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FDA Considerations and Recommendations for COVID-19 Vaccines (2026-2027 Formula)

Vaccines and Related Biological Products Advisory Committee Meeting, May 28, 2026

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Background

- VRBPAC meetings regarding COVID-19 vaccines formula updates:
  - April 6, 2022: initial discussion about framework for updating variant formulations
  - June 28, 2022: **bivalent** (**Wuhan/BA.4/5**) update recommended
  - Jan. 26, 2023: agreement on **periodic assessment in Spring** for a potential variant antigen update for the winter respiratory season; timing adjusted as needed
  - June 15, 2023: **XBB.1.5** update recommended
  - June 5, 2024: JN.1 lineage update recommended; June 13, 2025 FDA determined **KP.2 preference, if feasible**
  - May 22, 2025: **JN.1 lineage, LP.8.1 preference**, update recommended
- Decisions are based on totality of available evidence, including antigenicity of current/emerging variants, vaccine effectiveness, and candidate vaccine immunogenicity.
- Objective is to obtain independent expert advice on a potential variant formula update through an open and transparent process.

Evidence Used to Support Decisions

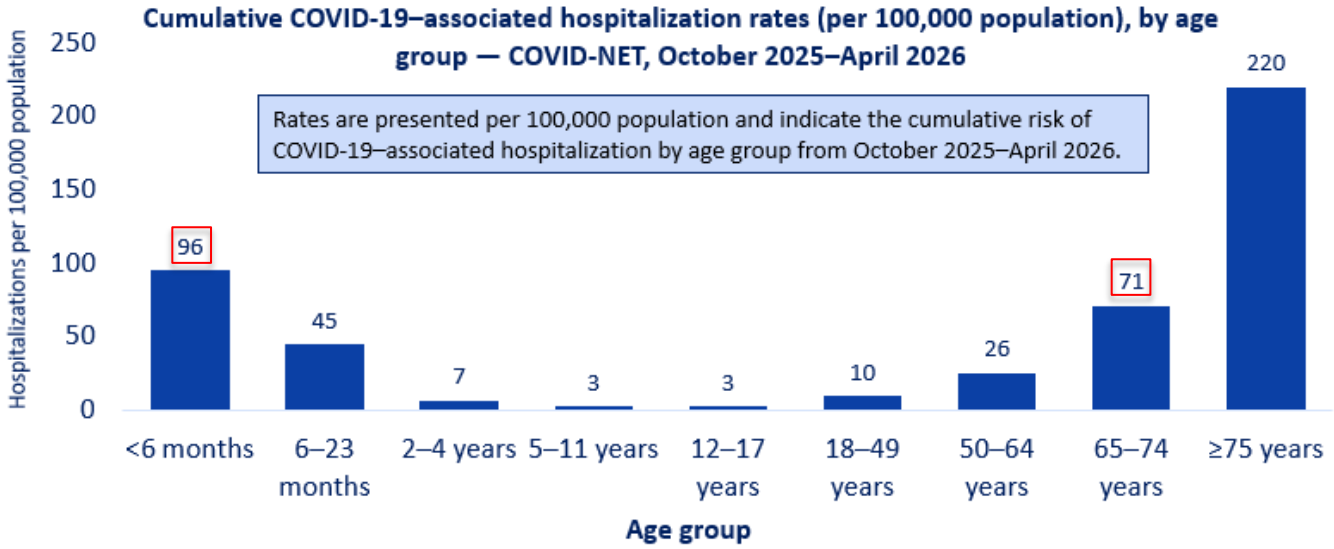
- **Variant surveillance**: circulating & emerging variants
- **Variant antigenicity data:** cross-neutralization by primary infection sera
- **Vaccine effectiveness data:** real-world effectiveness studies
- **Postvaccination serology studies:** neutralizing antibody responses
- **Candidate variant-updated vaccine immunogenicity data:** available nonclinical and human data

Key Challenges in Vaccine Strain Selection

- Months-long manufacturing timelines and manufacturer-specific constraints
- Unpredictable variant evolution and seasonality
- Declining surveillance and epidemiology data
- Limited nonclinical and clinical data for candidate updated vaccines
- Heterogeneous population immunity that influences disease risk and responses to vaccines

Populations at Risk for Severe COVID-19

- Pediatric population: lower accumulated immunity; generally lower severe disease, with infants at higher risk.
- Adult population: substantial but heterogenous immunity: highest severe disease risk among older adults.
- Immunocompromised people: at increased risk across age groups.

