Considerations for long-term protection against mpox

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CDC collaborative studies examining serologic response to JYNNEOS vaccinations

Study	Goals	Timepoints/Duration	Participant Information
• DRC • Healthcare personnel • Democratic Republic of the Congo, Tshuapa Province	• Safety • Immunogenicity • Effectiveness	• 2-year studies • Serum obtained on days 0, 14, 28, and 42, and 6, 12, 18, 24 months • Booster: 5 years • Serum obtained on days 0, 7, 14	• 1000 participants SC/SC liquid formulation • 600 participants SC/SC lyophilized formulation • ~170 participants (Booster)
• DC PEP++ • Expanded post-exposure prophylaxis in MSM with behaviors that increase risk for mpox • DC Health • Washington, DC	• Immunogenicity • Comparison between different routes of vaccination	• 2-year study • Days 0, 28, and 42-56 and 6 months • 12, 18, and 24 months planned.	• 330 participants • Participants with 2 timepoints (n=216), 3 timepoints (n=70), or all 4 timepoints (n=66)

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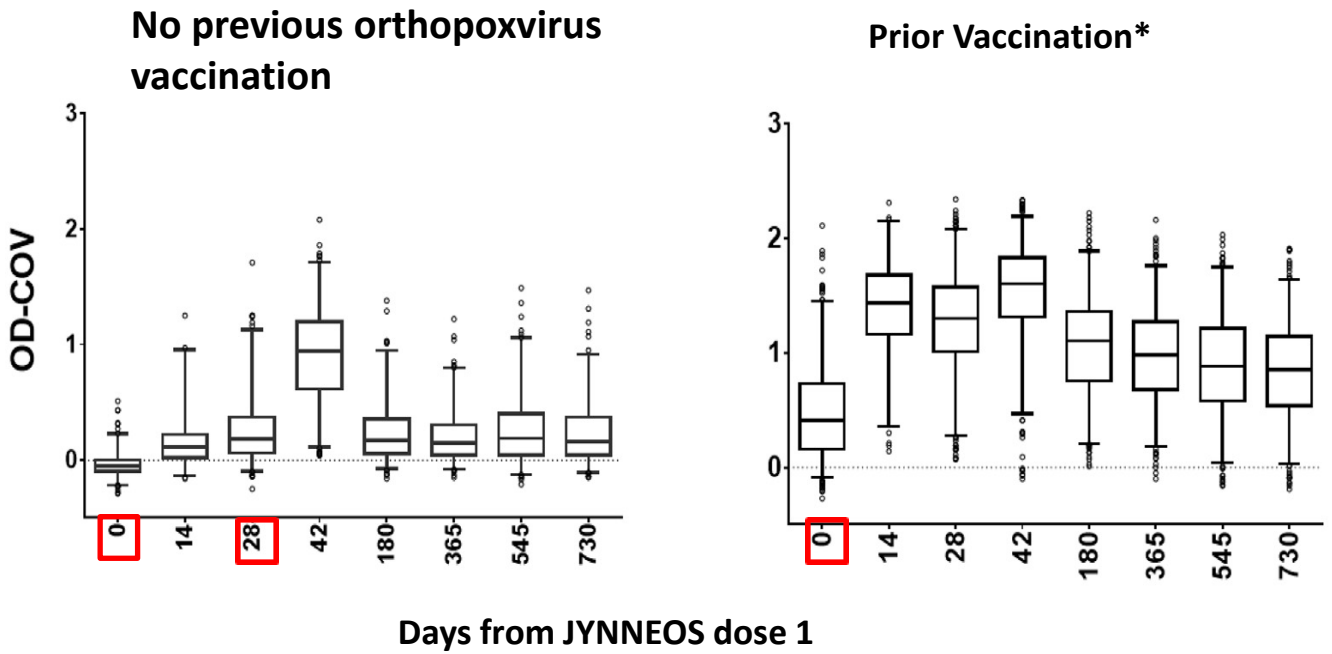
DRC study: Detection of IgG antibody after JYNNEOS vaccination

- Serum specimens tested for presence of orthopoxvirus-specific IgG antibody using an enzyme-linked immunosorbent assay (ELISA)
- Positivity determined by Optical Density (OD) – cutoff value (COV)
- Circulating IgG levels peaked slower and lower in persons who received no previous orthopoxvirus vaccine
- Circulating IgG levels stayed higher for a longer period of time in persons previously vaccinated



Priyamvada et al., Vaccine, 2022

*Prior vaccination was not with JYNNEOS; it was a vaccine to prevent smallpox that was received during childhood

