Monkeypox

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Questions

- What are the most common questions you are fielding about monkeypox?

- What are the most challenging questions you have received about monkeypox?

Learning objectives

1. Summarize the epidemiology of monkeypox in the current outbreak.

2. Describe the clinical manifestations, including atypical presentations, of monkeypox and the approach to diagnosis.

3. Outline approaches to supportive care, treatment, and prevention for people with or at risk for monkeypox.

A few words about terminology

- Calls are growing to rename monkeypox.
- The current name is inaccurate:
  - The name was bestowed in 1958, when the virus was identified in laboratory monkeys.
  - But, the environmental reservoir is likely rodents, not monkeys.
- Several variations are currently in use (**MPX, MPXV, MPV**), but there is no consensus.
- The viral clades (now called I and II instead of Congo Basin and West African) have already been renamed.
- The WHO, CDC, White House, and much of the medical literature refer to the illness as monkeypox.

https://www.nytimes.com/2022/08/23/health/monkeypox-name-stigma.html?searchResultPosition=1

Frontline clinicians play a crucial role in addressing this outbreak.

- **May 12, 2022:** Patient admitted in Boston with painful perirectal ulcers and scattered other lesions
- **May 14, 2022:** Two cases of MPX in the United Kingdom not related to travel
- **May 17, 2022:** Review of UK cases prompted MPX testing
- **May 18, 2022:** Diagnosis confirmed for patient in Boston

HEALTH

How Boston doctors diagnosed the first US case of monkeypox

It was an "aha moment."

Dr. Nesli Basgoz, an infectious disease specialist at MGH, diagnosed the first case of monkeypox in the US. *John Tlumacki/Boston Globe*

By Ross Cristantiello

May 30, 2022

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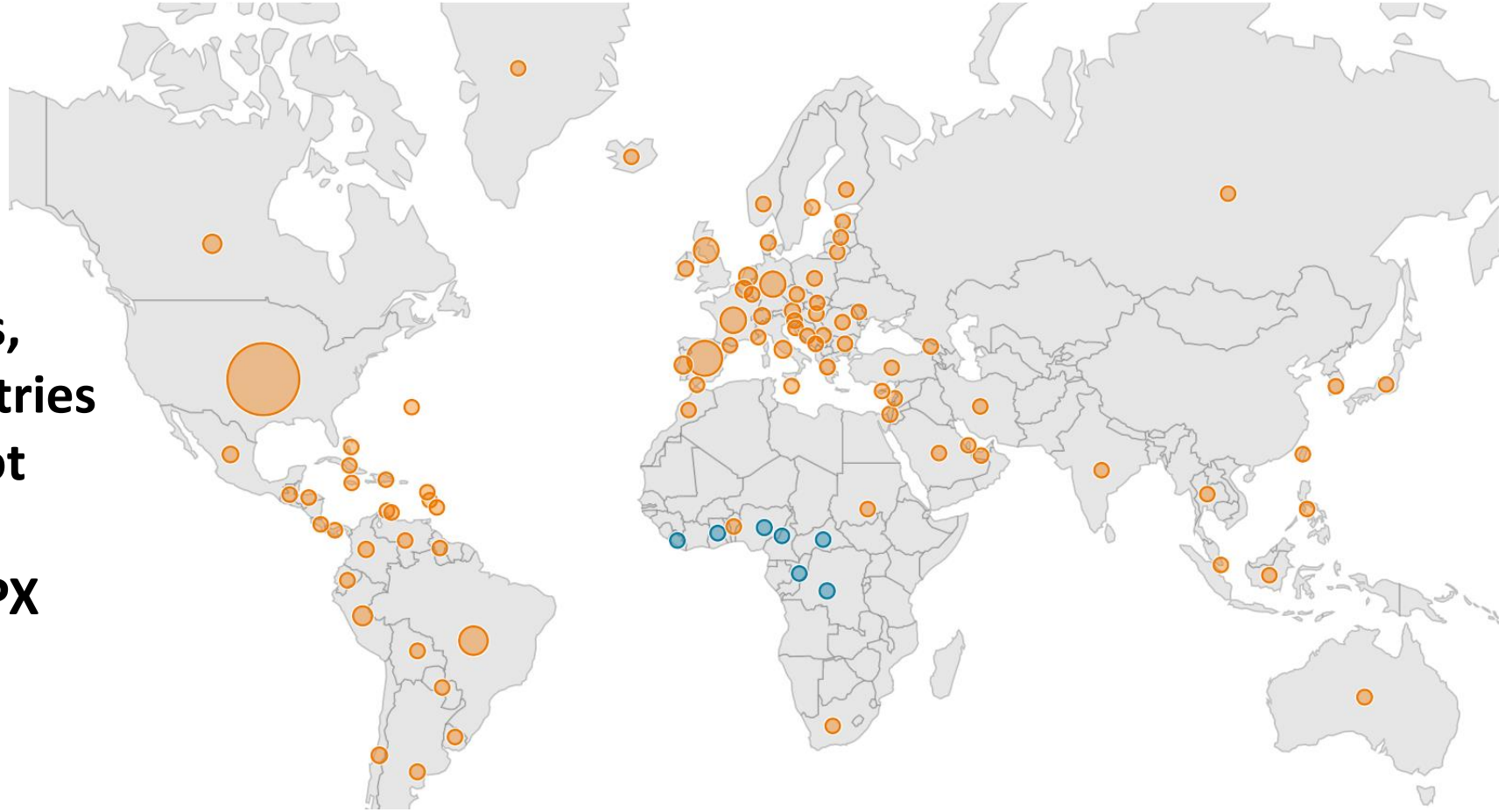
Basgoz N, N Engl J Med, 2022

