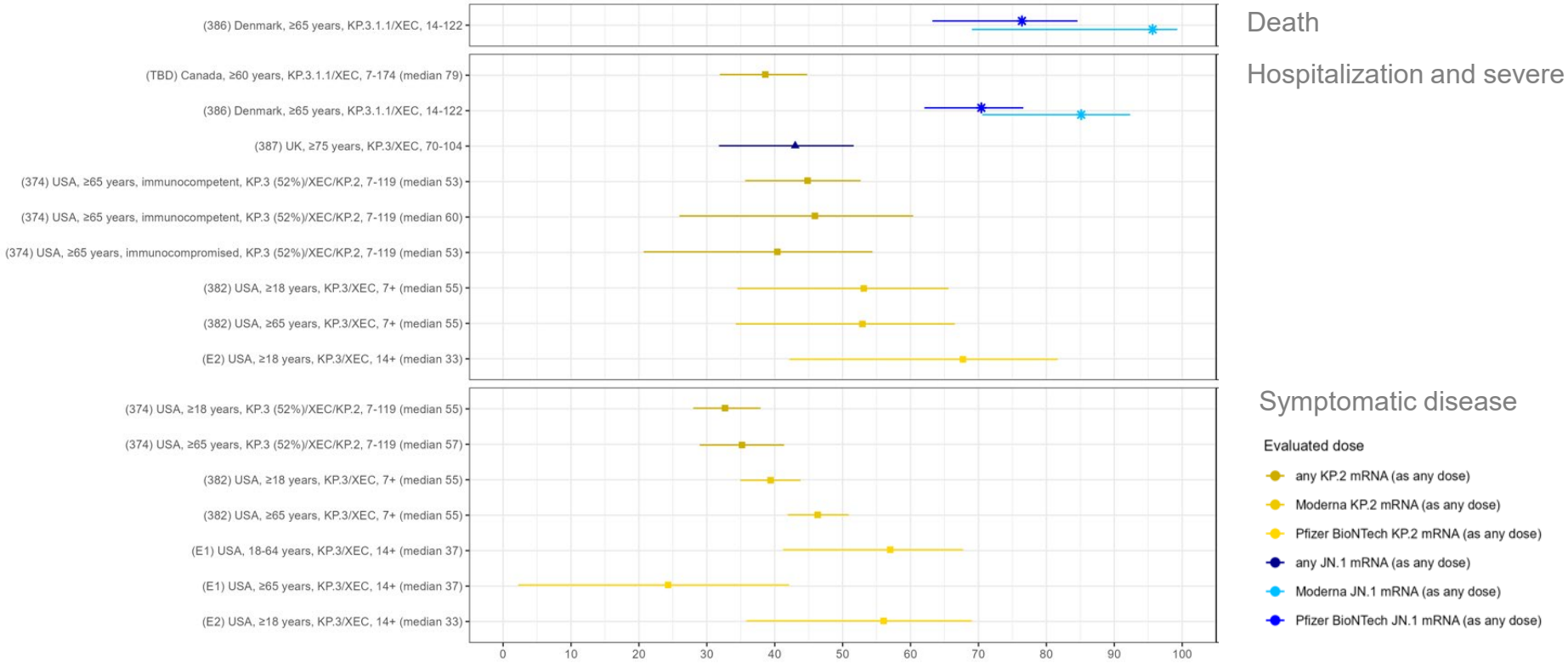


Neutralization titers (NT50) of convalescent plasma from individuals reinfected with JN.1 after BA.5 or BF.7 breakthrough infection (n = 29) (L) and those reinfected with JN.1/XDV + F456L after BA.5 or BF.7 breakthrough infection (n = 21) against SARS-CoV-2 variants KP.3.1.1, XEC, LF.7, LF.7.2.1, MC.10.1, NP.1 and LP.8.1.

The dashed line indicates the limit of detection (NT50=10). Geometric mean titers are labelled above each group, with fold changes relative to XEC and statistical significance indicated above the geometric mean titer labels. Wilcoxon rank-sum tests were used to determine p values.

Liu J, et al. Lancet Infect Dis; 2025. doi: 10.1016/S1473-3099(25)00015-5

5. Vaccine effectiveness (VE) estimates



Estimates of relative or up-to-date vaccine effectiveness (VE) within three months of a dose of a monovalent JN.1 or monovalent KP.2 mRNA vaccine during periods of JN.1 descendent lineage circulation.

The top panel shows VE estimates against death, followed by hospitalization and severe disease, and the bottom panel shows VE estimates against symptomatic disease. Analysis conducted by WHO using data from www.view-hub.org with published studies up to 5 May 2025.

