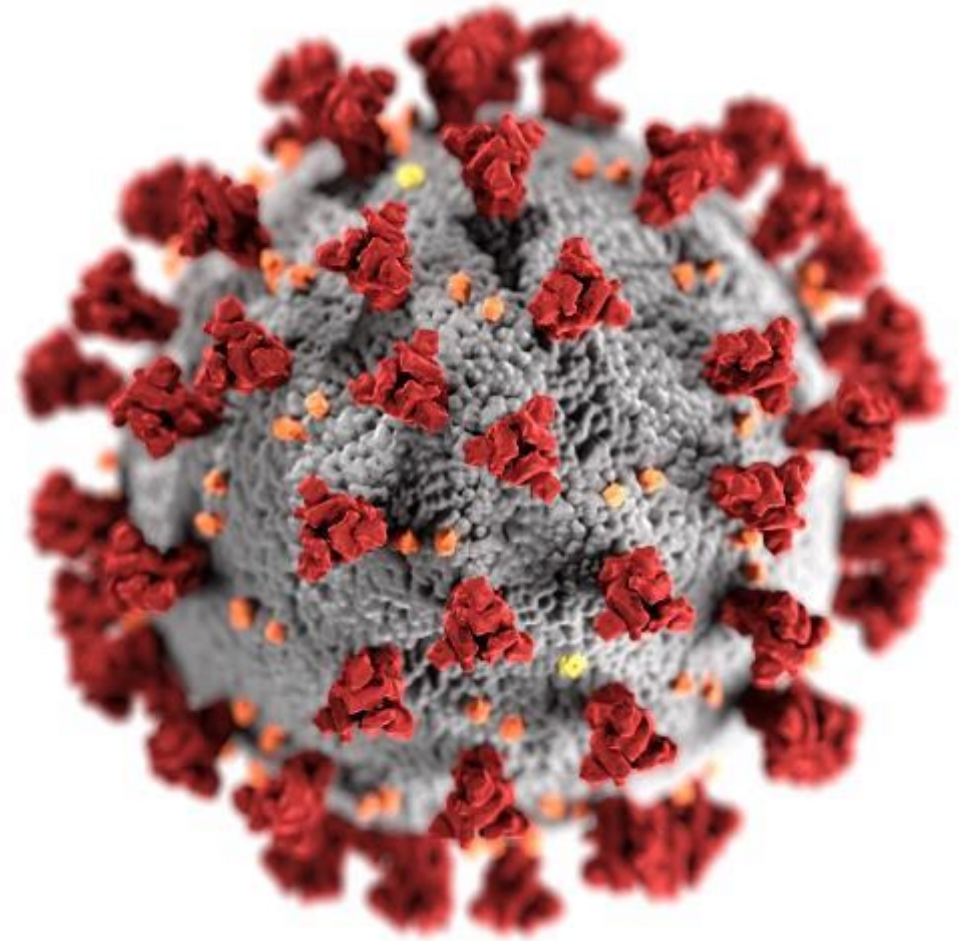


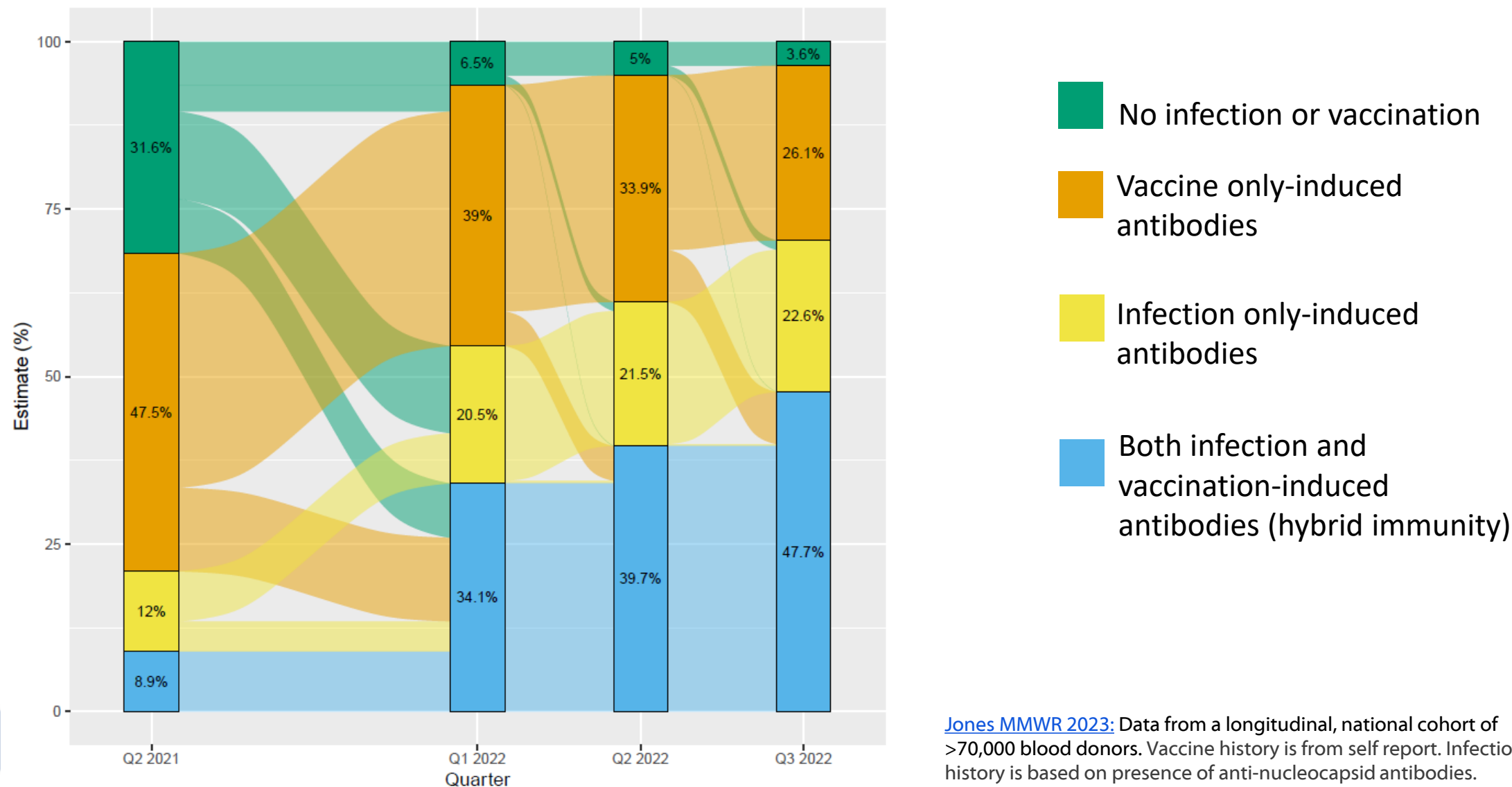
Infection-induced and hybrid immunity

Jefferson Jones, MD MPH FAAP
CDR, US Public Health Service

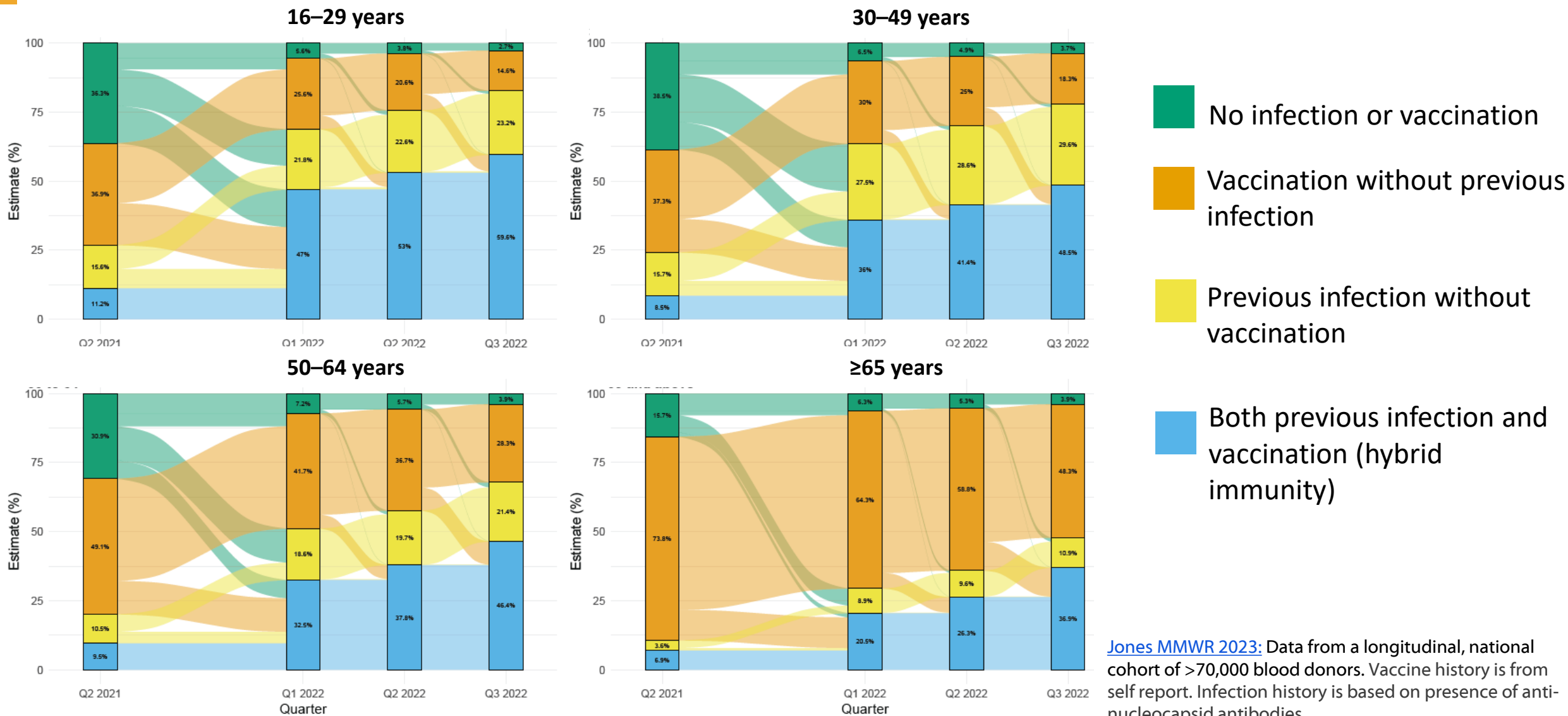


cdc.gov/coronavirus