2022 ACIP recommendations for persons at occupational risk for orthopoxvirus exposures

- Reviewed data indicated an anamnestic response occurs 2 years after the 2-dose series
- ACIP recommendations: persons (typically laboratorians) at occupational risk for variola virus and MPXV exposures should receive JYNNEOS booster doses every 2 years
- No data to indicate whether anamnestic response would occur >2 years after 2-dose series; standard-of-care for these persons working with research grade virus has been booster doses

WG's interpretation

- Significance of waning circulating antibody levels is unknown
- Anamnestic response elicited 2 years after JYNNEOS primary series
- 2022 ACIP recommendations were for exposures that are different from those experienced during the current outbreak

Real-world data during 2022/2023 U.S. mpox outbreak

- VE studies
  - 3 studies: NY State, Epic Cosmos, and Multijurisdictional Case-Control Studies
  - VE ranged from 36%–75% for 1 dose and 66%–89% for 2 doses
- Mpox cases among persons who received 2 doses have occurred: Some cases expected; reported as early as August 2022
- 2023 Chicago cluster involving persons who received 2 JYNNEOS doses*
  - No U.S. clusters of a similar size reported
  - No hospitalizations; opiates not typically prescribed for pain control
  - Sequences typical of B.1 variant of MPXV Clade IIb; no mutations that would confer increased pathogenicity

*For most, at least one dose (and often both doses) were administered subcutaneously

WG's interpretation

Third dose currently not indicated for entire population eligible for vaccination

Additional vaccine doses for immunocompromised persons, including persons with HIV

Safety of third dose of JYNNEOS

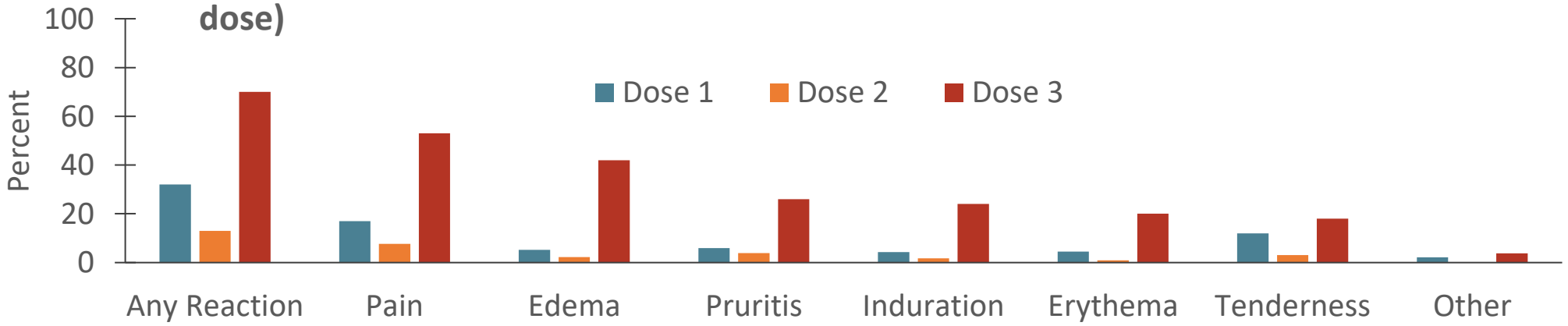
Current Knowledge

CDC's DRC study: Study of HCP shows increased adverse events among recipients of 3rd dose at 5 years after primary series

Limitation

- Study population may not be representative of U.S. population

Select vaccine-associated adverse events, by dose, healthcare personnel in Democratic Republic of Congo (n=706 for first and second doses and n=170 for 3rd dose)



