



# 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**

**February 22, 2023**

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

## EtR question

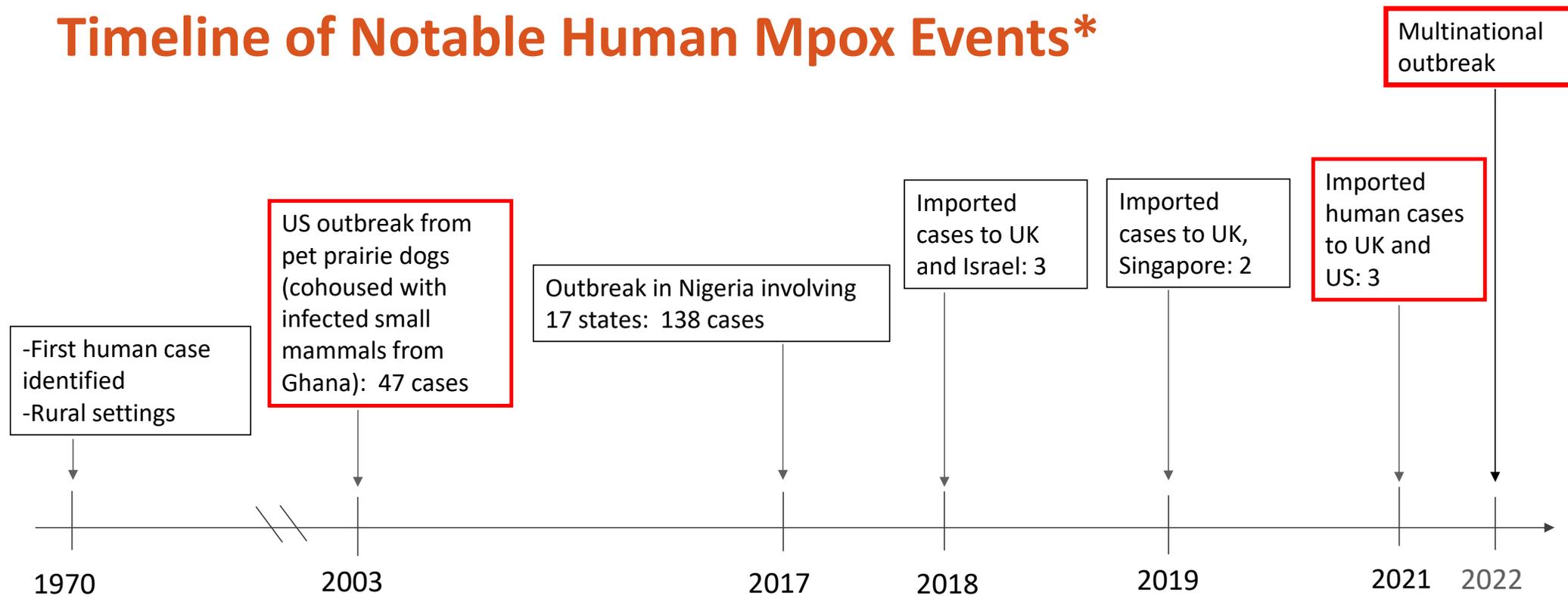
Does ACIP recommend the 2-dose\* JYNNEOS vaccine series for persons aged 18 years and older at risk of mpox during an mpox outbreak?<sup>§</sup>

\*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.