Link-Gelles R, et al. MMWR Morb Mortal Wkly Rep. 2025;74:73-82.
Hansen CH, et al. SSRN (preprint): https://ssrn.com/abstract=5227321
Rudolph AE, et al. bioRxiv (preprint). 2025; doi: 10.1101/2025.01.15.24319342.
Appaneal HJ, et al. Nat Commun. 2025;16:4033.
UK Health Security Agency. https://www.gov.uk/government/publications/epidemiology-of-covid-19-in-england/epidemiology-of-covid-19-in-england-january-2020-to-december-2024#vaccine-surveillance

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Summary of evidence: Virus evolution

There are persistent and increasing gaps in the reporting of cases, hospitalizations and deaths, from WHO Member States, making epidemiological trends difficult to infer. Nonetheless, in 2025, SARS-CoV-2 continues to circulate globally, causing severe disease, post COVID-19 condition, and death.

As of May 2025, currently circulating SARS-CoV-2 variants are derived from JN.1. The weekly proportion of Variant Under Monitoring (VUM) LP.8.1 among all SARS-CoV-2 sequences submitted to GISAID continues to increase. The weekly proportion of JN.1 (Variant of Interest, VOI) is slowly increasing, largely due to increases in LF.7 and its descendent variants, while all other VUMs (KP.3, KP.3.1.1, XEC, and LB.1) are declining.

Several JN.1 derived variants have independently evolved changes in the spike protein at epitopes known to be targeted by neutralizing antibodies.

Summary: Antigenic characterization and immunogenicity data

Published and unpublished data using antisera from naïve hamsters infected with JN.1, KP.2, KP.3.1.1, XEC or LP.8.1 or mice immunized with mRNA vaccine antigens JN.1, KP.2 or KP.3 showed that JN.1, KP.2, KP.3.1.1, XEC, and LP.8.1 are antigenically closely related to each other (approximately 1 antigenic unit in cartographic analysis, which corresponds to a two-fold-difference in neutralization).

In published and unpublished data from humans, vaccination with monovalent JN.1 or KP.2 antigens significantly increased neutralizing antibody titers against all JN.1 descendent lineages tested:

- Analysis of pre- and post-vaccination sera from JN.1 lineage (i.e. JN.1 or KP.2) immunized individuals demonstrated significant rises in neutralization of JN.1 and its descendent lineages, including KP.3.1.1, XEC, LF.7.2.1, and LP.8.1.
- Neutralization titers against LP.8.1 were generally modestly lower (2-fold reduction) than those against the homologous JN.1 or KP.2 antigen.

Summary: Vaccine effectiveness

Contemporary vaccine effectiveness (VE) estimates are relative (rVE), rather than absolute (comparing vaccinated to unvaccinated individuals), and demonstrate the added or incremental protection of recent vaccination over and above pre-existing infection- and vaccine-derived immunity.

Monovalent JN.1 or KP.2 COVID-19 vaccines were introduced into some vaccination programmes in the second half of 2024. There are only a few studies estimating rVE for the monovalent JN.1 or KP.2 mRNA COVID-19 vaccines during periods of JN.1 descendent lineage circulation. Both vaccines demonstrated additional protection—relative to pre-existing immunity—against symptomatic and severe COVID-19 during the first three to four months after vaccination.

Summary: Data from COVID-19 vaccine manufacturers

Immunization of naïve mice, as well as of mice previously immunized with SARS-CoV-2 variants, with monovalent JN.1 or KP.2 vaccines resulted in high neutralizing antibody titers against JN.1 and its derivatives including KP.2, KP.3.1.1, XEC, LP.8.1, and LF.7.2. However, neutralization titers against LP.8.1 were typically lower than those against the homologous immunizing antigen.

Immunization of naïve mice, as well as of mice previously immunized with SARS-CoV-2 variants, with monovalent LP.8.1 vaccine candidates elicited high neutralizing antibody titers against the homologous antigen. Cross-neutralizing antibody titers elicited against other JN.1 lineage variants including JN.1, KP.2, KP.3, KP.3.1.1, XEC, and LF.7.2 were similar or modestly higher than those elicited by JN.1 or KP.2 antigens.

In humans, vaccination with monovalent JN.1 or KP.2 antigens resulted in robust neutralizing antibody responses to JN.1 and descendent variants, including KP.3.1.1, XEC, LP.8.1, and LF.7.2. Analysis of pre- and post-vaccination sera from JN.1 or KP.2 immunized individuals showed some variation in neutralizing antibody titers against LP.8.1 and LF.7.2 across different studies. In most instances, they were similar or lower than those against the homologous JN.1 or KP.2 antigens.

TAG-CO-VAC Recommendation

Objective:

Achieve broadly cross-reactive vaccine-elicited immune responses in the context of continued SARS-CoV-2 evolution

Recommendation:

Monovalent JN.1 or KP.2 remain appropriate COVID-19 vaccine antigens; **monovalent LP.8.1** is a suitable alternative vaccine antigen.

JN.1: NextStrain: 24A, GenBank: PP298019, GISAID: EPI_ISL_18872762
LP.8.1: NextStrain: 25A; GenBank: PV074550.1; GISAID: EPI_ISL_19467828