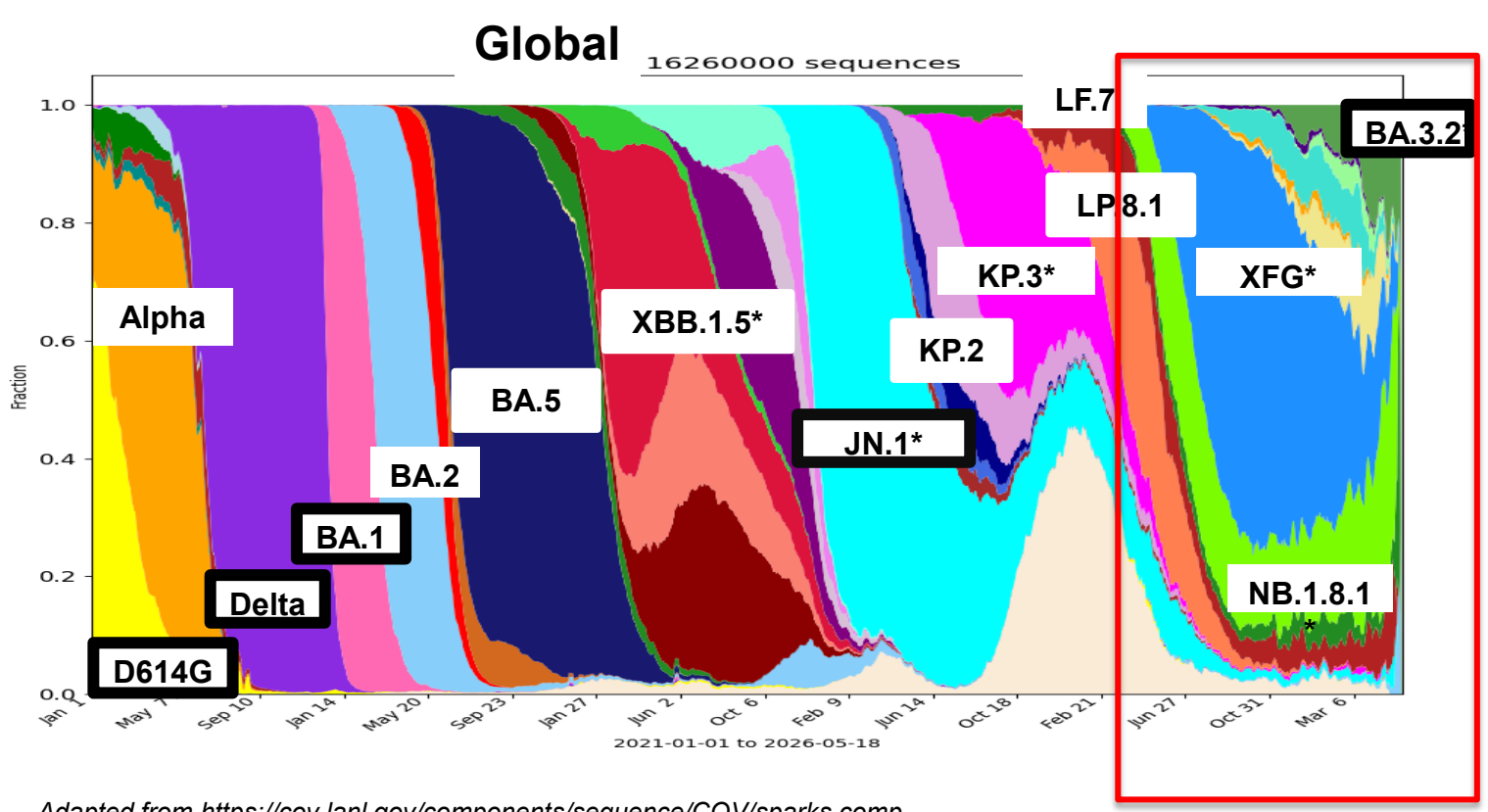


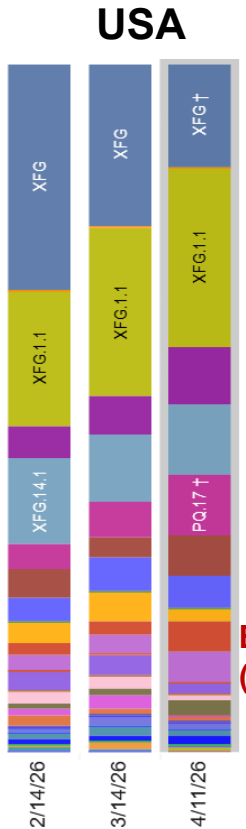
Additional Considerations

- **Humoral immunity wanes** even after multiple exposures, increasing susceptibility to re-infection and disease.
- **Vaccines generally elicit the strongest responses to matched variants**; cross-neutralizing responses may also be generated against antigenically related variants.
- **Neutralizing antibody titers are associated with protection**, but absolute protective thresholds are not known; other components of the immune response also contribute to protection.
- **Variant vaccines may differ in immunogenicity**.
- **Availability of candidate updated vaccines** need to be considered.