Shifts in vaccine-induced, infection-induced, and hybrid immunity against SARS-CoV-2 among blood donors aged ≥ 16 years — United States, Quarter 2 2021– Quarter 3 2022

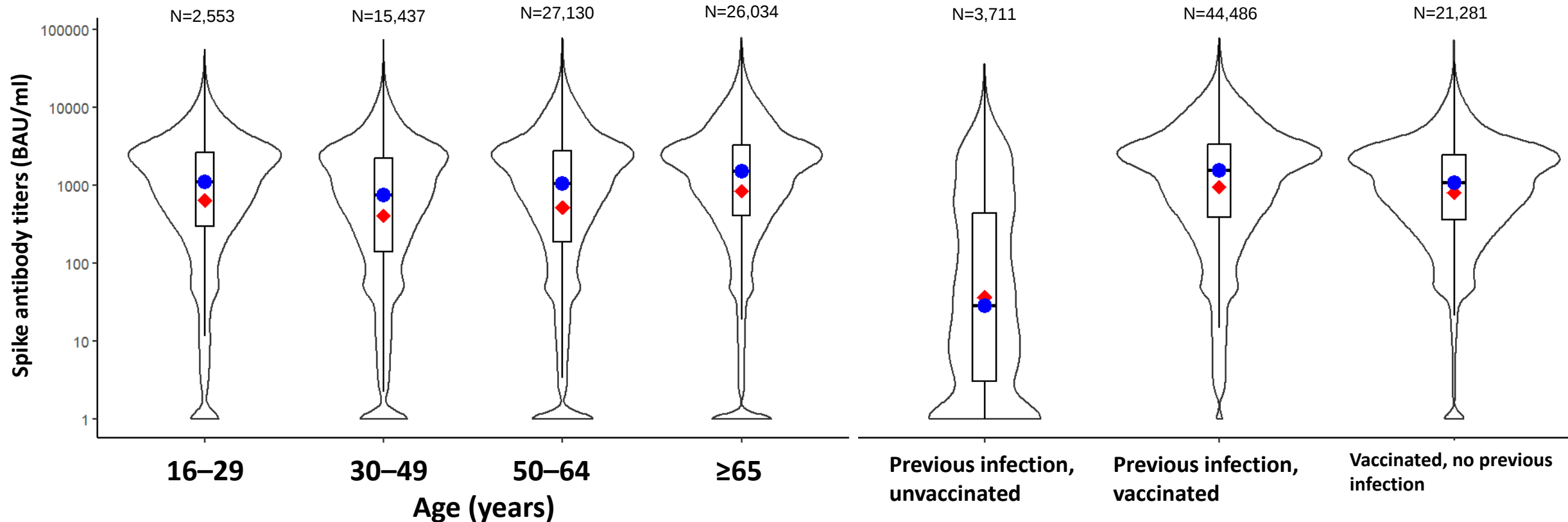


Shifts in vaccine-induced, infection-induced, and hybrid immunity against SARS-CoV-2 among people aged ≥16 years by age group — United States, Q2 2021–Q3 2022



[Jones MMWR 2023](#): Data from a longitudinal, national cohort of >70,000 blood donors. Vaccine history is from self report. Infection history is based on presence of anti-nucleocapsid antibodies.

