JYNNEOS Vaccine Safety Monitoring During the 2022 Mpox Outbreak – United States

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CDC Mpox vaccine safety data sources

- Vaccine Adverse Event Reporting System (VAERS)
- Vaccine Safety Datalink (VSD)
- V-safe after vaccination health checker
- Single-patient emergency Investigational New Drug (EIND) procedures

VAERS

VAERS is the nation's early warning system for vaccine safety

VAERS

Vaccine Adverse Event Reporting System

CDC + FDA

Co-Managed by CDC and FDA

http://vaers.hhs.gov

JYNNEOS EUA* required reporting to VAERS for adverse events and vaccine administration errors

- The vaccination provider is responsible for MANDATORY reporting of the following listed events following JYNNEOS to VAERS:
  - Vaccine administration errors whether or not associated with an adverse event
  - Serious adverse events (irrespective of attribution to vaccination)
  - Cases of cardiac events including myocarditis and pericarditis
  - Cases of thromboembolic events and neurovascular events

*EUA indications: intradermal injection for individuals aged ≥18 and subcutaneous injection for individuals aged <18 years; Fact Sheet for Healthcare Providers Administering Vaccine: Emergency Use Authorization of Jynneos (Smallpox and Monkeypox Vaccine, Live, Non-Replicating) for Prevention of Monkeypox Disease in Individuals Determined to be at High Risk for Monkeypox Infection (fda.gov)

VAERS: JYNNEOS surveillance methods

- VAERS reports received and processed by January 20, 2023
- Adverse event reporting rates were calculated by dividing the number of VAERS reports by the number of vaccine doses administered in the U.S.
  - Vaccine doses administered during May 22–January 13 and reported to CDC by January 23, 2023
    - Dose 1: 698,188
    - Dose 2: 426,980
    - Total: 1,125,168

VAERS: JYNNEOS report characteristics, n = 1,817

Characteristic	n (%)
Sex	
Male	1,415 (78)
Female	238 (13)
Not reported	164 (9)
Age	
0-17	25 (1)
18-64	1,501 (83)
≥65	83 (5)
Not reported	208 (11)
Other vaccines on same day	
Yes	45 (2)
No	1,772 (98)

Characteristic	n (%)
Dose in series	
1	1,013 (56)
2	471 (26)
Not reported	333 (18)
Route of administration	
Intradermal	1,001 (55)
Subcutaneous	378 (21)
Intramuscular	211 (12)
Not reported	227 (12)

VAERS: vaccine administration error reports

- Represent 50% of all JYNNEOS VAERS reports
  - Of these, 96% did not report an adverse health event
- Error reporting rate
  - Intradermal: 937 per million doses administered
  - Subcutaneous: 306 per million doses administered
- Errors frequently reported with attempted intradermal administration:
  - Absence of a wheal without vaccine leakage (42%)
  - Vaccine leakage from injection site (12%)

VAERS: adverse health event reporting rates per million doses administered by route of administration

Subcutaneous	rate
All adverse health events	639
Injection site erythema	107
Injection site swelling	107
Injection site pain	99
Pain	96
Fatigue	80
Erythema	77
Headache	77
Dizziness	74
Injection site pruritus	66
Pyrexia	66

Intradermal	rate
All adverse health events	685
Injection site erythema	152
Dizziness	129
Injection site swelling	112
Urticaria	110
Injection site pruritus	93
Erythema	78
Syncope	73
Pruritus	72
Hyperhidrosis	70
Loss of consciousness	69

Serious Adverse Event definition

- Death
- A life-threatening adverse event
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- A congenital anomaly/birth defect
- An important medical event that based on appropriate medical judgement may jeopardize the individual and may require medical or surgical intervention to prevent one of the outcomes listed above

VAERS: serious adverse events reported after JYNNEOS*, n = 26

SAE reporting rate: 22 reports per million doses administered

- Myocarditis (n=5)
- Death (n=2)**
- Pericarditis (n=2)
- Urticaria (n=2)
- Appendicitis
- Aseptic meningitis
- Asthenia
- Atrial fibrillation
- Cellulitis
- Chest pain
- Dehydration
- Idiopathic thrombocytopenic purpura
- Injection site discoloration
- Injection site pain
- Injection site scar
- Methemoglobinemia
- Retrograde amnesia
- Rhabdomyolysis
- Sudden hearing loss

*The report of an adverse event to VAERS is not documentation that a vaccine caused the event.