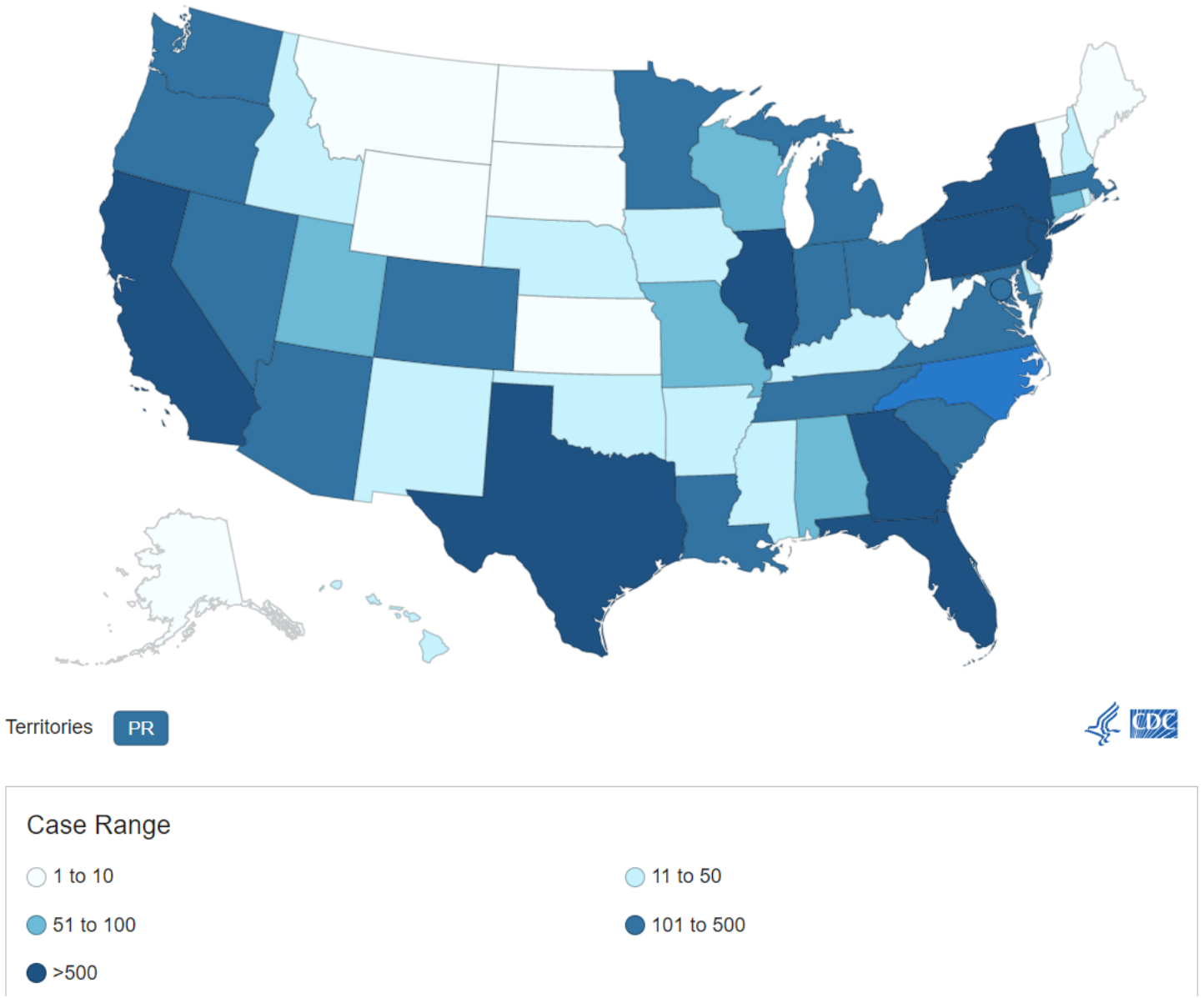
The MPX outbreak is global.

