



Evidence to Recommendations Framework: Vaccination with JYNNEOS During Mpox Outbreaks

Agam Rao, MD

CAPT, US Public Health Service

Poxvirus and Rabies Branch

Centers for Disease Control and Prevention

Advisory Committee on Immunization Practices

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Evidence to Recommendations Framework

Evidence to Recommendations (EtR) Framework

- Structure to describe information considered in moving from **evidence** to ACIP vaccine **recommendations**
- Provide transparency around the impact of additional factors on deliberations when considering a recommendation



EtR Domains

EtR Domain	Question(s)
Public Health Problem	<ul style="list-style-type: none">Is the problem of public health importance?
Benefits and Harms	<ul style="list-style-type: none">How substantial are the desirable anticipated effects?How substantial are the undesirable anticipated effects?Do the desirable effects outweigh the undesirable effects?
Values	<ul style="list-style-type: none">Does the target population feel the desirable effects are large relative to the undesirable effects?Is there important variability in how patients value the outcome?
Acceptability	<ul style="list-style-type: none">Is the intervention acceptable to key stakeholders?
Equity	<ul style="list-style-type: none">What would be the impact of the intervention on health equity?
Feasibility	<ul style="list-style-type: none">Is the intervention feasible to implement?
Resource Use	<ul style="list-style-type: none">Is the intervention a reasonable and efficient allocation of resources?

EtR question

Does ACIP recommend the 2-dose* JYNNEOS vaccine series for persons aged 18 years and older at risk of mpox during an mpox outbreak?[§]

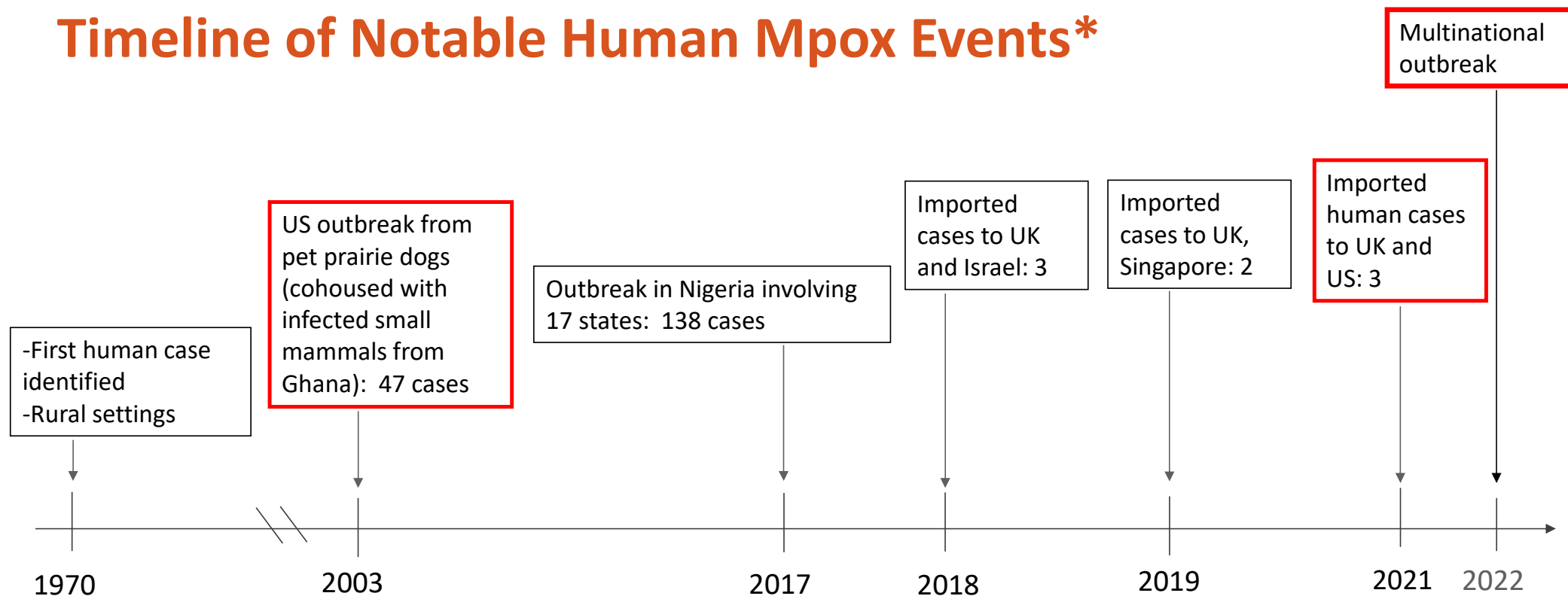
*Dose 2 administered one month after dose 1

§ Public health authorities determine whether there is an mpox outbreak; a single case may be considered an mpox outbreak at the discretion of public health authorities. Other circumstances in which a public health response may be indicated include ongoing risk of introduction of mpox into a community due to disease activity in another geographic area.