**Reported causes of death: drowning, cocaine toxicity.

Myocarditis and pericarditis

Myocarditis and pericarditis

- Myocarditis and pericarditis have occurred following either primary vaccination or revaccination with live vaccinia virus smallpox vaccines
  - The mechanism is poorly understood, and it was unknown whether persons who receive JYNNEOS might experience myocarditis or pericarditis
- Epidemiologic analysis groupings:
  - Myocarditis with or without pericarditis
  - Pericarditis
- Surveillance risk interval: symptom onset within 30 days after vaccination

Case definitions available at: DOI: 10.15585/mmwr.mm7027e2

Myocarditis rate per million persons during 30-day period

Observed after JYNNEOS

Data source	Dose 1 cases	doses	rate per million (95% CI)	Dose 2 cases	doses	rate per million (95% CI)
VAERS	2	726,851	2.75 (0.33–9.94)	3	445,019	6.74 (1.39–19.70)
Vaccine Safety Datalink	1	37,646	27 (0.67–148)	1	21,919	46 (1.15–254)

Expected

- Historical myocarditis population background rates per million persons:
  - U.S. military in 2002[1]: 21.6
  - MarketScan database, males 18–64 yrs in 2017–2019[2]: 2.7 – 7.5
- Historical myocarditis rates after live, replicating smallpox vaccines (Dryvax or ACAM2000) ranged from 78 to 5,230 cases per million persons[1,3]

References:
1) Halsell, et all. DOI: 10.1001/jama.289.24.3283; 2) Oster, et al. DOI: 10.1001/jama.2021.24110 ;
3) Mandra, et al. DOI: 10.1017/dmp.2020.478

Pericarditis rate per million persons during 30-day period

Observed after JYNNEOS

Data source	Dose 1 cases	doses	rate per million (95% CI)	Dose 2 cases	doses	rate per million (95% CI)
VAERS	4	726,851	5.50 (1.50–14)	2	445,019	4.49 (0.54–16.23)
Vaccine Safety Datalink	0	37,646	0	0	21,919	0

Expected

- Historical pericarditis population background rates per million persons:
  - Italy, 2001–2005[1]: 22.8
  - U.S. Nationwide Inpatient Sample database, 2003–2012[2]: 4.7
- Historical pericarditis rate after live, replicating smallpox vaccines (Dryvax or ACAM2000) was 925 cases per million persons in one U.S. military study[3]

References:
1) Imazio, et al. DOI: 10.1136/hrt.2006.104067; 2) Kumar, et al. DOI: 10.1159/000445206;
3) Engler, et al. DOI:10.1371/journal.pone.0118283

V-safe

V-safe Mpox: active vaccine safety monitoring

- Smartphone-based system that uses text messaging to initiate web-based survey monitoring for adverse events following vaccination
- V-safe is used to:
  - Characterize the basic safety profile of a vaccine when given outside a clinical trial setting
  - Provide information for public health communication around vaccine safety
  - Facilitate reporting to the Vaccine Adverse Event Reporting System (VAERS) for medically attended adverse events following vaccination
- V-safe supplements CDC's other vaccine safety monitoring systems, VAERS and Vaccine Safety Datalink (VSD)