Data Highlights

Variant Landscape:
Dominant Variant Waves and Co-circulating Subdominant Variants





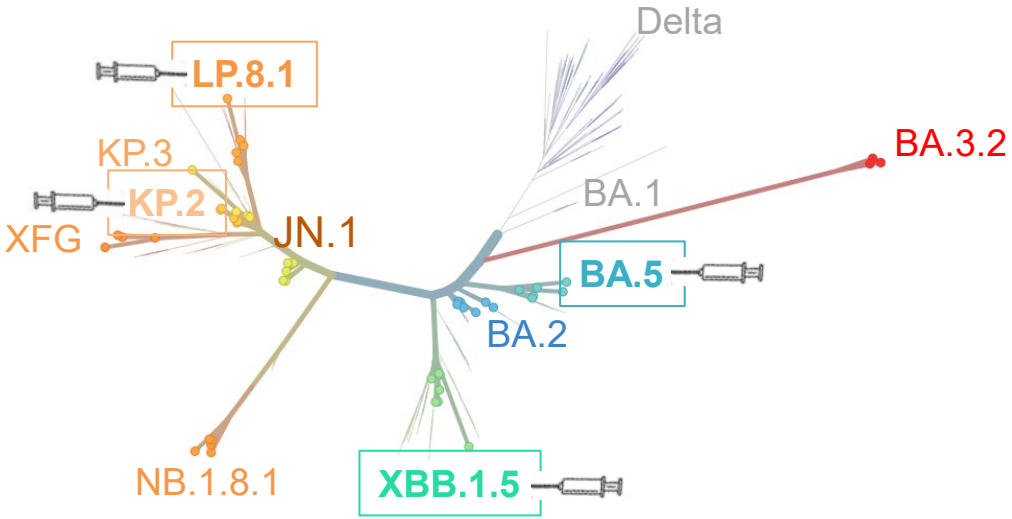
BA.3.2 (3-7%)

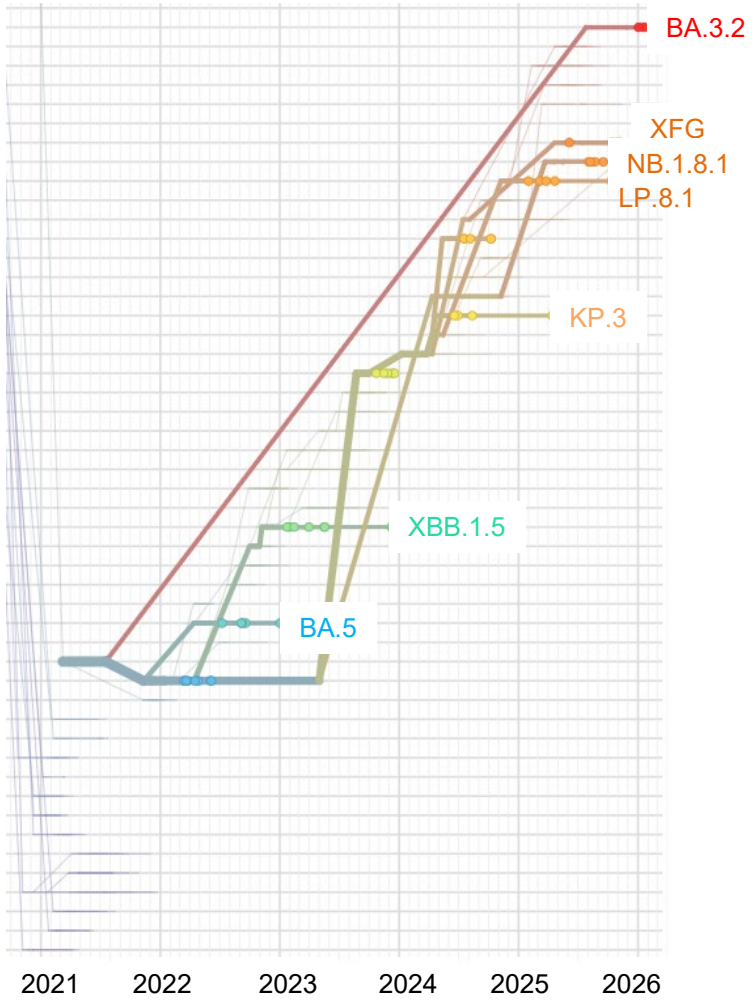
Adapted from https://cov.lanl.gov/components/sequence/COV/sparks.comp