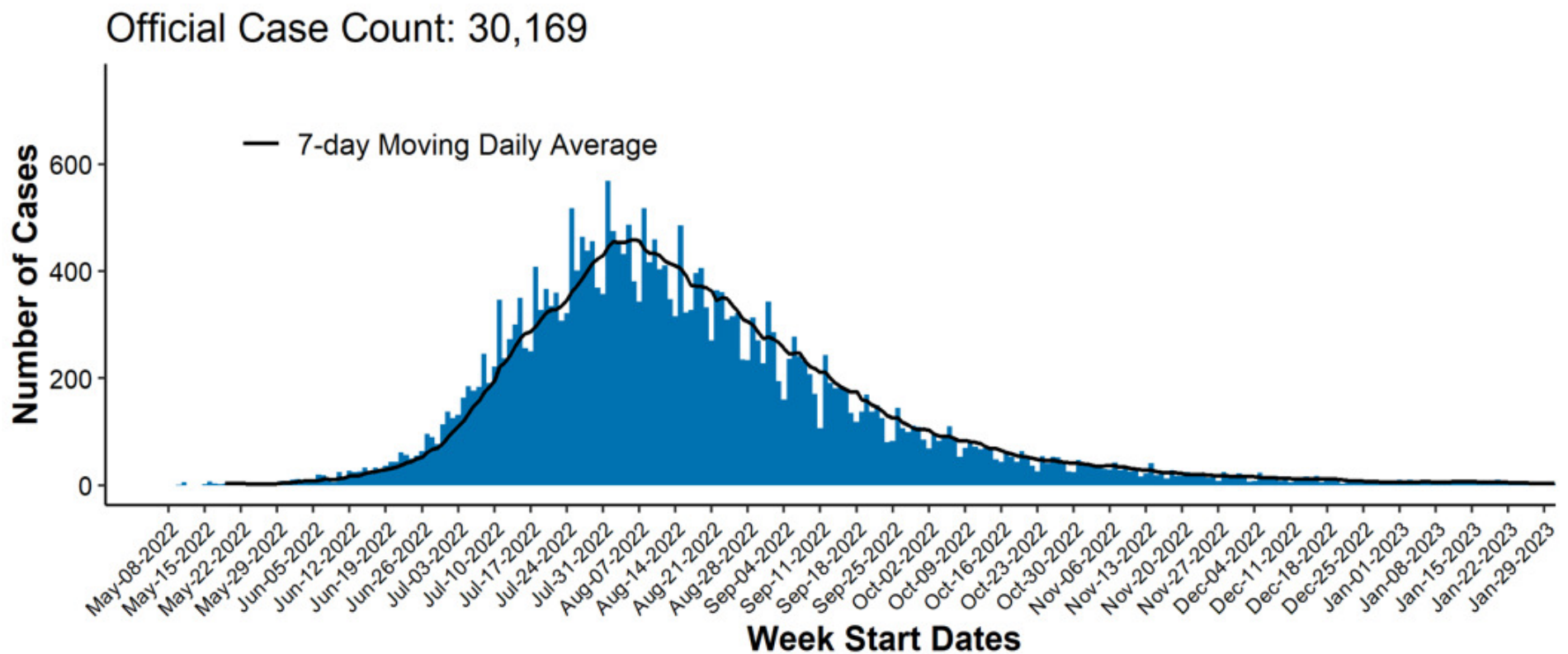
EtR Domain: Public Health Problem

Timeline of Notable Human Mpox Events*



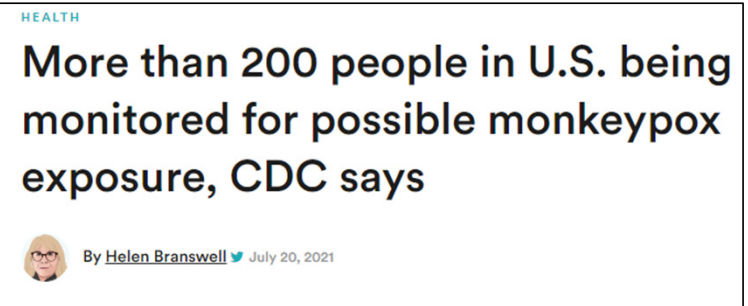
*During 1970-2021, mpox was endemic in 9 African countries: Cameroon, Central African Republic, Cote d'Ivoire, Democratic Republic of Congo, Gabon, Liberia, Nigeria, Republic of Congo, and Sierra Leone; during recent years, there has been a re-emergence of human cases after decades of no reported cases