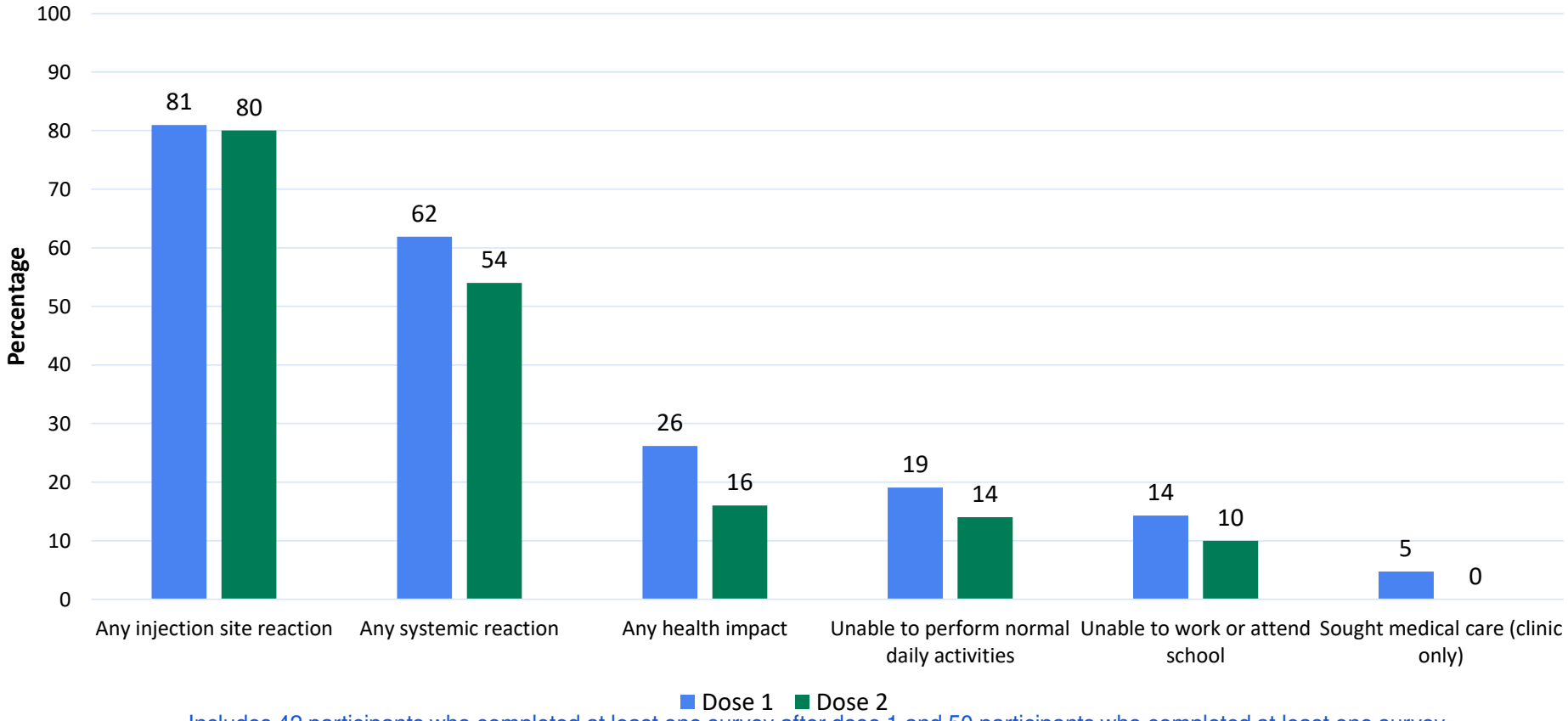
V-safe Mpox: characteristics of active participants*

Characteristic	N=181 n	(%)
Age in years		
18-49	112	(61.9)
50-64	56	(30.9)
≥65	13	(7.2)
Gender identity		
Male	139	(76.8)
Female	28	(15.5)
Transgender	7	(3.9)
None of the above or unknown	7	(3.9)
Immunocompromised**	32	(17.1)

Characteristic	N=181 n	(%)
Race/Ethnicity		
White, non-Hispanic	111	(61.3)
Hispanic	28	(15.5)
Asian, non-Hispanic	11	(6.1)
Black, non-Hispanic	10	(5.5)
Multiracial, non-Hispanic	10	(5.5)
Other race, non-Hispanic	2	(1.1)
Unknown race or ethnicity	9	(5.0)

