Centers for Disease Control and Prevention

Evidence to Recommendations Framework: Vaccination with Jynneos for Adolescents at Risk of Mpox During Outbreaks

Faisal Syed Minhaj, PharmD, MPH

Poxvirus and Rabies Branch

Centers for Disease Control and Prevention

Advisory Committee on Immunization Practices

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Evidence to Recommendations (EtR) Framework

- Structure to describe information considering in moving from evidence to ACIP vaccine recommendations

- Provides transparency around the impact of additional factors on deliberations when considering a recommendation

EtR question

- Does ACIP recommend the 2-dose* JYNNEOS vaccine series for persons 12–17 years of age at risk of mpox during an mpox outbreak§?

*Dose 2 administered one month after dose 1

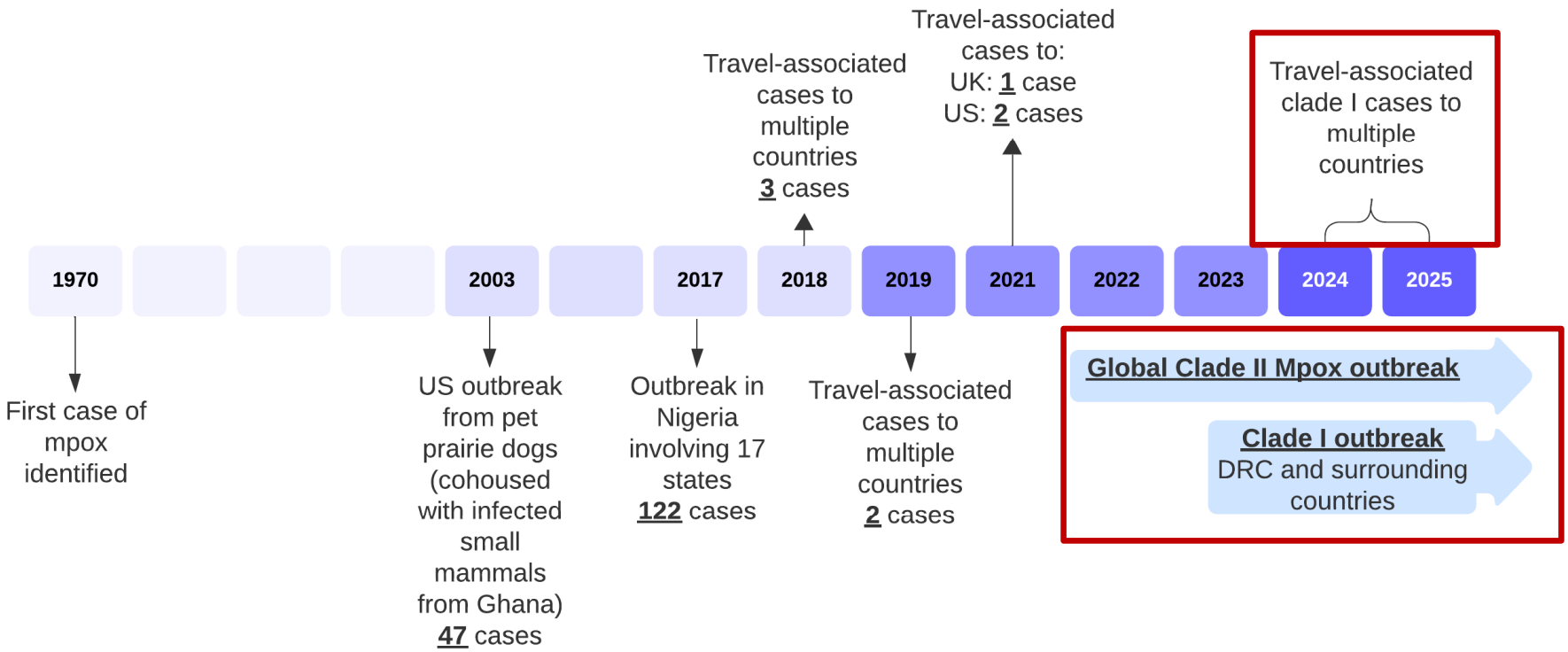
§Public health authorities determine whether there is an mpox outbreak; a single case may be considered an mpox outbreak at the discretion of public health authorities. Other circumstances in which a public health response may be indicated include ongoing risk of introduction of mpox into a community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

Evidence to Recommendation Domains

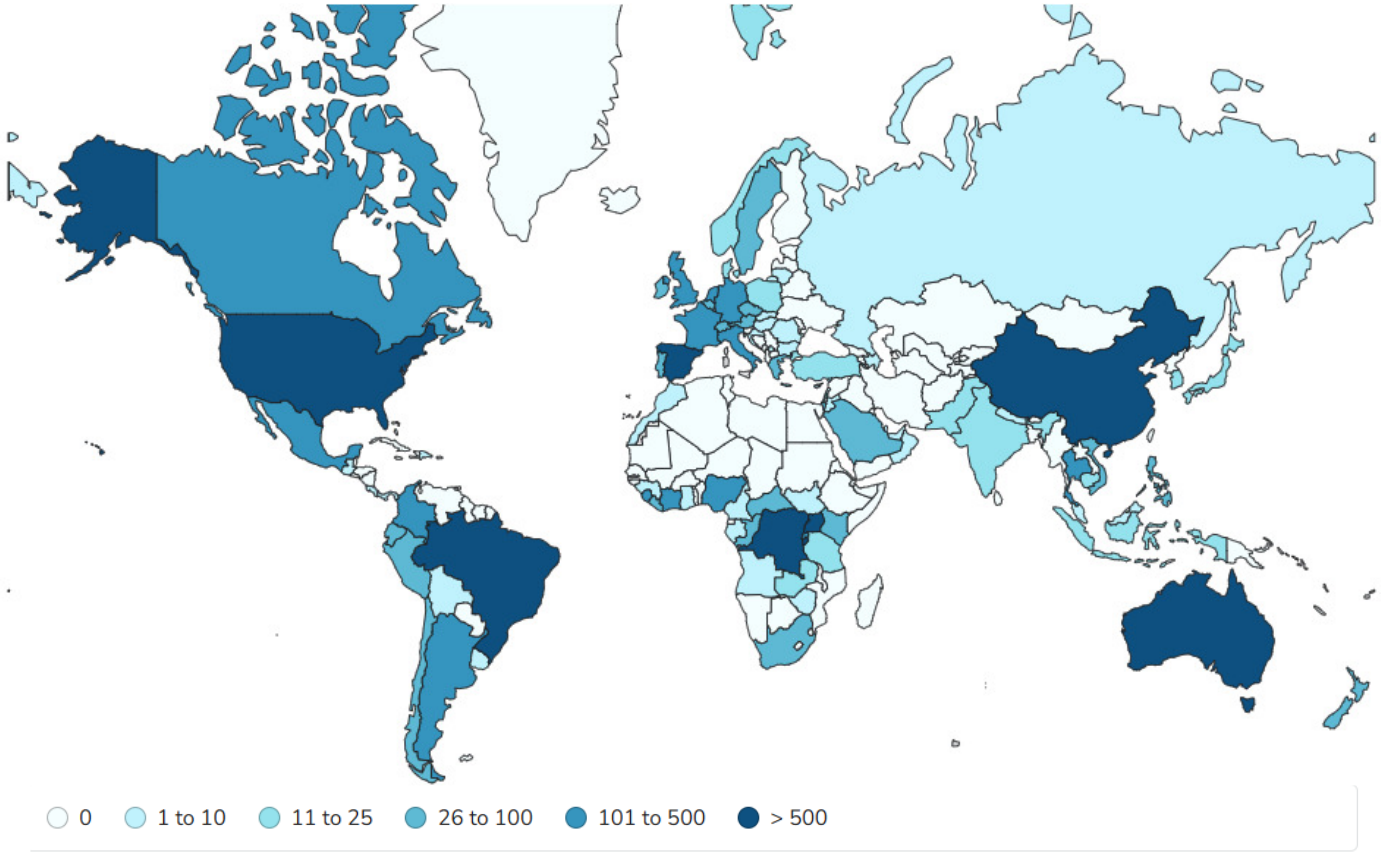
EtR Domain	Question(s)
Public Health Problem	• Is the problem of public health importance?
Benefits and Harms	• How substantial are the desirable anticipated effects? • How substantial are the undesirable anticipated effects? • Do the desirable effects outweigh the undesirable effects?
Values	• Does the target population feel the desirable effects are large relative to the undesirable effects? • Is there important uncertainty or variability in how much people value the main outcome?
Acceptability	• Is the intervention acceptable to key stakeholders?
Equity	• What would be the impact on health equity?
Feasibility	• Is the intervention feasible to implement?
Resource Use	• Is the intervention a reasonable and efficient allocation of resources?