U.S. mpox case trends as of February 9, 2023



Many contacts monitored during investigations and some secondary cases have occurred

- United States, July 2021: Traveler returning from Nigeria
 - 223 contacts monitored
 - No high-risk exposures and no secondary transmissions
 - Contacts included flight crew and fellow passengers on international and domestic flights, friends, Ride-share driver
- United Kingdom, 2019 and 2021
 - 2019: Healthcare personnel developed mpox after presumed exposure while changing bedding of mpox patient
 - 2020: Two household contacts of mpox patient developed mpox



Typical manifestations of mpox



From Basgoz N, Brown CM, Smole SC, et al. Case 24-2022: A 31-Year-Old Man with Perianal and Penile Ulcers, Rectal Pain, and Rash. Epub ahead of print. Copyright © Jun 15 2022. Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society



Above: Shared with permission from patients

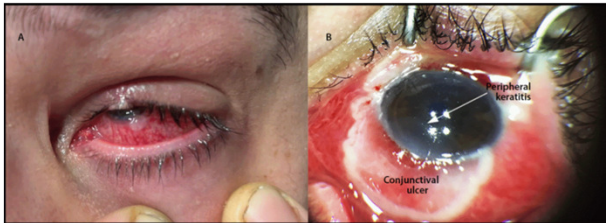


- Lesions often perianal and/or affecting genitals
- Rectal pain
- Abdominal pain
- Rectal bleeding
- Tenesmus



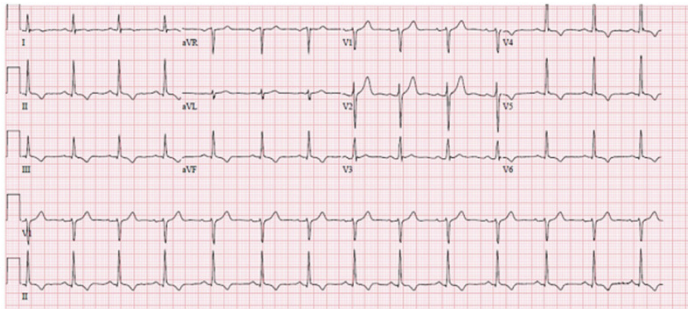
https://www.cdc.gov/mmwr/volumes/71/wr/mm7132e3.htm?s_cid=mm7132e3_w

Severe manifestations: Ocular lesions, neurologic complications, myopericarditis, and some mucosal lesions



Left: Keratitis and conjunctival ulcer

Cash Goldwasser S, Labuda SM, McCormick DW et al. (2022) Ocular monkeypox, United States—July-September 2022. MMWR. 2022 Oct

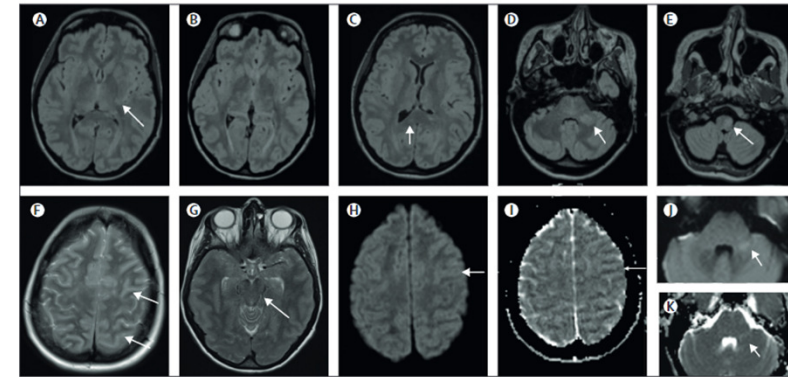


Above: NSR with TWI in inferior and anterolateral leads of ECG. Patient with mpox and no underlying medical conditions. Other signs and symptoms: SOB, decreased exercise tolerance, elevated Tn (0.35ng/mL reference <0.07 ng/mL) indicating myocarditis

Rodriguez-Nava G, Kadlecik P, Filardo TD et al. Myocarditis Attributable to Monkeypox Virus Infection in 2 Patients, United States, 2022. Emerg Infect Dis. 2022 Dec;28(12):2508-2512.