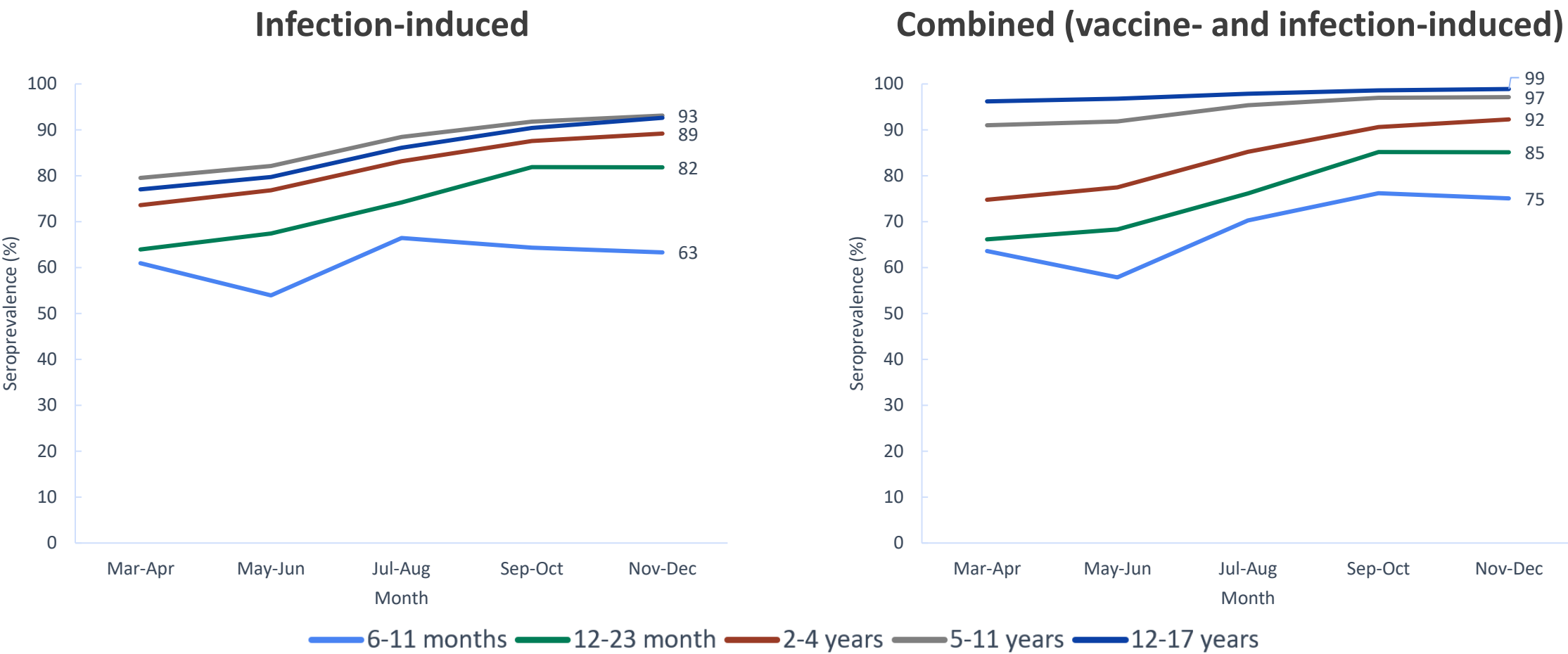
Quantitative anti-spike antibody titers by age group and by infection and vaccine status, Jul-Oct 2022



Source: CDC (unpublished). Data from nationwide blood donor cohort
Vaccine history is from self report. Infection history is based on presence of anti-nucleocapsid antibodies.

Pediatric infection-induced and combined (vaccine- and infection-induced)

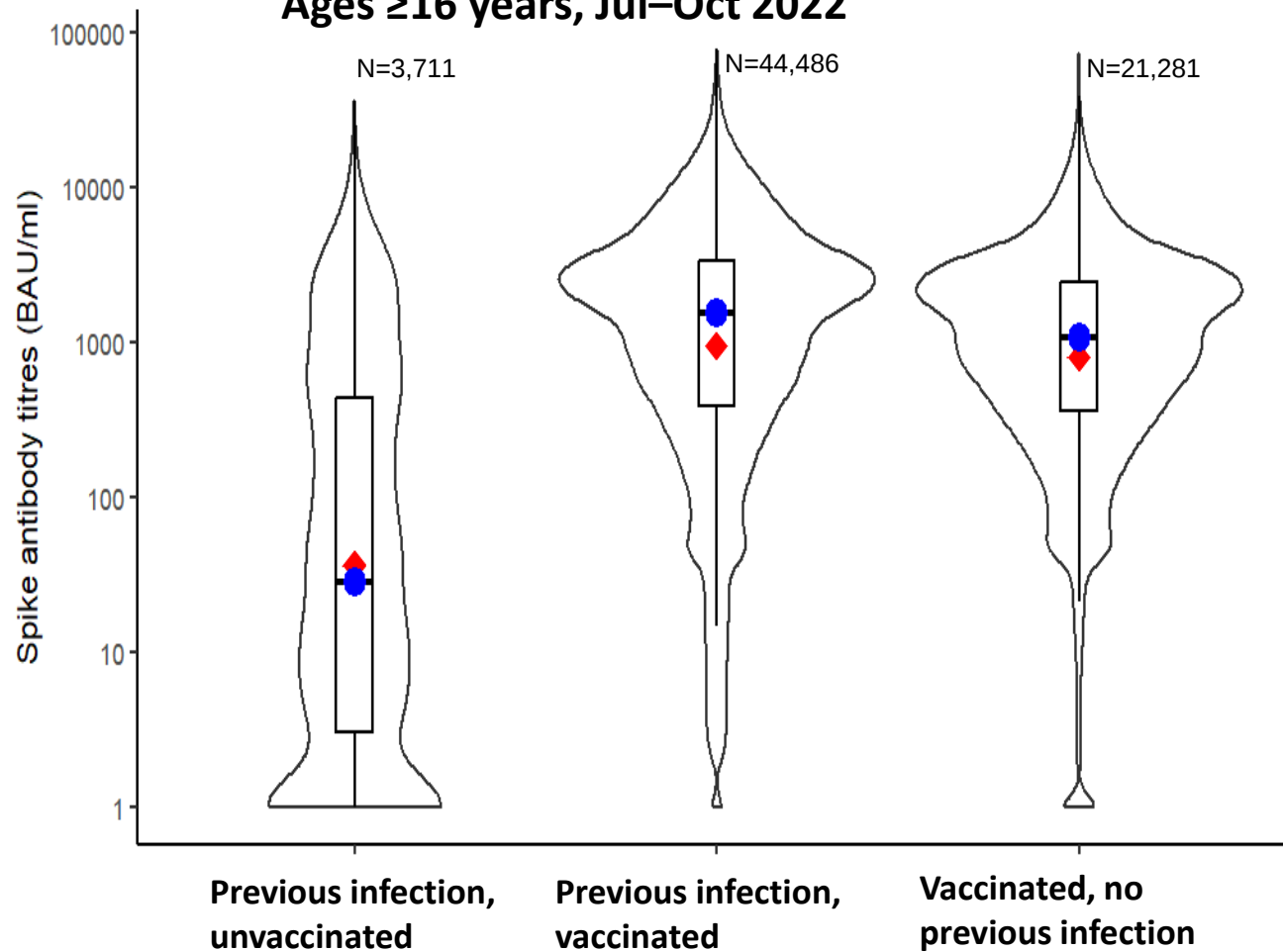
Seroprevalence from U.S. commercial laboratories — March–December 2022