Minhaj et al, unpublished data, 2023

Safety of third dose of JYNNEOS in persons with HIV

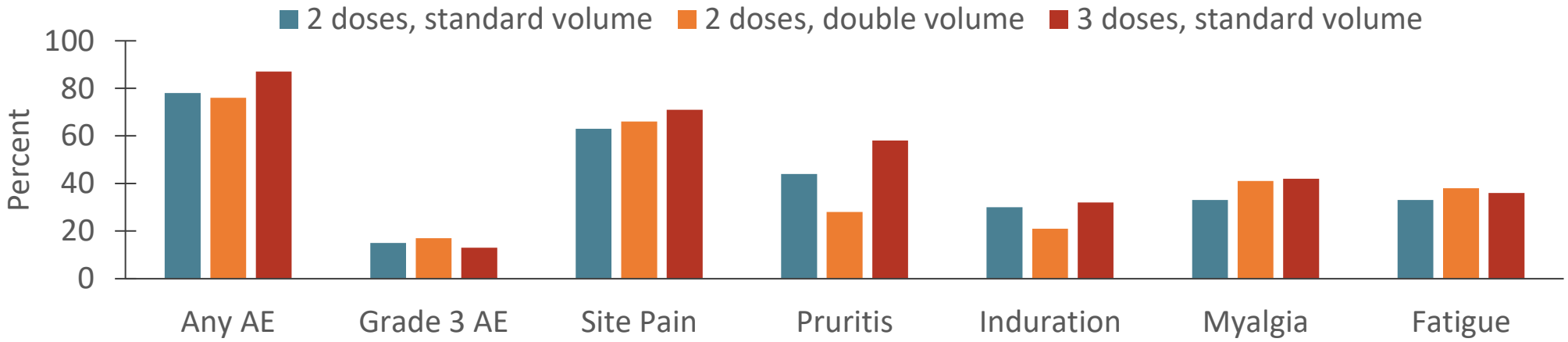
Current Knowledge

Study of persons with HIV (CD4 100–500) shows increased adverse events (albeit not significant) among recipients of third dose at week 12

Limitation

Small numbers of total subjects; only 30 patients received third dose; difficult to know likelihood of increased adverse events

Select vaccine-associated adverse events, by dose, among persons with HIV in the United States (n=87 for 1st and 2nd doses, n= 30 for third dose)



Overton 2020 Vaccine

WG's interpretation

Third dose might result in more adverse events; this could deter some persons from receiving first and second doses

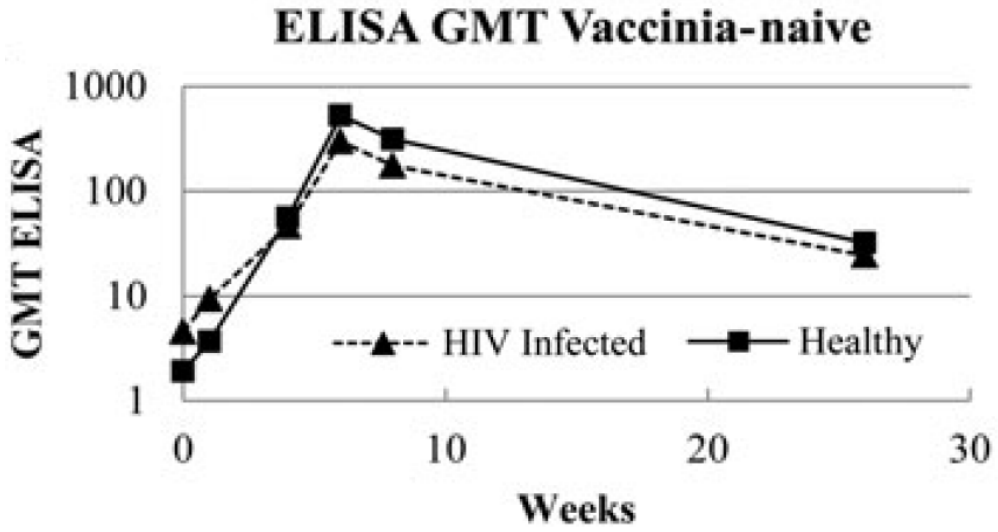
Serologic Response to JYNNEOS among persons with HIV

Current Knowledge

- For nearly 600 persons with CD4 >200*, serologic response to 2-dose series equivalent to response in persons without HIV

Limitation

- No assessment of serologic response for persons with CD4 <100



* measured in cells/mm^3

Greenberg 2013 J Infect Dis; Overton 2015 Open Forum Infect Dis;