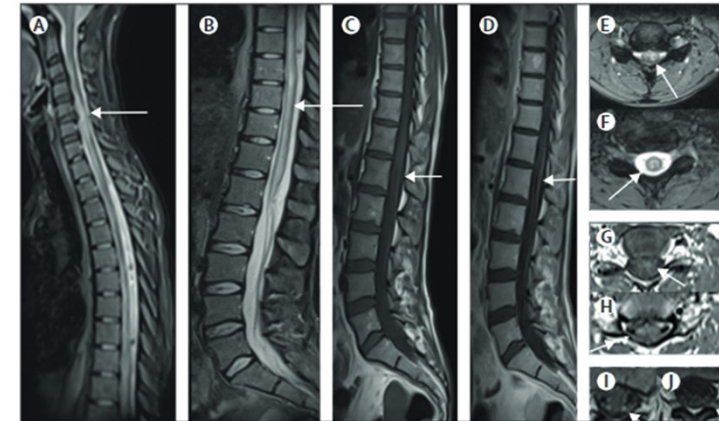
Complications associated with some mucosal lesions

- Painful or obstructing rectal, urinary tract, oral and genital lesions and strictures
- Lesions might expose muscle or bone



Above: encephalitis

Right: transverse myelitis



Cole J, Choudry S, Kular S, et al. Monkeypox encephalitis with transverse myelitis in a female patient. Lancet Infect Dis. 2022 Dec 2:S1473-3099(22)00741-1.

Severe manifestations from uncontrolled viral spread in severely immunocompromised patients



Carrubba S, Geevarghese A, Solli E et al. Novel severe oculocutaneous manifestations of human monkeypox virus infection and their historical analogues. *Lancet Infect Dis.* 2023 Jan 23:S1473-3099(22)00869-6.



Menezes YR, Miranda AB. Severe disseminated clinical presentation of monkeypox virus infection in an immunosuppressed patient: first death report in Brazil. *Rev Soc Bras Med Trop.* 2022 Aug 29;55:e0392.

Public health importance

Work group interpretation

Are outbreaks of mpox of public health importance?

☐ No ☐ Probably no ☐ Uncertain ☐ Probably yes ☒ Yes ☐ Varies

EtR Domain: Benefits and Harms

Early Estimates and Population-based, adjusted VE measures*

- Vaccine performance
 - Comparison of incidence between vaccinated and unvaccinated persons in 43 U.S. jurisdictions: Mpox incidence among unvaccinated was 7.4 (95% CI=6.0-9.1) times that among persons who received only 1 dose of JYNNEOS vaccine ≥ 14 days earlier, and 9.6 (95% CI = 6.9–13.2) times that among persons who received dose two ≥ 14 days earlier
- Population-based, adjusted measures of vaccine effectiveness (VE) using electronic medical records
 - Retrospective, population-based cohort study conducted in Israel; 5 mpox infections among subjects vaccinated with 1 SC dose and 16 among unvaccinated subjects. VE for dose 1 was 86% (95% CI = 59-95%)
 - Nationwide U.S. case-control study with 1:4 ratio of cases matched to controls; adjusted VE was 35.8% (95% CI: 22.1-47.1%) for one dose and 66.0% (95% CI: 47.7-78.1%) for 2 doses, regardless of vaccination route

Early Estimates and Population-based, adjusted VE measures*

- Population-based, adjusted measures of VE using case-control studies
 - Case-control study of adult MSM (18-49 years of age) in 12 U.S. jurisdictions; adjusted VE was 76% (95% CI: 48-89%) for two doses (interim results)
 - New York State case-control study of adult male mpox cases matched to STI controls; adjusted VE was 68% (95% CI: 25-86%) for one dose and 89% (95% CI: 44-98%) for two doses (preliminary results)



PEP effectiveness and infections following single dose

- France: 10% (11 of 108) of those administered JYNNEOS after mpox exposure became symptomatic with mpox disease soon after vaccination (IQR 1-6, median 5 days), although clinical course mild among those persons
- France: Observational study involving people who received single, SC dose; 4% (12 of 276) infected during month after vaccination, none with serious infection
- NYC: Cohort study of individuals with high-risk exposure; VE was 77% with PEP <14 days after last exposure and 79% with PEP <14 days after first exposure



Benefits

Work group interpretation

How substantial are the desirable anticipated effects of mpox vaccine during an outbreak?