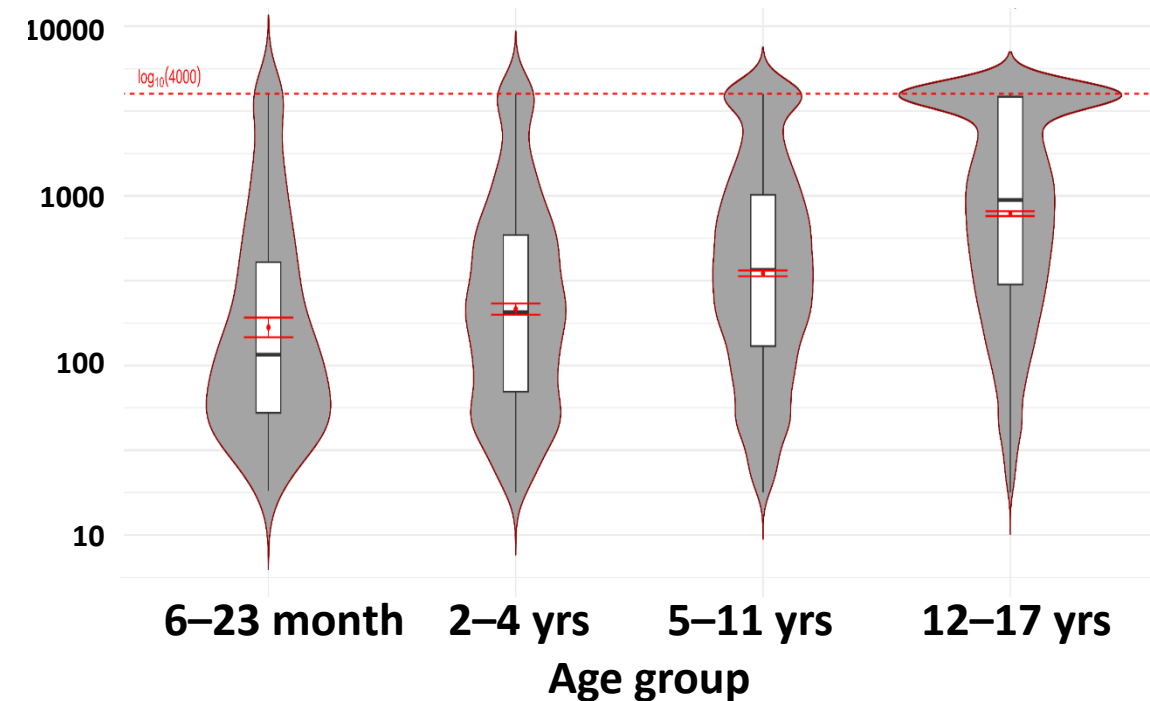
Source: <https://covid.cdc.gov/covid-data-tracker/#pediatric-seroprevalence> and unpublished data (CDC) Data from repeat, cross-sectional study on blood specimens collected by commercial laboratories. Vaccine history is unknown in this study. Infection-induced seroprevalence estimated from blood specimens tested for anti-nucleocapsid antibodies: the number of specimens per 2-month collection period were, by age group: 6–11 months: 157; 12–23 months: 724; 2–4 years: 2,165; 5–11 years: 9,247; and 12–17 years: 14,570. Combined (vaccine- and infection-induced seroprevalence estimated from specimens tested for both spike and nucleocapsid antibodies: >99% of samples tested for anti-nucleocapsid antibodies were tested for anti-spike antibodies.