EtR Domain: Public Health Problem

Mpox current situation

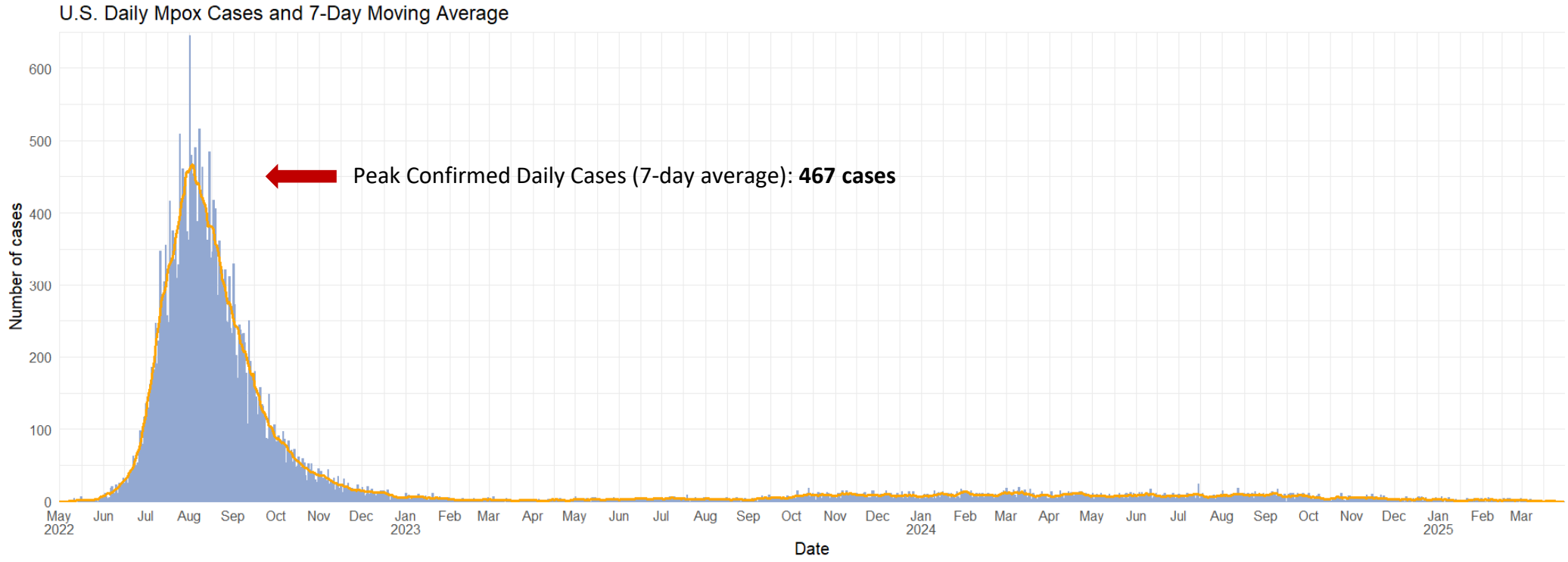


Global distribution of confirmed mpox cases, January 1, 2024 – March 26, 2025

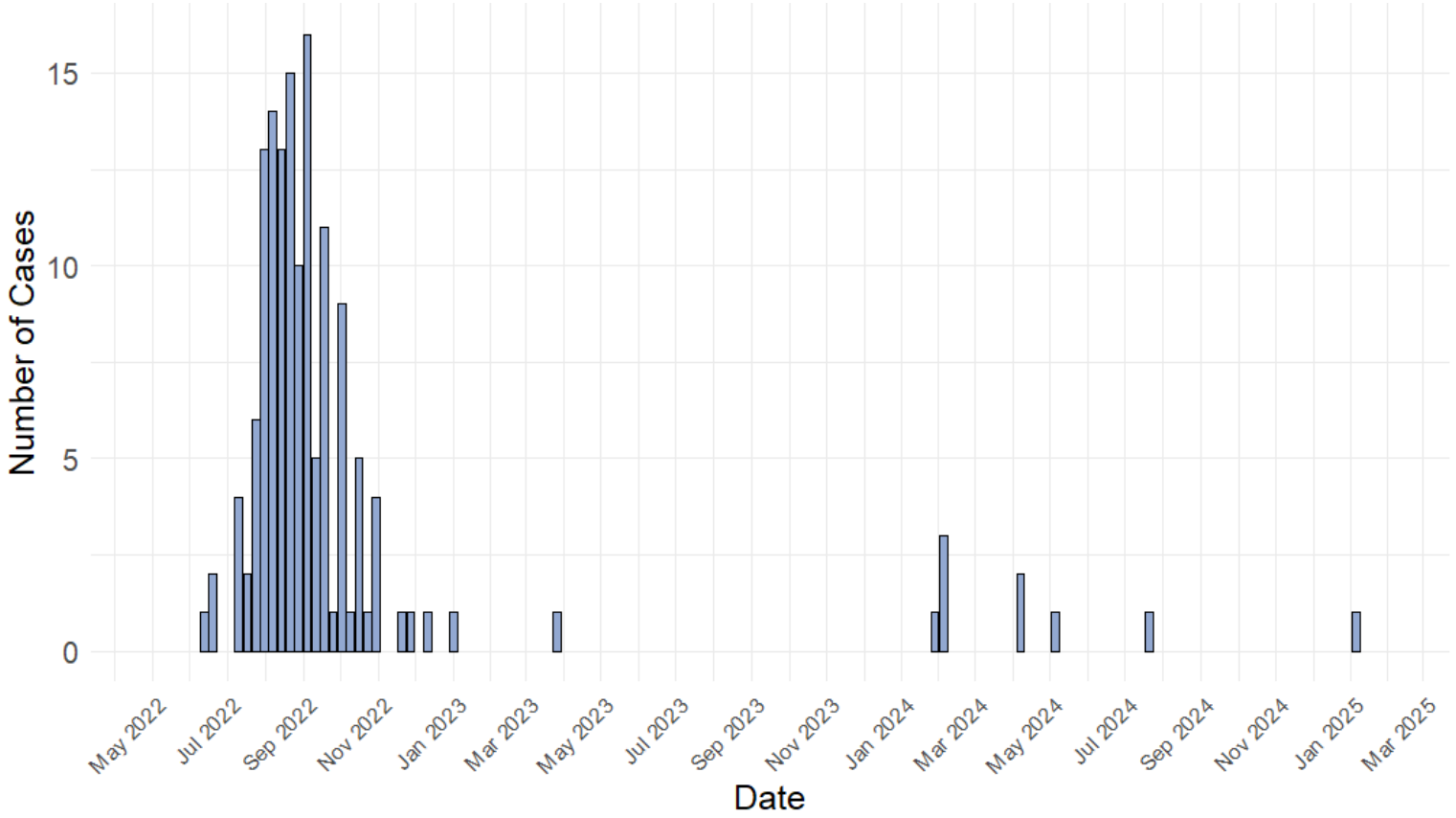


Global distribution of confirmed clade I mpox cases January 1, 2024 – April 13, 2025

United States mpox case count and 7-day moving Average – May 2022 through March 2025



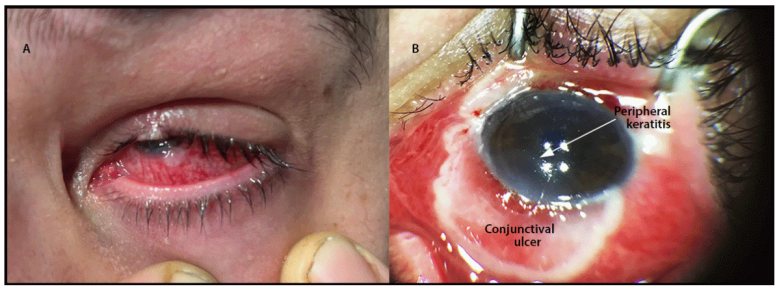
U.S. mpox case counts in pediatrics, May 2022 through March 2025



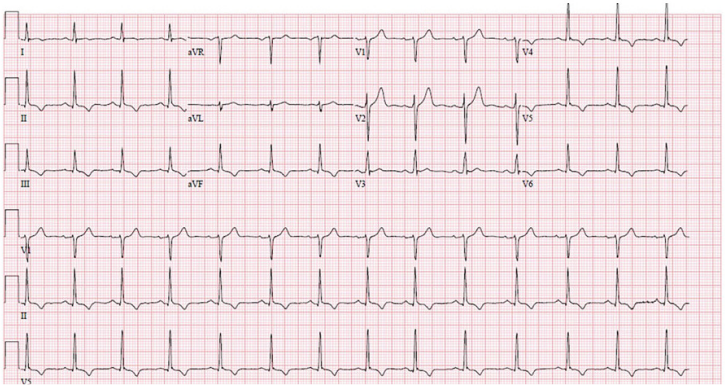
Age group	Case Count
12-17	92
6-11	17