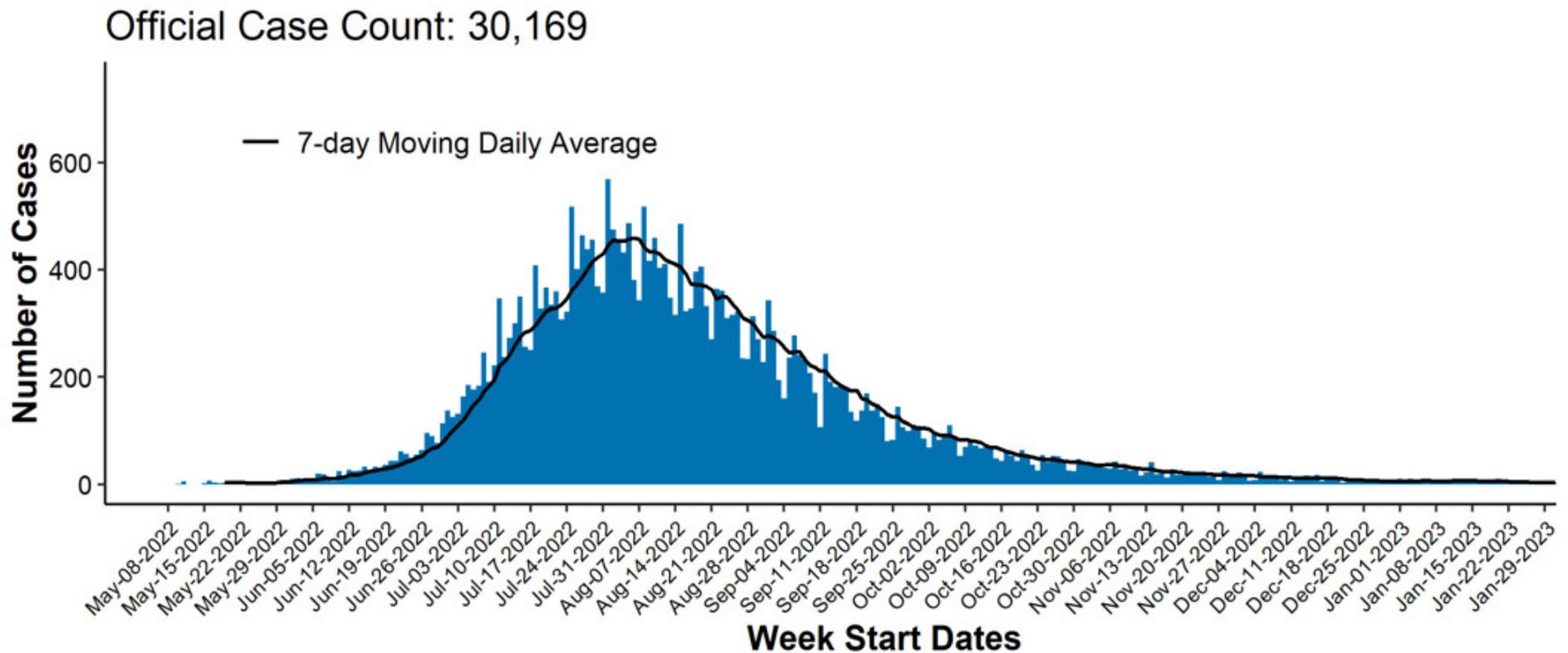
# **EtR Domain: Public Health Problem**

# 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

HEALTH

**More than 200 people in U.S. being monitored for possible monkeypox exposure, CDC says**



By [Helen Branswell](#) July 20, 2021

# 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

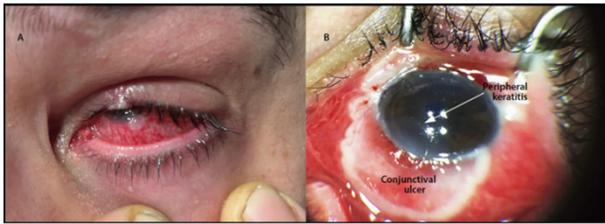


- Lesions often perianal and/or affecting genitals
- Rectal pain
- Abdominal pain
- Rectal bleeding
- Tenesmus



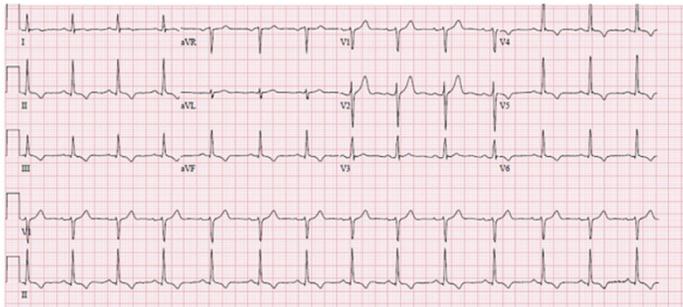
[https://www.cdc.gov/mmwr/volumes/71/wr/mm7132e3.htm?s\\_cid=mm7132e3\\_w](https://www.cdc.gov/mmwr/volumes/71/wr/mm7132e3.htm?s_cid=mm7132e3_w)

# 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

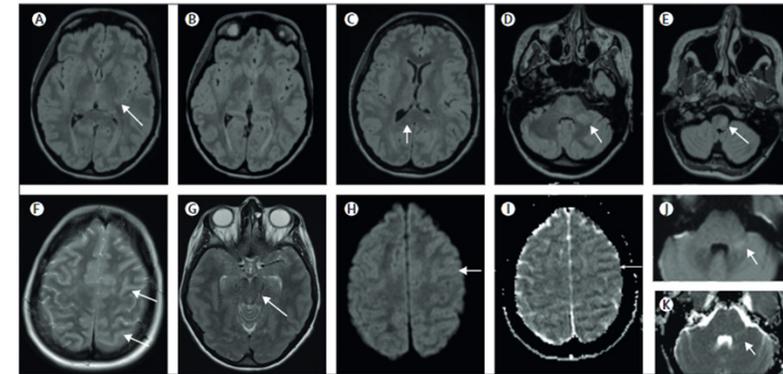


Above: NSR with TWI in inferior and anterolateral leads of ECG. Patient with mpox and no underlying medical conditions. Other signs and symptoms: SOB, decreased exercise tolerance, elevated Tn (0.35ng/mL reference <0.07 ng/mL) indicating myopericarditis

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.