How substantial are the desirable anticipated effects?

☐ Minimal ☐ Small ☐ Moderate ☒ Large ☐ Don't know ☐ Varies

Vaccine Safety: Subcutaneous administration

- During May 22, 2022 – January 13, 2023, a total of 1,125,168 JYNNEOS vaccine doses were administered. CDC monitored JYNNEOS safety using VAERS and VSD for vaccine recipients of all ages
- Adverse events (AEs)
 - The most common AEs reported were nonserious and included injection site reactions, consistent with prelicensure studies
 - Reported at similar rates for doses received by intradermal and subcutaneous administration
 - Serious adverse events were rare among adults



Harms

Work group interpretation

How substantial are the undesirable anticipated effects of mpox vaccine during an outbreak?

How substantial are the desirable anticipated effects?

☐ Minimal ☒ Small ☐ Moderate ☐ Large ☐ Don't know ☐ Varies

Benefits / Harms

Work group interpretation

What is the balance between the desirable effects relative to the undesirable effects?

Do the desirable effects outweigh the undesirable effects?



Favors intervention



Favors comparison



Favors both



Favors neither




Unclear



EtR Domain: Values

Vaccination values extrapolated from 2022 outbreak data

- Populations at highest risk concerned about mpox
 - In August, 53.1% of American Men's Internet Survey (AMIS) respondents had concerns about getting mpox
 - During October-December, an AMIS survey showed that those with high mpox concern had 3.5 times odds of being vaccinated
 - Interest in vaccine high
 - During Aug-Nov, >85% of respondents in the American Transformative HIV Study (AMETHST) were interested in vaccine
 - During Aug-Dec, 50% of Porter-Novelli survey responders who identified as LGBTQ+ felt that vaccination is important to protect from mpox
 - During Oct-Nov, >70% of MSM in a San Francisco survey of persons experiencing homelessness reported that they would accept or have accepted vaccination
- 

Target population sentiments

Work group interpretation

Does the target population feel that the desirable effects are large relative to undesirable effects?

Does the target population feel that the desirable effects are large relative to undesirable effects

☐

No

☐

Probably no

☐

Uncertain



Probably yes

☐

Yes

☐

Varies



Uncertainty or variability in how much people might value vaccination

- During 2022 mpox outbreak, willingness to be vaccinated was dynamic, and dependent on perceived vulnerabilities
- There is clear demand for JYNNEOS vaccination, but many remain unvaccinated for unclear reasons
- Demographics of future outbreaks unclear; unknown if values expressed by population most affected by the 2022 mpox outbreak can be extrapolated to all other populations



Target population sentiments

Work group interpretation

Is there important uncertainty about or variability in how much people value the main outcomes?

Is there important uncertainty about or variability in how much people value the main outcomes



Important
uncertainty
or variability



Possibly important
uncertainty or
variability



Probably no
important
uncertainty or
variability



No important
uncertainty or
variability



No known
undesirable
outcomes

EtR Domain: Acceptability

Stakeholder perceptions: Sermo survey of clinicians

- Sermo*: Online community of >1.3 million clinicians
- July 31 - August 1, 2022 survey results of U.S. clinicians (n=415): 69% felt U.S. without enough mpox vaccine to handle outbreak
- September 12, 2022 survey of U.S. clinicians (n=62)
 - 66% had treated at least one mpox patient
 - 76% knew where a patient could get JYNNEOS vaccination
 - 86% wanted to be able to provide vaccination in their office

Sermo Barometer Reveals Growing Concern Among Global Physicians Regarding Monkeypox

August 8, 2022

As WHO declares a global health emergency, 65% of doctors say their countries do not have enough vaccines

New York, NY – With the spread of monkeypox on the rise and the World Health Organization (WHO) declaring a global health emergency, findings from a recent survey conducted by Sermo, a physician-first online community and leader in global HCP insights, show there is high concern about public misinformation spreading. The survey also found that while 71% of respondents would recommend vaccination as a preventative measure to a patient who was concerned about contracting monkeypox, 65% of doctors say their country does not have enough vaccines.