Antibody titers depend more on history of infection and vaccination than age

National blood donor seroprevalence study
Ages ≥ 16 years, Jul–Oct 2022



National pediatric commercial lab seroprevalence study
Ages 6 months–17 years, Nov–Dec 2022, among specimens with antibodies*

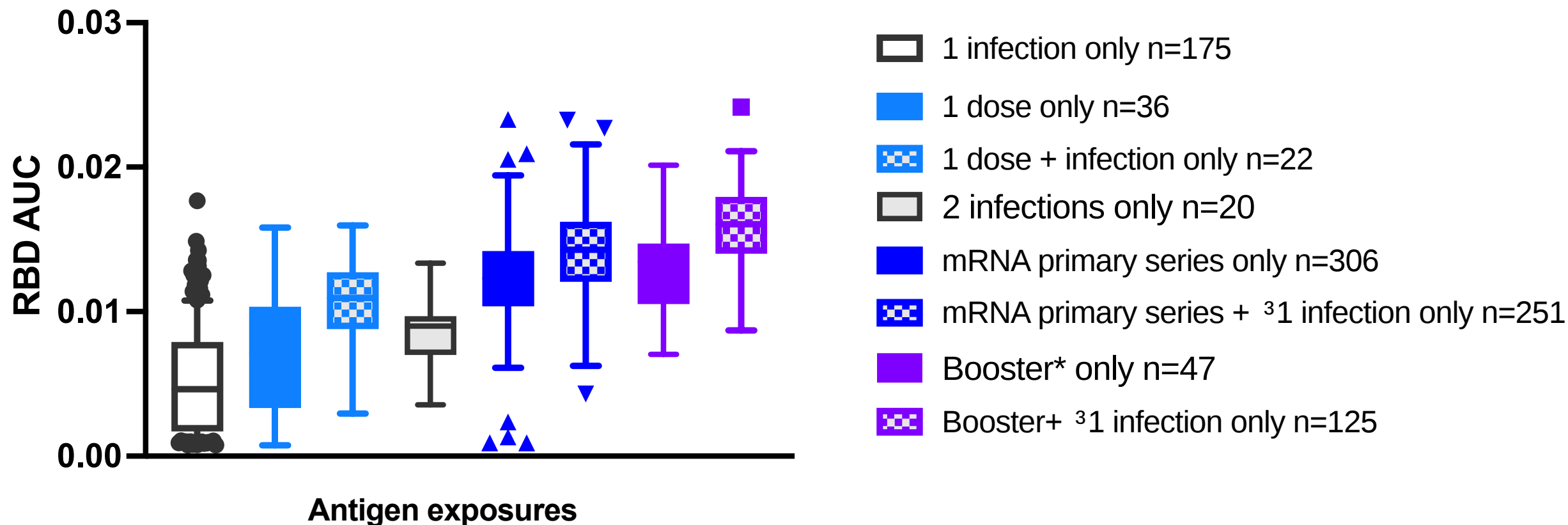


*Does not include specimens with no detectable antibodies
Source: CDC (unpublished)



RBD Ab levels by history of infection and vaccination status—children 6 mo—17+ yrs, PROTECT study

6 months — 17+ years



Blood draw within 6 months of immune modifying event, time between immune modifying events is ≤ 365 days.