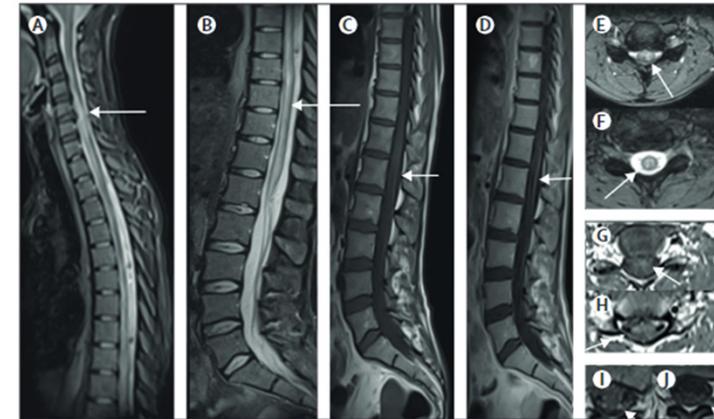
## Complications associated with some mucosal lesions

- 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



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.

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.

# 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  $\geq 14$  days earlier, and 9.6 (95% CI = 6.9–13.2) times that among persons who received dose two  $\geq 14$  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?

|   |                                |  |   |                                     |                                 |
|---|--------------------------------|--|---|-------------------------------------|---------------------------------|
| <b>How substantial are the desirable anticipated effects?</b> |                                |  |   |                                     |                                 |
| <input type="checkbox"/> Minimal                              | <input type="checkbox"/> Small | <input type="checkbox"/> <u>Moderate</u> | <input checked="" type="checkbox"/> Large | <input type="checkbox"/> Don't know | <input type="checkbox"/> 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

Over two-thirds of physicians 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  /aries

# 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

- ☐ Undesirable consequences clearly outweigh desirable consequences in most settings
- ☐ Undesirable consequences probably outweigh desirable consequences in most settings
- ☐ Balance between desirable and undesirable consequences is closely balanced or uncertain
- ☐ Desirable consequences probably outweigh undesirable consequences in most settings
- X** **Desirable consequences clearly outweigh undesirable consequences in most settings**
- ☐ 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<sup>§</sup>

\*Dose 2 administered one month after dose 1

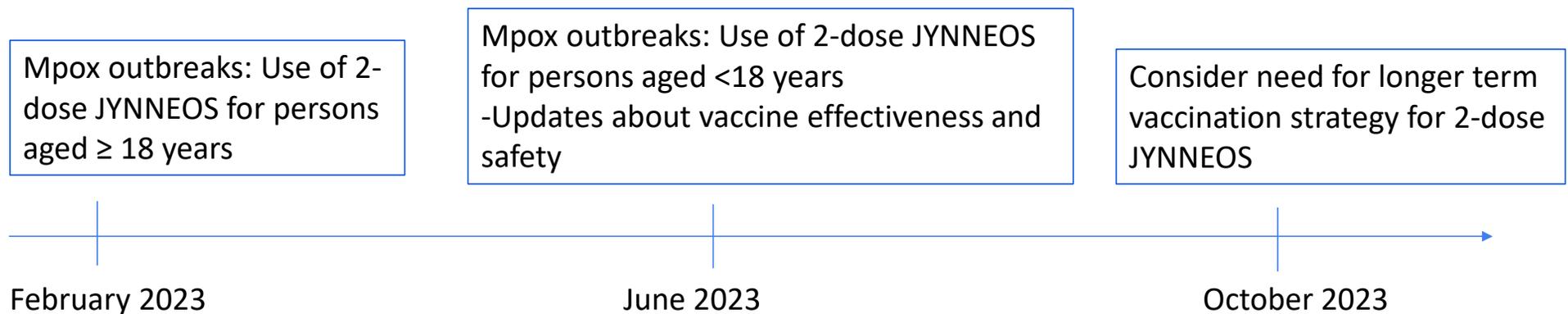
§ Public health authorities determine whether there is an mpox outbreak; a single case may be considered an mpox outbreak at the discretion of public health authorities. Other circumstances in which a public health response may be indicated include ongoing risk of introduction of mpox into a community 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<sup>§</sup>



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

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

# Acknowledgements

- Amanda Cohn
  - Rosalind Carter
  - Kevin Delaney
  - Catherine McLean
  - Faisal Minhaj
  - Sascha Ellington
  - Jonathan Duffy
  - Dani Moulia
  - Anna Chard
  - Manisha (Mo) Patel
  - Adam Cohen
  - Tom Shimabukuro
  - Rita Helfand
  - Melinda Wharton
  - Emily Mosites
  - Dan Filardo
  - Grace Marx
  - Amy Lansky
  - Rachel Kachur
  - Christine Prue
  - Saskia Voss
  - Dan Payne
  - Michael Yeh
  - David Hopkins
  - Brett Petersen
  - Jane Zucker
  - Jennifer Rosen
  - Eli Rosenberg
  - Sara Oliver
  - Robbie Goldstein
- 

# Questions?

For more information, contact CDC  
1-800-CDC-INFO (232-4636)  
TTY: 1-888-232-6348 [www.cdc.gov](http://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