1-5	23
<1	15
Total	**147**

Typical mpox manifestations

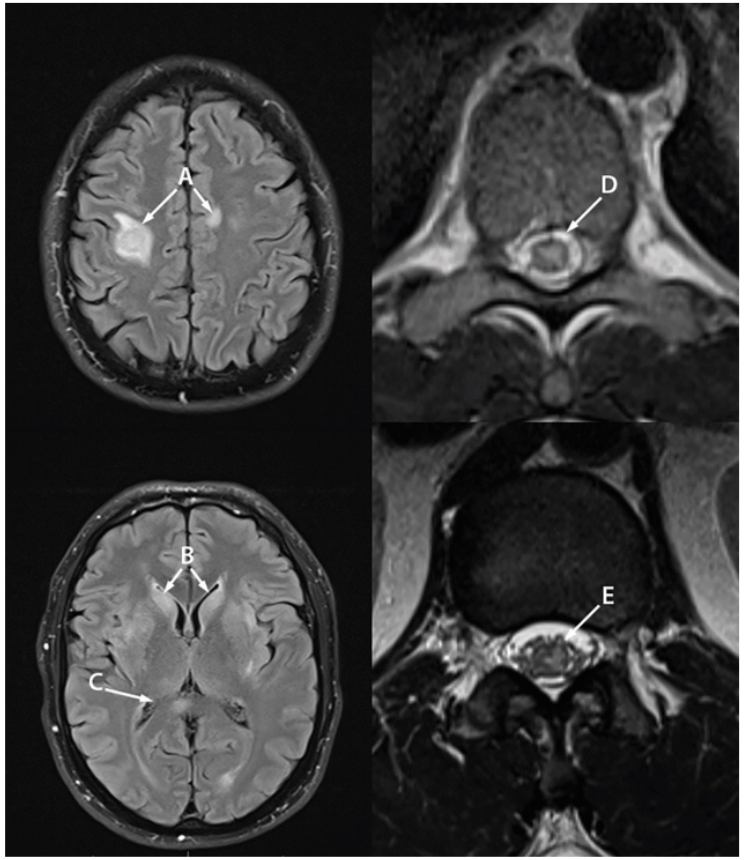
Severe manifestations of mpox



Keratitis and conjunctival ulcer

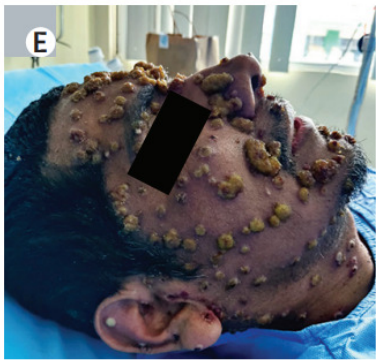


T-wave inversions in inferior and anterolateral leads of a patient with mpox with elevated Tn, SOB, decreased exercise tolerance



Encephalomyelitis in a patient with mpox

Severe manifestations from uncontrolled viral replication in severely immunocompromised



Carrubba S. Lancet Infect Dis. 2023 May;23(5):e190-e197.
Mitjà O. Lancet. 2023 Mar 18;401(10380):939-949.