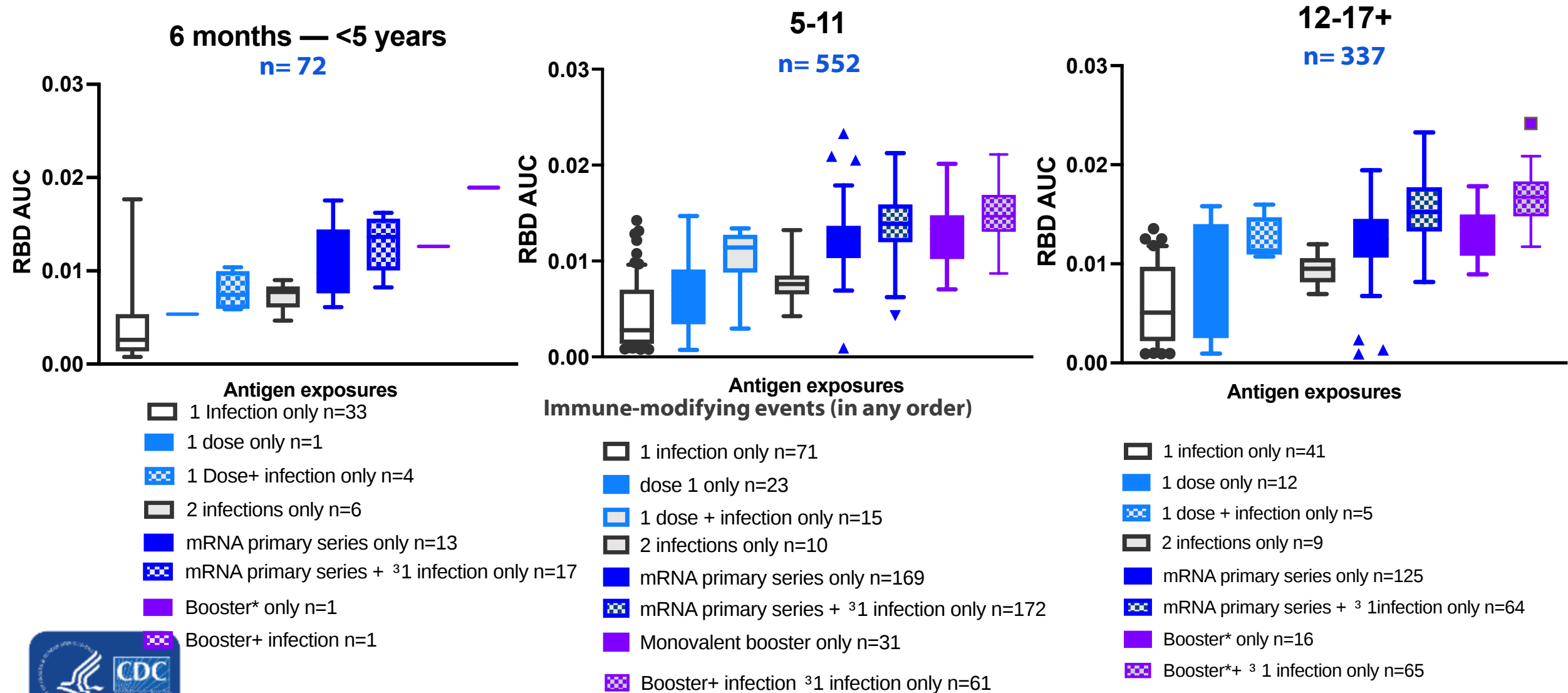
RDB AUC: area under the curve of receptor-binding domain antibodies, a quantitative measure of binding antibodies.

*Booster Bivalent and monovalent boosters grouped together.

Lyski, Z and Porter, C. Unpublished data from the PROTECT cohort. PROTECT protocol: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9377426/>



RBD Ab levels by history of infection and vaccination status by age group—children 6 mo—17+ yrs, PROTECT study



SARS-CoV-2 neutralizing antibody (nAb) studies

- In unvaccinated persons, infection-induced nAb titers highest against variants similar to the variant that infected the person¹
- nAb titers in people with hybrid immunity may wane slower than in people vaccinated without infection²
 - Infection after vaccination may be moderated by imprinting³
- Omicron
 - Omicron variants demonstrate greater escape from neutralization than older variants^{1–2,4–6}
 - Additional vaccine doses beyond primary series increase Omicron nAb titers^{4,5}
 - Hybrid immunity results in higher Omicron nAb titers than immunity from infection or vaccination alone, including to recent Omicron subvariants⁴



[1 Rössler 2022 NEJM](#); [2 Qu 2022 NEJM](#); [3 Wheatley Trends Immunol 2021](#); [4 Kurhade 2023 Nat Med](#);
[5 Gaebler 2022 OFID](#); [6 Barateau 2023 Sci Transl Med](#)