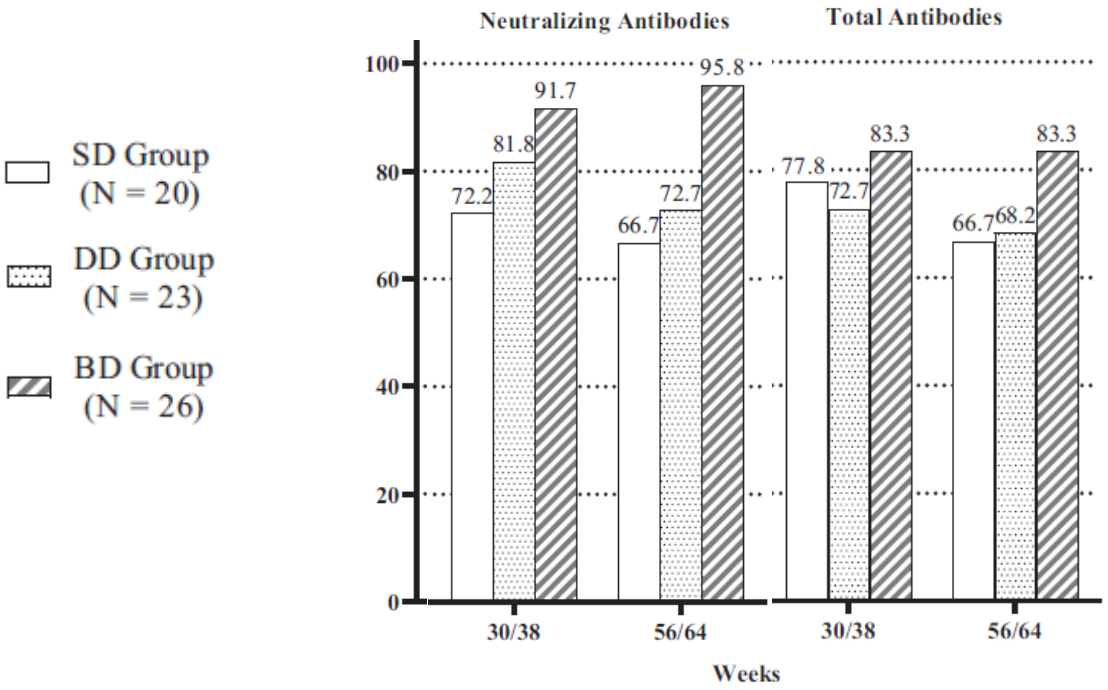
Serologic Response to JYNNEOS among persons with HIV

Current Knowledge

- For persons with CD4 100-500* and lifetime nadir <200*, serologic response of 3 doses is similar to 2 doses
- Review of unpublished data: No correlation between low CD4 count and antibodies after vaccine

Limitation

- Serologic correlate of protective immunity unknown
- Small number of subjects: only 26 subjects in 3-dose arm



* measured in cells/mm^3

Overton 2020 Vaccine

VE of JYNNEOS in persons with self-reported immunocompromise (including HIV)

Current Knowledge

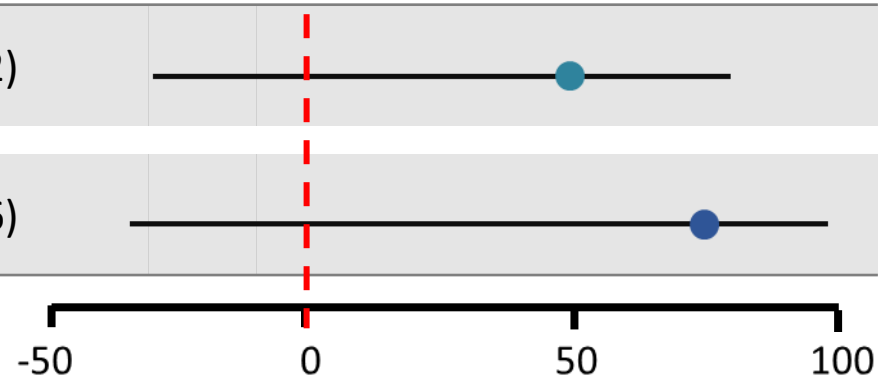
VE point estimates for persons who are immunocompromised* lower than for general population of vaccinated persons for both 1 and 2 doses

* predominately HIV (CD4 cell count not specified)

Limitation

- Estimates do not differ statistically from estimates for general population
- Few persons for whom this was evaluated; Confidence Intervals wide

	Cases	Controls	Adjusted† VE (95% CI)
Partial vaccination VE, immunocompromised	22	52	51.0% (-27.6–81.2)
Full vaccination VE, immunocompromised	9	31	70.2% (-37.9–93.6)



†Adjusted for age, race/ethnicity, immunocompromised status, reported close contact with a confirmed/suspected mpox case in 3 weeks prior to index event, and month of index event
https://www.cdc.gov/mmwr/volumes/72/wr/mm7220a3.htm?s_cid=mm7220a3_w

Severity of infections among fully vaccinated: National reporting and anecdotal reports

Current Knowledge

- >10,000 mpox cases among persons with HIV; however no confirmed reports of severe mpox illness after full vaccination
- CDC reviewed data reported from health departments for fully vaccinated persons with mpox and confirmed none were hospitalized due to severe manifestations of mpox
- Anecdotally, CDC told there was a severe case in a patient who was not fully vaccinated; however, details not known