Are outbreaks of mpox of public health importance?

No Probably no Uncertain Probably Yes Yes

Varies

EtR Domain: Benefits and Harms

Adolescent safety and immunogenicity study summary

- Adolescent arm met pre-specified criteria for non-inferiority
  - GMT ratio of adolescents to adults was 1.60 (CI 1.32, 1.95)
- Vaccine was safe and well tolerated in adolescents
  - Solicited systemic and local AEs were similar between adolescents and adults
    - Systemic: 74% (CI 69, 79) vs 73% (CI 66, 79)
    - Local: 88% (CI 84, 91) vs 91% (CI 87,95)
  - Unsolicited related AEs: mainly injection site related
  - Dizziness in adolescents is common with vaccine administration in this age group and is not likely to represent a safety concern

CDC's vaccine safety data sources for JYNNEOS

- **Vaccine Adverse Event Reporting System (VAERS)**
  - National passive reporting system
- **Vaccine Safety Datalink (VSD)**
  - Large linked healthcare data
- **V-safe**
  - Web-based survey of vaccinees
- **Single-patient Emergency Investigational New Drug (EIND) procedures**
  - EIND provided vaccine access for individuals <18 years of age prior to EUA
  - Collected adverse event information from the vaccination provider 28 days after each dose

Adverse events among individuals <18 years of age 2022–2023

- **Vaccine adverse event reporting system (VAERS)[1]**
  - At least 1,245 vaccinees nationwide
  - One report of syncope
  - Three reports of unspecified mild local and systemic reactions
- **VSD[2]**
  - 88 vaccinees
  - No adverse events of special interest observed
- **V-safe[1]**
  - No participants were <18 years of age
- **EIND[3]**
  - 57 vaccinees
  - 21% reported local or systemic reactions. No serious adverse events were reported

1) https://pubmed.ncbi.nlm.nih.gov/38647241/ 2) https://pubmed.ncbi.nlm.nih.gov/39565485/ 3) https://pubmed.ncbi.nlm.nih.gov/36480476/

How substantial are the *desirable* anticipated effects

Minimal Small Moderate Large

☐ Don't Know ☐ Varies

How substantial are the *undesirable* anticipated effects

Minimal Small Moderate Large

Don’t Know

Varies

Do the desirable effects outweigh the undesirable effects?

Favors Intervention

Favors Both

Favors Comparison

Favors Neither

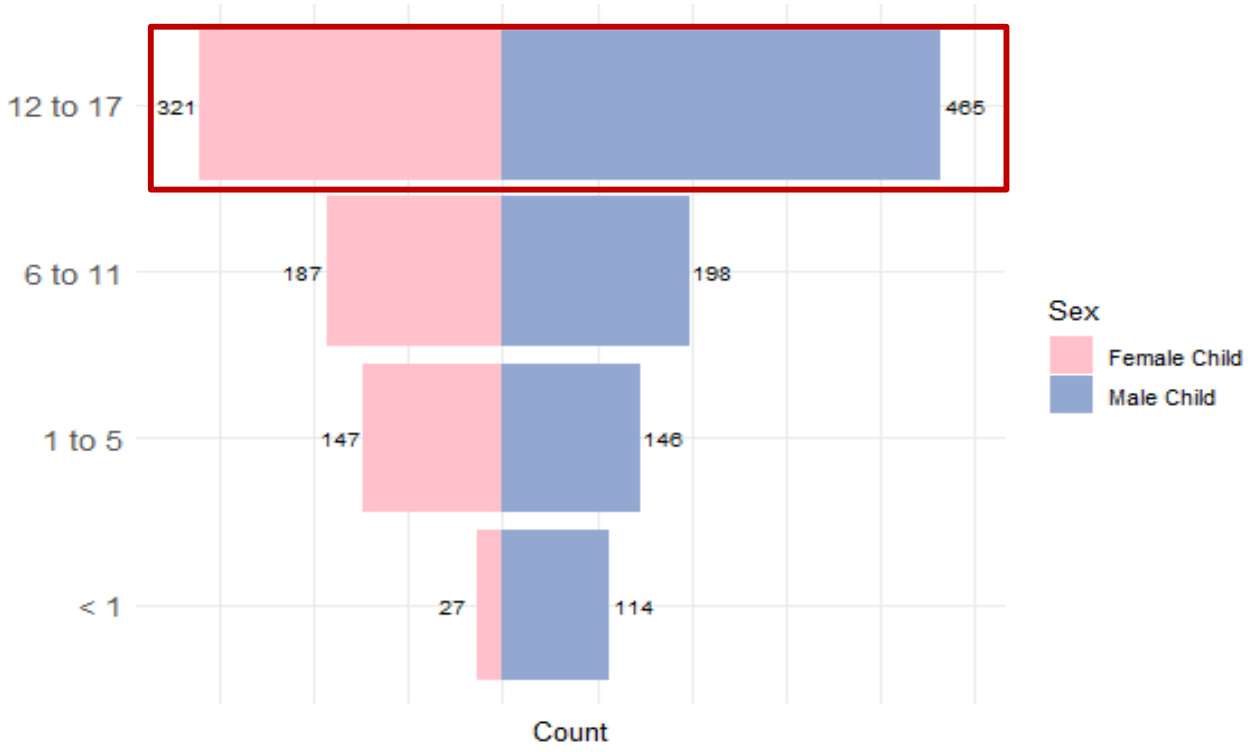
Unclear

EtR Domain: Values

Values Considerations

- NIH rapidly completed trial recruitment
- Participants were supportive in participating to help friends
- When an outbreak occurred (i.e., 2022 global outbreak), pediatric close contacts were vaccinated
- Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) youth advisors were surveyed and 12/13 respondents were supportive of vaccination
- We do not know what type of outbreak would occur in the future, and how adolescents would perceive their risk or acceptability of vaccine

JYNNEOS first doses administered to children 17 years and younger by sex May 2022 – September 2024