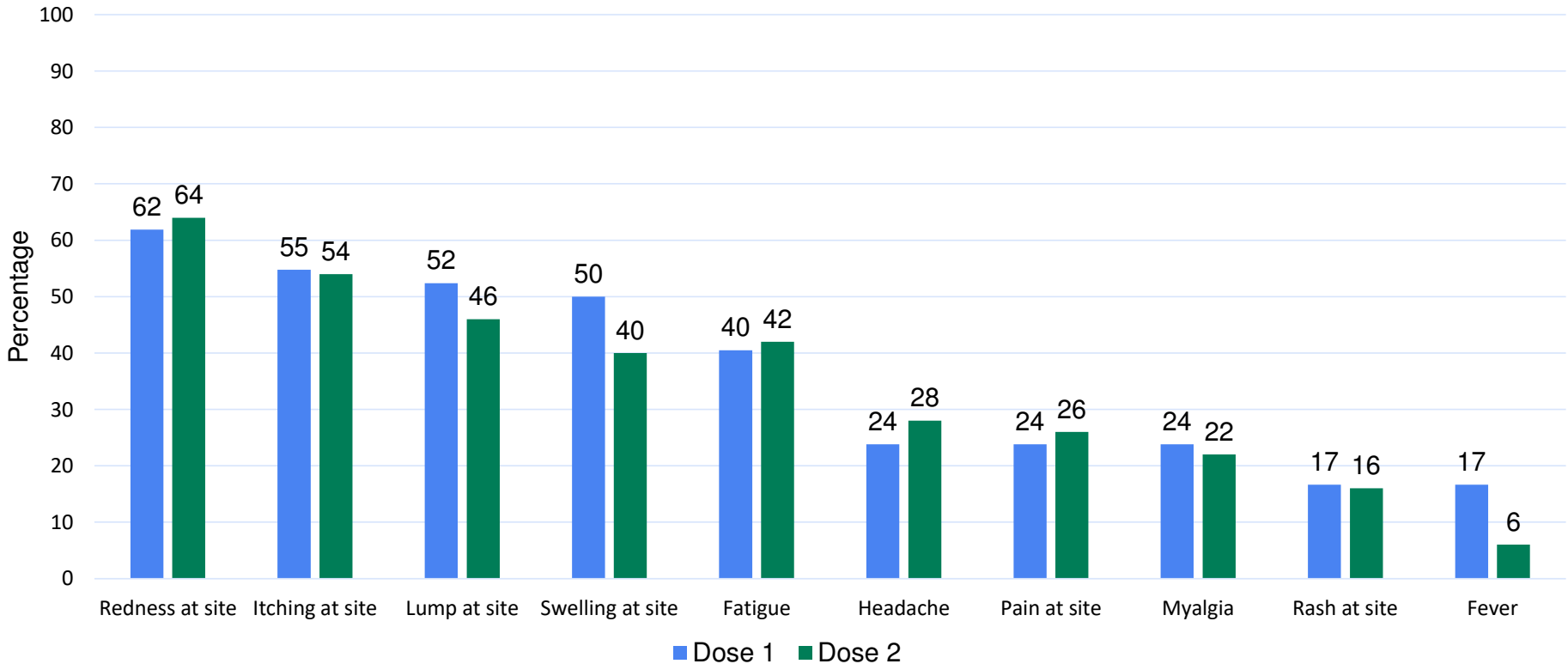
*active participants defined as having completed at least one survey, November 16, 2022 – January 29, 2023
**defined as self-report of immunocompromising condition or taking immunosuppressive medications at the time of vaccination

V-safe Mpox: reactions and health impact events reported by v-safe participants at least once in days 0-7 after vaccination, by dose



Includes 42 participants who completed at least one survey after dose 1 and 50 participants who completed at least one survey after dose 2, data collected November 16, 2022 – January 29, 2023

V-safe Mpox: top injection site and systemic reactions reported by v-safe participants at least once in days 0-7 after Mpox vaccination, by dose



Includes 42 participants who completed at least one survey after dose 1 and 50 participants who completed at least one survey after dose 2, data collected November 16, 2022 – January 29, 2023

Adverse Events in persons <18 years of age

Single-patient emergency Investigational New Drug (EIND) procedures

- CDC facilitated JYNNEOS EIND authorizations from FDA for 65 persons aged <18 years prior to the EUA being issued on August 9, 2022
  - CDC solicited information from vaccine providers about adverse events occurring during the 28 days after each dose
- Ages: 4 months to 17 years
- Sex: 58% male
- Adverse events reported:
  - Dose 1: 10 (18%) of 57
  - Dose 2: 5 (21%) of 24
  - Injection site reactions: pain, erythema, swelling, and induration
  - Systemic adverse events: fever, fatigue, and headache
- No serious adverse events were reported

VAERS: reports for persons aged <18 years

- JYNNEOS vaccine was administered to 1,245 persons aged <18 years in the U.S during this surveillance period
- VAERS received 25 reports for persons aged <18 years
  - Ages from 12 through 17 years
  - Vaccine administration errors, n = 21 (84%)
    - e.g., administered intradermal dose instead of subcutaneous dose
  - Only 1 adverse health event reported: syncope
  - No serious adverse events reported

Conclusions

Conclusions

- JYNNEOS post-licensure and post-authorization vaccine safety surveillance findings to date are consistent with those observed in clinical trials
- No new or unexpected safety concerns have been identified
- Serious adverse events were rare among adults, and none have been identified among persons aged <18 years
- VAERS and Vaccine Safety Datalink data do not suggest an increased risk for myocarditis or pericarditis following JYNNEOS, but the possibility of a small risk cannot be excluded

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