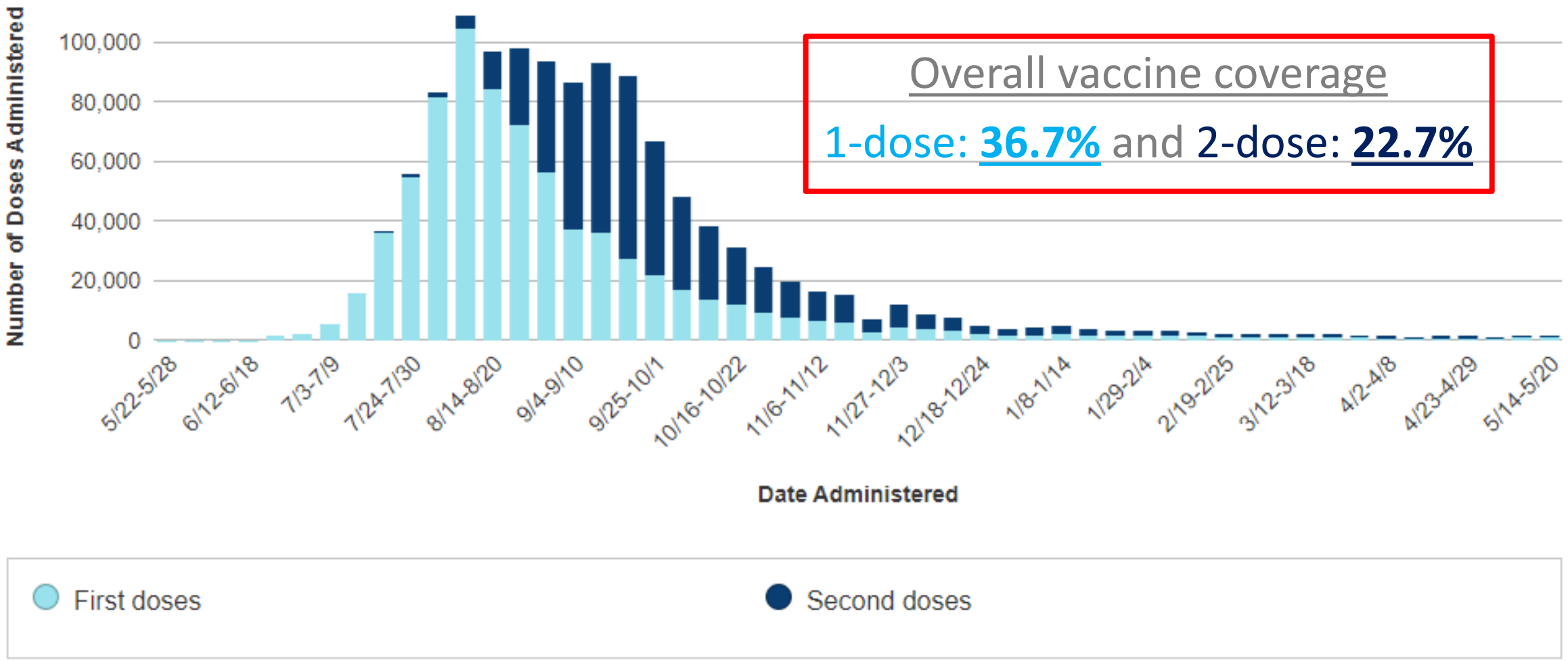
Limitation

- Data extrapolated from surveillance and consultation data; no formal review of electronic health records linked to vaccine registries
- Not known whether persons who do not respond to 2 doses of JYNNEOS would respond to a third dose

WG's interpretation

There is no convincing data to indicate patients with moderate-severe immunocompromise would benefit from an additional dose of JYNNEOS

First and Second Doses of JYNNEOS Vaccine Administrations–United States, May, 2022 to May 2023



Conclusions

- WG prefers no CDC recommendation for third JYNNEOS dose at this time, including for persons with advanced HIV or other severe immunocompromise
- WG emphasized several strategies
  - Encourage 2-dose vaccinations among persons who do not have immunity*
  - Prevent or minimize life-threatening manifestations
    - Optimizing immune function (e.g., with HIV antiretrovirals), ideally before mpox exposure
    - Using CDC interim treatment considerations[§] to manage patients with (or at risk of) severe manifestations of mpox

*e.g., persons who have not had mpox

[§] Rao et al. 2023. MMWR

Next steps

- Continue to collect and evaluate any existing data, particularly about use of JYNNEOS in immunocompromised persons
- Attempt to characterize severity of mpox cases experienced by people who received 2 JYNNEOS doses
- Continue ongoing VE studies
- Update CDC interim clinical considerations* if additional JYNNEOS vaccine doses are recommended

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Questions and Comments?

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.