Age group	Total first doses
12-17	798
6-11	391
1-5	293
<1	150
Total	**1,632**

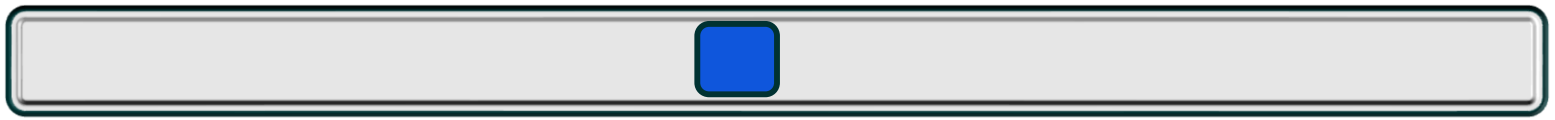
Persons with no age data available were removed from the analysis

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

No Probably no Uncertain Probably Yes Yes

Varies

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

Data available for acceptability domain

Survey administered to Adolescent Medicine Trials Network (ATN) providers

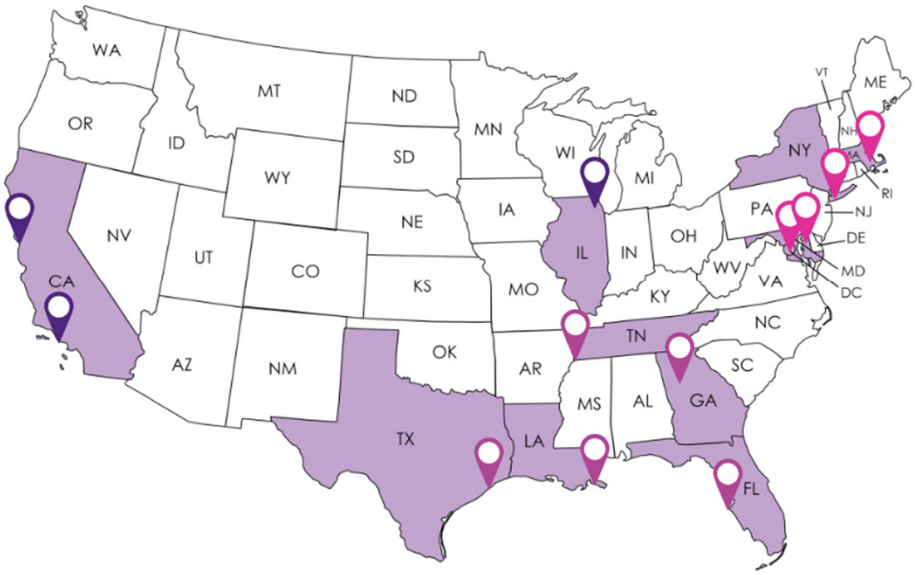
Survey of mothers of adolescents and younger children

Data available for acceptability domain

Survey administered to Adolescent Medicine Trials Network (ATN) providers

Survey of mothers of adolescents and younger children

ATN V Sites



Eastern U.S.

Washington, D.C.
Children's National Hospital

New York City, New York
Callen-Lorde Community Health Center

Boston, Massachusetts
The Fenway Institute

Western & Midwestern U.S.

San Francisco, California
Bridge HIV, San Francisco Department of Public Health

Los Angeles, California
Children's Hospital Los Angeles

Chicago, Illinois
Adolescent and Young Adult Research (AWAR) @ The CORE Center

Southern U.S.

Houston, Texas
Baylor College of Medicine/ Texas Children's Hospital

New Orleans, Louisiana
Tulane University Adolescent Medicine

Tampa, Florida
University of South Florida

Atlanta, Georgia
Emory University

Memphis, Tennessee
St. Jude Children's Research Hospital

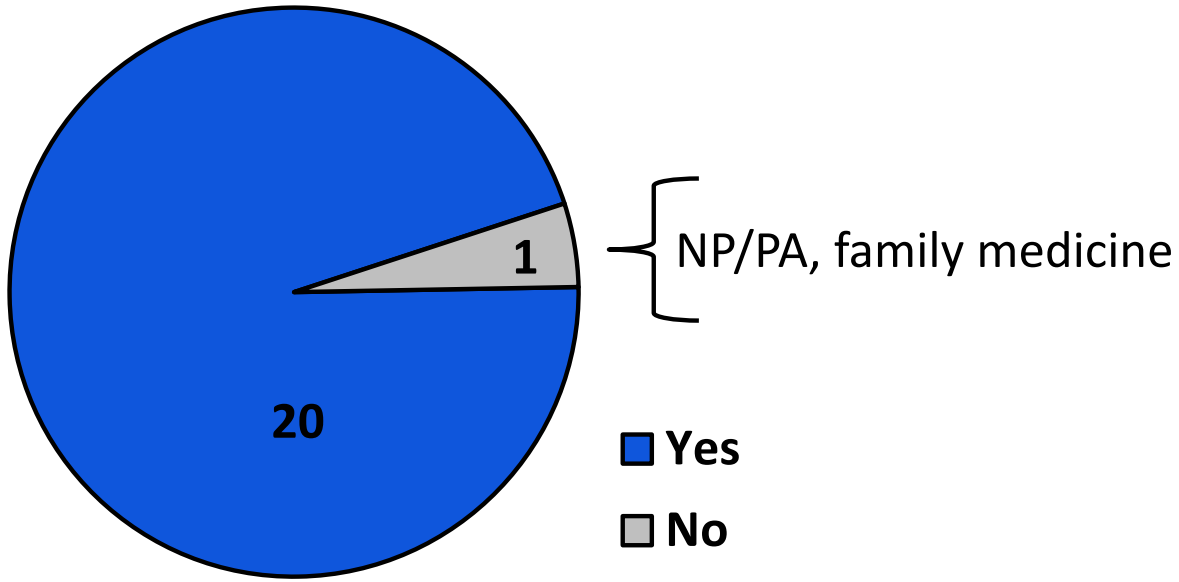
Survey to Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) providers

- Distributed to clinicians for 1 week in January 2025
- 23 providers responded
  - 21 (91%) treat 12–17-year-olds at risk for mpox
- Among those 21 providers:
  - 17 (81%) offer vaccines in clinic; 11 (52%) offer mpox vaccine.
  - Type of practice:
    - 19 (90%) university-based;
    - 1 (5%) FQHC;
    - 3 (14%) community-based.