Other SARS-CoV-2 immunity laboratory study highlights

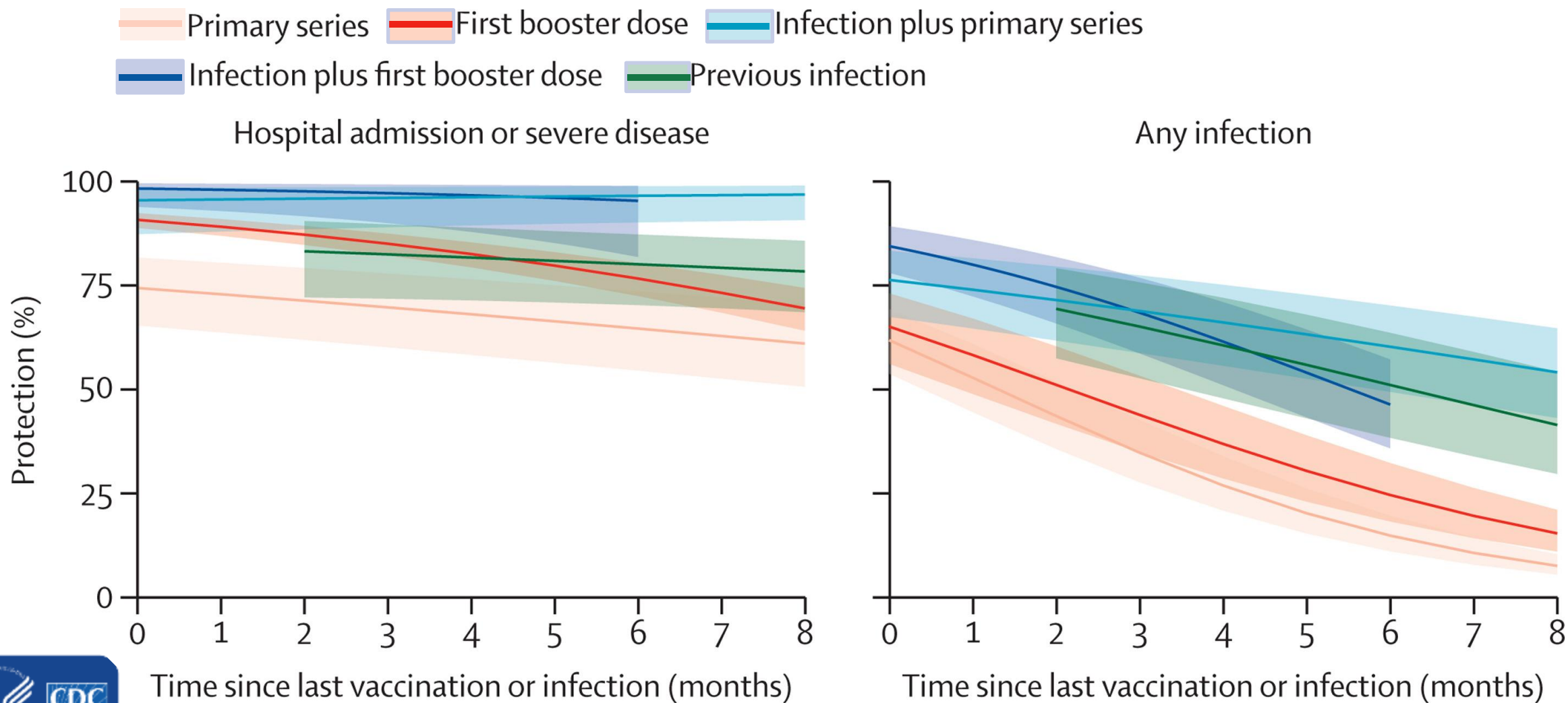
- Hybrid immunity appears to result in stronger more robust immune response using other measures as well, including
 - Infection-induced and hybrid immunity result in higher IgA titers than vaccine-induced immunity^{1,2}
 - Hybrid immunity may result in higher proportion of anti-spike memory B cells than vaccination alone³
 - Hybrid immunity induces T cells and antibodies directed against non-spike viral antigens⁴
- T-cell immunity from both infection and vaccination well preserved against Omicron⁴
 - Cellular immunity likely important in preventing severe disease⁵



¹ Barateau 2023 Sci Transl Med; ² Sheikh-Mohamed Immunol Rev 2022;

³ Bednarski 2022 mBio; ⁴ Naranbhai 2022 Cell ; ⁵ Moss 2022 Nature

Systematic review of protection against Omicron from infection, hybrid with monovalent primary series, and hybrid with first monovalent booster



Conclusions

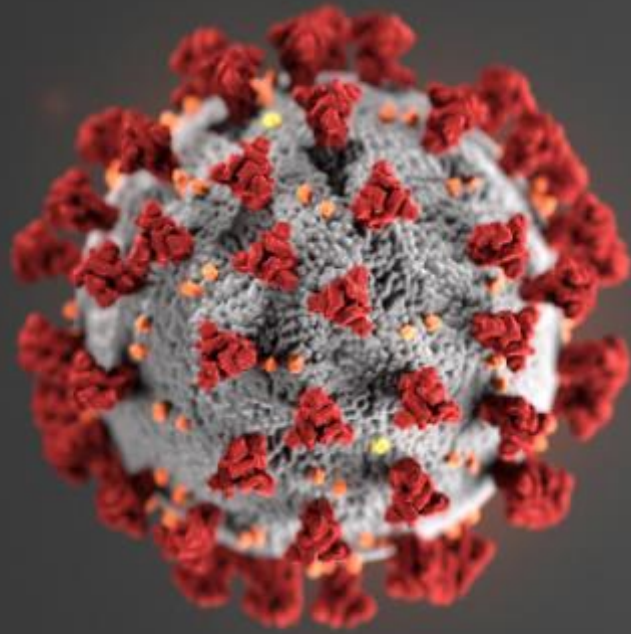
- SARS-CoV-2 infection can cause severe disease, death, and long-term morbidity, whereas COVID-19 vaccination is safe and effective at preventing severe COVID-19 disease
- The proportion of people with immunity from infection or hybrid immunity has increased
- Immunity following vaccination and infection wanes over time, and both monovalent primary series vaccination and history of pre-Omicron infection provided much lower protection during Omicron than during prior COVID-19 waves
- Compared with protection from infection or vaccination alone, hybrid immunity likely better protects against infection and severe disease with Omicron
- Stronger protection is likely provided when the infecting variant is similar to the circulating variant, but this may be complicated by imprinting
- Current protection likely influenced by both cumulative number of vaccine doses, number of times infected, and timing of most recent vaccination or infection, and how closely the circulating variant matches the vaccine or prior infection
- Conclusions apply to both children and adults



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- PROTECT team





For more information, contact CDC
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TTY: 1-888-232-6348 www.cdc.gov

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.