The barometer survey included 1,011 physician respondents from 20 countries, with key findings including:

Concerns About Misinformation

Seventy-eight percent of physician respondents expressed concern about the spread

* <https://app.sermo.com/barometer/unitedstates>

Stakeholder perceptions: Health departments

- Health departments have been requesting JYNNEOS and organizing vaccination campaigns



MONKEYPOX

New York City opens more monkeypox vaccination appointments today



By [Derick Waller](#)

Tuesday, July 12, 2022



Jurisdiction	Total Allocated Eaches as of Feb 08 2023, 12pm	Total Requested as of Feb 08 2023, 12pm	Total Shipped as of Feb 08 2023, 12pm
All Jurisdictions	1,183,813	857,493	857,393
Alabama	8,383	4,523	4,523
Alaska	1,080	600	600
American Samoa	60	40	40
Arizona	19,773	12,173	12,173
Arkansas	4,260	2,460	2,460
California	112,309	114,189	114,189
California - Los Angeles	73,802	65,522	65,522
Colorado	19,525	12,805	12,805
Connecticut	8,928	6,328	6,328
Delaware	2,795	1,655	1,655
District of Columbia	31,455	27,415	27,415
Federated States of Micronesia	20	20	20
Florida	112,680	74,720	74,720
Georgia	54,502	33,582	33,582
Guam	120	80	80
Hawaii	4,472	3,272	3,272
Idaho	2,420	1,380	1,380

<https://aspr.hhs.gov/SNS/Pages/JYNNEOS-Distribution.aspx>

Vaccine equity pilot program

- Enabled jurisdictions to request more than their allotted amount of JYNNEOS vaccine
- Established to
 - Support innovative ways to address vaccination disparities
 - Encourage vaccination coordination between health departments and community-based organizations
 - Promote innovation to strengthen existing vaccination infrastructure



**15
Jurisdictions**

**28
Programs**



~25k Doses

Acceptability

Work group interpretation

Is the intervention acceptable to key stakeholders

Is the intervention acceptable to key stakeholders

☐ No

☐ Probably no

☐ Uncertain

☐ Probably yes

☒ Yes

☐ Varies

EtR Domain: Resource Use

Resource Use

- JYNNEOS vaccine is provided from HHS' Strategic National Stockpile (SNS) free-of-charge
- Vaccines are a good use of resources during an outbreak
- Costs and challenges associated with mobile, pop-up vaccination sites
- Cost-effectiveness analysis of vaccine implementation during the current outbreak planned, but not currently available



Resource Use

Work group interpretation

Is the intervention a reasonable and efficient allocation of resources

Is the intervention a reasonable and efficient allocation of resources

☐

No

☐

Probably no

☐

Uncertain

☐

Probably yes

☐

Yes

☒

Varies



EtR Domain: Equity

Equity

- No groups or settings disadvantaged by recommendation for JYNNEOS use during mpox outbreaks
- Effectiveness same for all immunocompetent persons
- Implementation to assure equitable access will be important particularly among persons who are at high risk for severe outcomes
- Might facilitate broad acceptance of the recommendation (e.g., by insurance companies, health departments) because endorsed by ACIP after rigorous review of evidence



Equity

Work group interpretation

What would be the impact on health equity

What would be the impact on health equity?

- | | | | |
|------------------------------------|---|---|--|
| <input type="checkbox"/> Reduced | <input type="checkbox"/> Probably Reduced | <input type="checkbox"/> Probably no impact | <input checked="" type="checkbox"/> Probably increased |
| <input type="checkbox"/> Increased | <input type="checkbox"/> Varies | <input type="checkbox"/> Don't know | |

EtR Domain: Feasibility

Feasibility

- Feasibility of conducting vaccine campaigns in communities, at events, and within public health facilities demonstrated in 2022
- Can be integrated into providers' practices
 - Standing orders available
 - Immunization Information Systems requirements for reporting vaccinations same as COVID-19 vaccines
 - JYNNEOS can be stored refrigerated for 8 weeks
- Wide range of vaccinators can administer JYNNEOS



WG discussions

- JYNNEOS vaccination probably sustainable during outbreaks
- Vaccine access is an important concern
 - Increased and convenient access
 - Low stigma
- Considerations to ensure vaccine equity
 - Strong ties with community-based organizations
 - Support vaccination events
 - Engage trusted messengers
 - Ensure access (including in rural areas)

Feasibility

Work group interpretation

Is the intervention feasible to implement?