Provider Characteristics	N = 21 n (%)
Provider type	
Physician	16 (76)
NP/PA	5 (24)
Specialty	
Adolescent medicine	10 (48)
Pediatrics	3 (14)
Medicine and pediatrics	3 (14)
Family medicine	3 (14)
Internal medicine	1 (5)
Pediatric ID	1 (5)

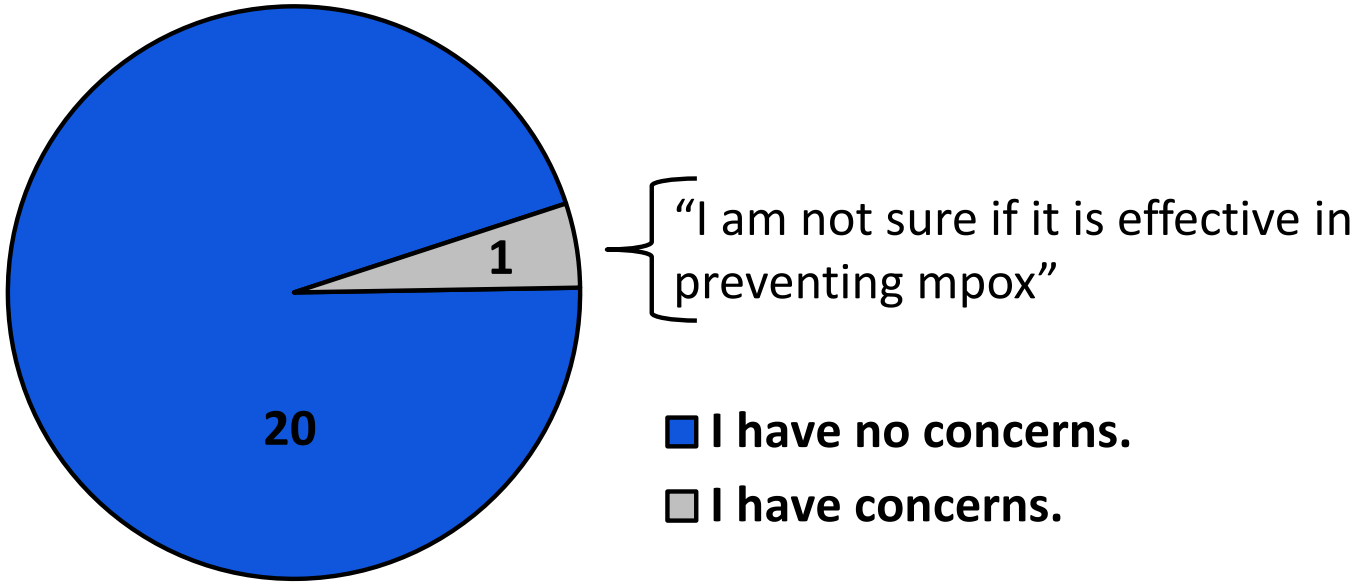
Survey to ATN providers (N = 21)

If CDC recommended the mpox vaccine for 12–17-year-olds with risk factors, would you recommend it for eligible patients?



Survey to ATN providers (N = 21)

What are your concerns about recommending mpox vaccine for your eligible 12–17-year-old patients?



Survey to ATN providers (N = 21)

What are challenges associated with offering the mpox vaccine in your practice?

Statement	N = 21 n (%)
There are no challenges in my practice	**5 (24)**
There are challenges	**16 (76)**
It is costly for the clinic to stock	7 (33)
Patients are unfamiliar with mpox vaccine	5 (24)
I do not know if there are challenges	4 (19)
It is costly for patients	3 (14)
I do not know how to access mpox vaccine	2 (10)
I do not have enough staff trained to administer this vaccine	1 (5)
I am unfamiliar with mpox	1 (5)
I am unfamiliar with mpox vaccine	1 (5)
Other	1 (5)

Data available for acceptability domain

Survey administered to Adolescent Medicine Trials Network (ATN) providers

Survey of mothers of adolescents and younger children

Online survey of Mothers with children ≤18 years

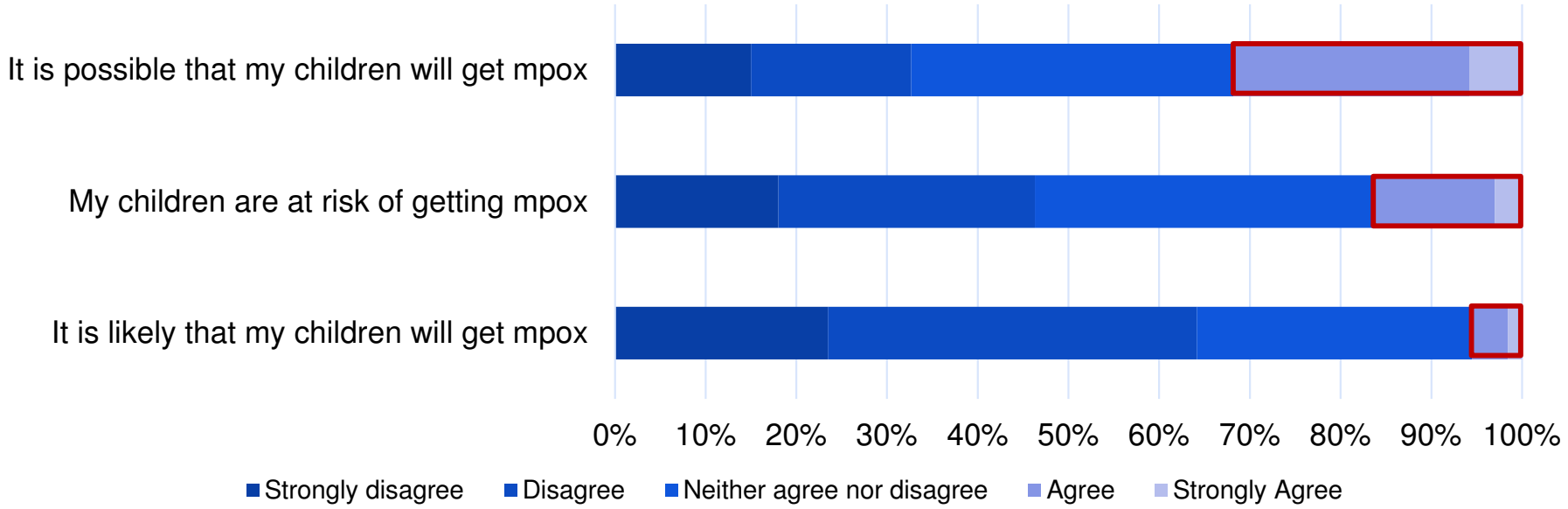
- Total surveyed: 566
- Unclear the age of all children of the mothers
  - Oldest child mean age 9.6 (SD 4.8)
  - 43% of the population had their oldest child age between 12-17 years
- Timeframe: July 2022
- Variety of household incomes were represented

Variable	n (%)
Receipt of all or some CDC recommended immunizations	510 (90)
Race/Ethnicity	
Black	59 (10)
Hispanic	40 (7.1)
Asian/NHOPI/Native American	19 (3.4)
White	439 (78)
Other	9 (1.6)
Number of children	
One	238 (42)
Two	205 (36)
Three	78 (14)
More than three	45 (8.0)

Below $15,000	$15,000 - $24,999	$25,000 - $34,999	$35,000 - $49,999	$50,000 - $74,999	$75,000 - $99,999	$100,000 - $149,999	$150,000 or more
24	39	70	66	119	105	81	62