51,257 cases, 99% in countries that have not historically reported MPX



https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html

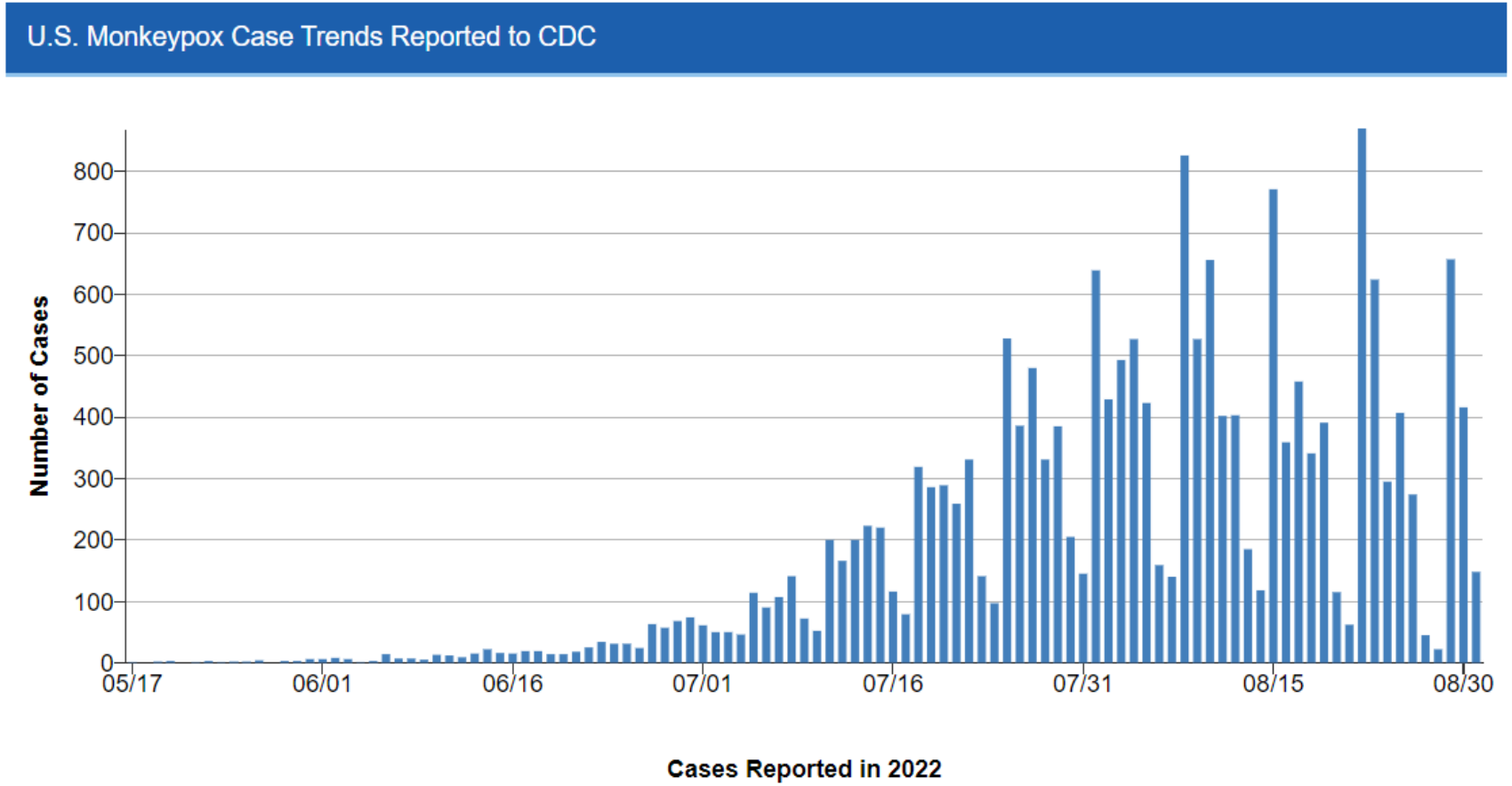
18,989 cases in the United States as of August 31, 2022 at 2 PM