June 2025-May 2026

https://www.cdc.gov/covid/php/variants/variants-and-genomic-surveillance.html

Variant Phylogeny

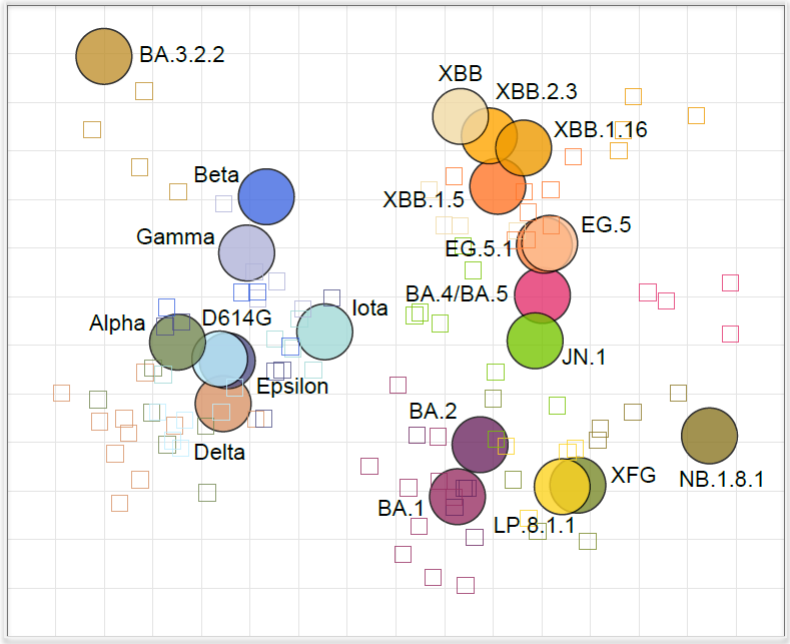




adapted from Nextstrain.org/ncov/reference

Antigenic maps: JN.1-lineage cluster with drift variants is distinct from BA.3.2.2

Hamster primary infection sera



T. Wang & C. Weiss labs, FDA/CBER, L. Katzelnick, NIH/NIAID

Effectiveness of Recent Vaccines

- **CDC data presented today**
  - **2024-2025 COVID-19 vaccination*** provided additional protection against medically-attended illness among children and adults, including immunocompromised adults; more robust against severe outcome
  - **2025-2026 COVID-19 vaccination*** (interim VE) indicates additional protection against COVID-19-associated urgent care/ED/hospitalizations
- ***Additional publications supporting vaccine effectiveness***
  - Skowronski *et al*. 2026 Euro Surveill. 31(18):260031
  - Hansen, *et al.* 2025 Lancet Inf Dis. 25(12):1293-1302
  - Abdul Aziz *et al.* 2025 Vaccine 67:127870

*mRNA vaccines were used

Recap of Immunogenicity Data

Supporting data from today's presentations and published literature

- **Postvaccination human sera**
  - **LP.8.1 mRNA COVID-19 vaccines** elicit robust cross-neutralizing responses against antigenically similar JN.1-lineage variants, including NB.1.8.1, but responses against BA.3.2.2 are significantly reduced compared with JN.1-lineage variants.
  - **BA.3.2.2 candidate mRNA vaccine** increases neutralization of BA.3.2.2 but responses were lower than expected (~7 fold), with reduced cross-neutralization of JN.1-lineage variants.
  - **Adults with prior antigenic exposures** show low-level neutralizing antibody titers against BA.3.2.2, but the clinical significance is unknown.
- **Nonclinical studies**
  - **LP.8.1 and XFG vaccines** elicit robust cross-neutralizing responses against antigenically similar JN.1-lineage variants, including NB.1.8.1, but reduced cross-neutralization of BA.3.2.2.
  - **BA.3.2.2 vaccines** elicit lower than expected homologous neutralization with reduced cross-neutralizing of JN.1-lineage variants.

Harmonization Efforts for Recommendations for Variant Antigen Updates to COVID-19 Vaccines

- FDA technical working group meetings with manufacturers regarding available clinical/nonclinical data using current and candidate vaccines

- Discussions with international regulatory authorities regarding potential recommendations for updates

Summary

- Current variant trends favor emerging JN.1-lineage variants (e.g., NB.1.8.1), while the persistence or potential dominance of divergent BA.3.2.2 remains unclear.

- LP.8.1- and XFG-based vaccines elicit cross-neutralizing antibody responses against antigenically-related JN.1 variants, but titers are much lower against BA.3.2.2.

- BA.3.2.2-based vaccines improve responses to BA.3.2.2 but may have lower intrinsic immunogenicity and weaker responses against JN.1-lineage variants.

Voting question for the committee

- For the 2026-2027 Formula of COVID-19 vaccines in the U.S., does the committee recommend JN.1-lineage XFG variant as the preferred variant for an updated monovalent vaccine?

Please vote “Yes” or “No” or “Abstain”

Discussion topic for the committee

- Please discuss circumstances that may warrant recommendation of a non-JN.1 lineage variant (e.g., BA.3.2) for COVID-19 vaccine use in the U.S.