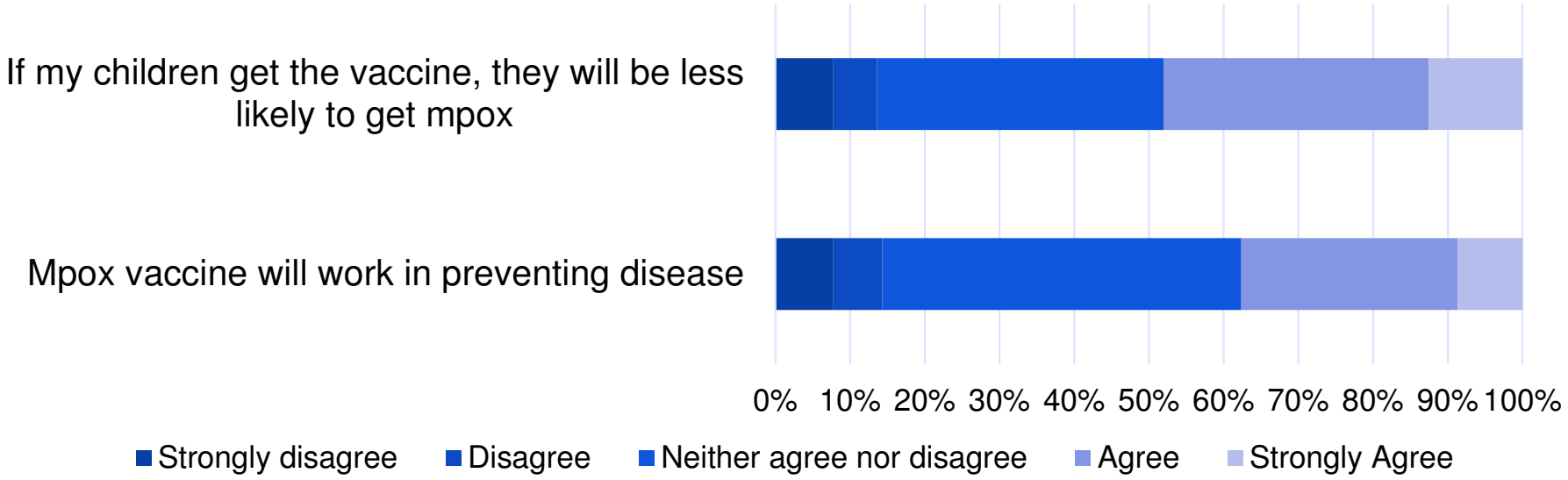
Liu S, Chu H. Patient Educ Couns. 2023 Sep;114:107842.

Low belief that children were at risk of getting mpox



Liu S, Chu H. Patient Educ Couns. 2023 Sep;114:107842.

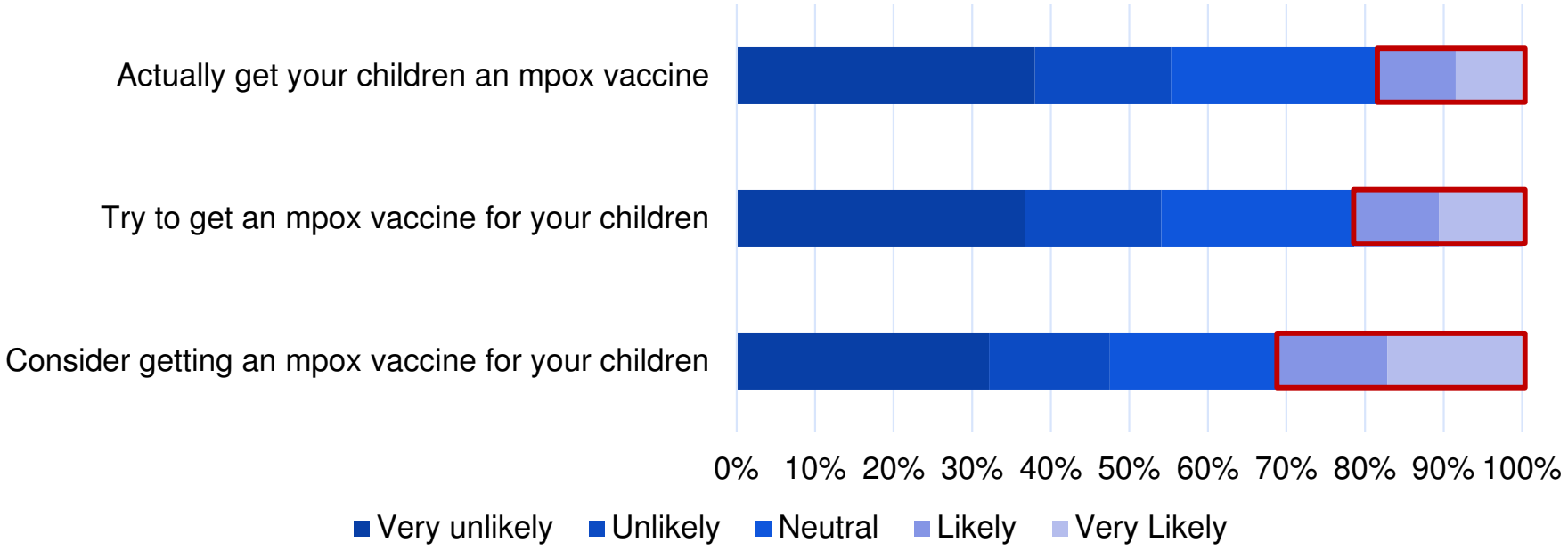
Some agreement that vaccination will impact disease



Liu S, Chu H. Patient Educ Couns. 2023 Sep;114:107842.

Likelihood to vaccinate is numerically low, but higher than expected

- Asked “what is the likelihood that you will”:



Liu S, Chu H. Patient Educ Couns. 2023 Sep;114:107842.

Summary of Acceptability data

- Mothers from the survey do not view their children at risk for mpox.
  - However, the intent to vaccinate is higher than expected.
- Vaccines were primarily given to adolescents both through public health and STI clinics.
- Among 21 surveyed ATN providers who provide care for at-risk adolescents:
  - Over half already offer the mpox vaccine.
  - 95% would recommend mpox vaccines for eligible patients and do not have concerns about recommending the vaccine.
  - Majority expressed challenges associated with offering the vaccine; most common concern was financial cost to the clinic.