Is the intervention feasible to implement

☐

No

☐

Probably no

☐

Uncertain

☐

Probably yes



Yes

☐

Varies



Summary of EtR #1

Domains		Domains		Domains	
Benefits: How substantial are the desired anticipated effects	Large	Values: Does the target population feel desirable effects are large	Probably Yes	Impact on health equity	Probably increased
Harms: How substantial are undesirable anticipated effects?	Small	Is there important uncertainty about or variability in values?	Possibly important uncertainty or variability	Feasible to implement?	Yes
Benefit / Harm:	Favors intervention	Acceptable to stakeholders?	Yes	Balance of consequences:	
Overall certainty of the evidence for the critical outcomes	Moderate	Reasonable and efficient allocation of resources?	Varies		

Balance of Consequences

<input type="checkbox"/> Undesirable consequences clearly outweigh desirable consequences in most settings	<input type="checkbox"/> Undesirable consequences probably outweigh desirable consequences in most settings	<input type="checkbox"/> Balance between desirable and undesirable consequences is closely balanced or uncertain
<input type="checkbox"/> Desirable consequences probably outweigh undesirable consequences in most settings	<input checked="" type="checkbox"/> Desirable consequences clearly outweigh undesirable consequences in most settings	<input type="checkbox"/> There is insufficient evidence to determine the balance of consequences

Proposed wording

ACIP recommends the 2-dose* JYNNEOS vaccine series for persons aged 18 years and older at risk of mpox during an mpox outbreak[§]

*Dose 2 administered one month after dose 1

§ Public health authorities determine whether there is an mpox outbreak; a single case may be considered an mpox outbreak at the discretion of public health authorities. Other circumstances in which a public health response may be indicated include ongoing risk of introduction of mpox into a community due to disease activity in another geographic area.



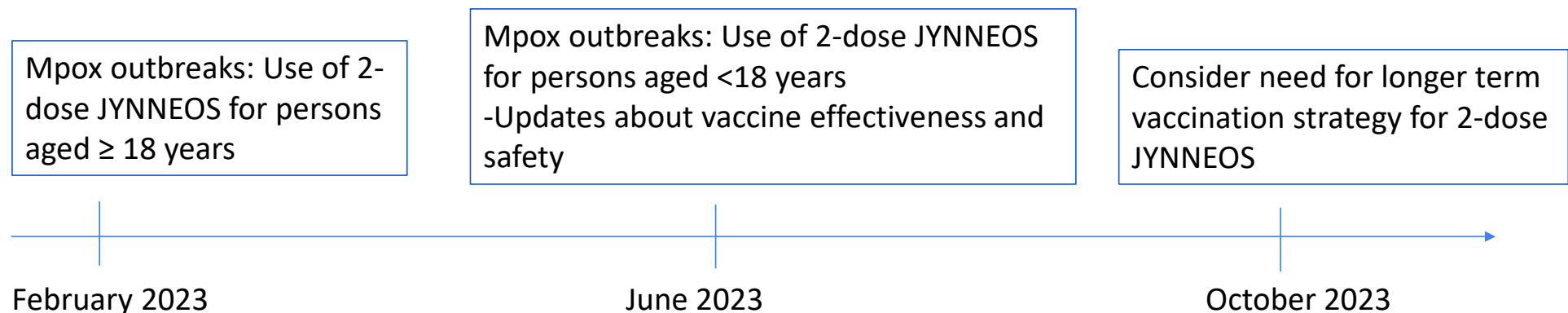
Clinical Considerations

- In outbreak setting, vaccine is ideally given pre-exposure but may also be given as post-exposure prophylaxis (PEP) , although evidence not been reviewed by ACIP for PEP at this time
- Complete 2-dose vaccine series should be given regardless of timing of exposure
- Although ACIP has not reviewed the evidence, if there are vaccine supply shortages, ID route of administration can be used



Tentative timeline for ACIP discussions and votes*


Current US mpox vaccination strategy remains active: Populations at high risk should continue to be vaccinated[§]



*February 2023 and June 2023 votes do not impact existing recommendations for the current mpox outbreak.

[§] <https://www.cdc.gov/poxvirus/monkeypox/interim-considerations/overview.html>

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Questions?

For more information, contact CDC
1-800-CDC-INFO (232-4636)
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.

National Center for Emerging and Zoonotic Infectious Diseases
Division of High-Consequence Pathogens and Pathology