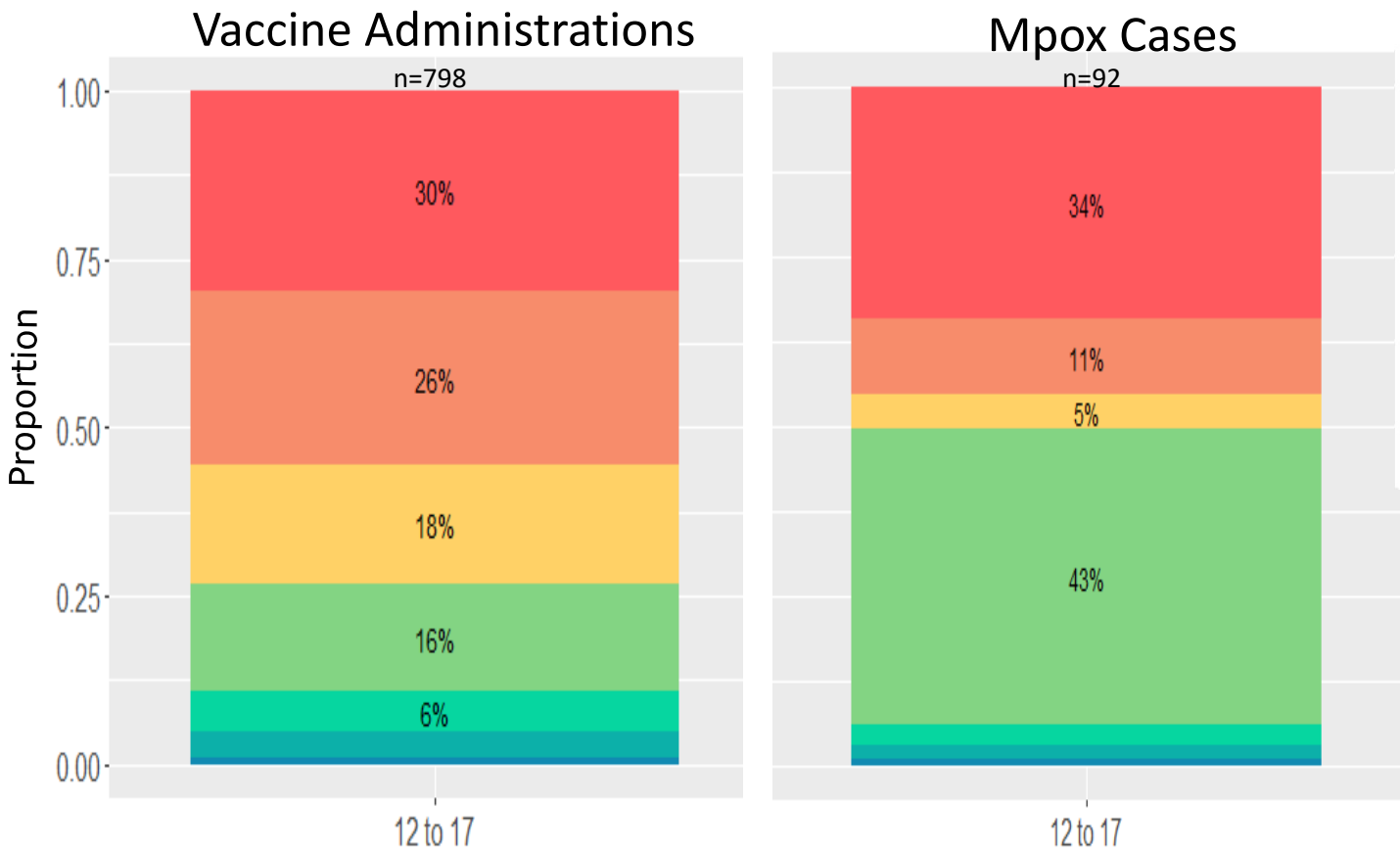
Is the intervention acceptable to key stakeholders?

No Probably no Uncertain Probably Yes Yes

Varies

EtR Domain: Health Equity

Vaccine administrations* and cases in adolescents by race and ethnicity, May 2022 – March 2025



*Vaccine administration through September 2024 Case data through March 2025

+Includes 3 mpox cases indicating Multiple races. Multiple races was not reported for vaccine administration data.

If Hispanic or Latino was indicated for ethnicity, Race/ethnicity is indicated as Hispanic or Latino; if Hispanic or Latino ethnicity was not indicated, Race/ethnicity is indicated as Race

Health Equity

- No groups or settings would be disadvantaged by recommendation for JYNNEOS use during mpox outbreaks.
- Immunogenicity is the same for immunocompetent persons 12-17 years.
- Implementation of vaccine should assure equitable access.
- Endorsement by ACIP could facilitate broad acceptance of recommendation (e.g., insurance, health departments, pharmacies).

What would be the impact on health equity?

Reduced | Probably Reduced | Probably no impact | Probably Increased | Increased

☐ Varies ☐ Don't know

EtR Domain: Feasibility

Feasibility Considerations

- Wide range of vaccinators can administer vaccine (e.g., pediatricians, pharmacists, public health nurses)
- Wide range of potential facilities: public health, STI clinic, adolescent health clinic, pediatrician offices
- Same Immunization Information Systems (IIS) requirements and reporting infrastructure as other vaccines
- Limitations to access
  - Poor access in rural communities
  - Cost of vaccine and 10 vial minimum ordering quantity could hinder practices stocking vaccine
  - Pediatricians may defer to STI/adolescent clinics

Feasibility considerations (cont.)

- Two doses, 28 days apart requires follow up and reminders
- JYNNEOS, once thawed/refrigerated, is good for either 4 or 8 weeks, allowing some time to schedule a second dose.
- Frozen storage is ~18 months

Is the intervention feasible to implement?

No Probably no Uncertain Probably Yes Yes

Varies

EtR Domain: Resource Use

Resource Use

- JYNNEOS is commercially available
  - Similar mechanisms for billing/reimbursement
    - Medicaid/Medicare/317 funding
  - Requires similar resources to other vaccine outbreak responses
- Generally, vaccines are a good use of resources during an outbreak
- Cost-effectiveness of vaccination during a future outbreak in adolescents is uncertain

Is the intervention a reasonable and efficient allocation of resources?

No | Probably no | Uncertain | Probably Yes | Yes

Varies

Balance of Consequences

Summary of Work Group Interpretation of EtR Domains

EtR Domain	Work Group Interpretation
Public Health Problem	Yes
Benefits and Harms	
Benefits	Large
Harms	Small
Benefit>Harm?	Favors intervention
Values	
Desirable>Undesirable?	Probably yes
Uncertainty?	Possibly important OR probably no important uncertainty or variability
Acceptability	Probably yes
Equity	Probably increased
Feasibility	Probably yes
Resource Use	Probably yes

Balance of consequences

Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between the desirable and undesirable consequences is *closely balanced or uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings	There is insufficient evidence to determine the balance of consequences

Proposed Recommendation 1

- ACIP recommends the 2-dose* JYNNEOS vaccine series for persons 12 to 17 years of age 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.