https://www.cdc.gov/poxvirus/monkeypox/response/2022/us-map.html

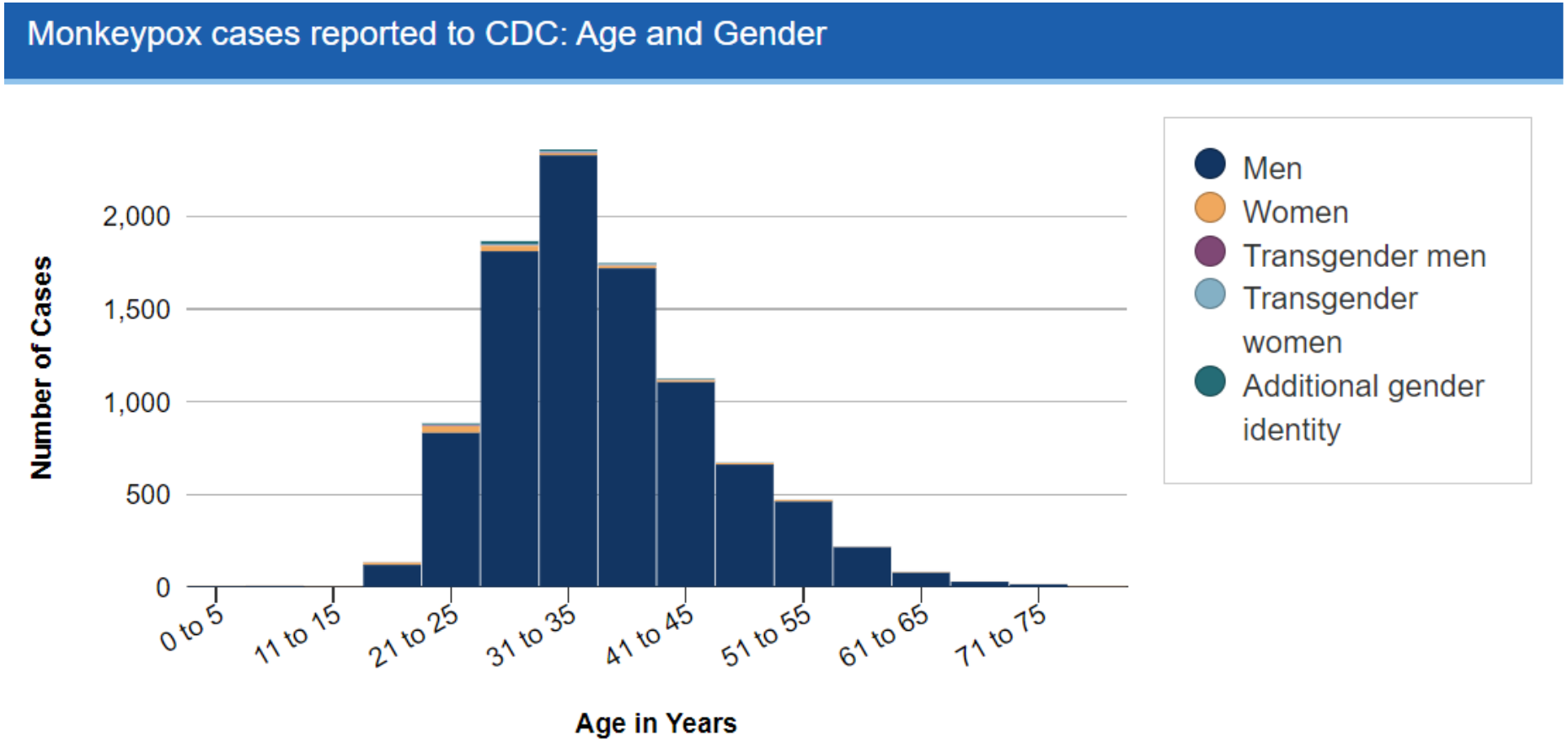
MPX diagnoses may be declining.

Trends of monkeypox cases reported to CDC since May 17, 2022, the start of the response to the current outbreak in the United States. Data include cases with reporting date.*



https://www.cdc.gov/poxvirus/monkeypox/response/2022/mpx-trends.html

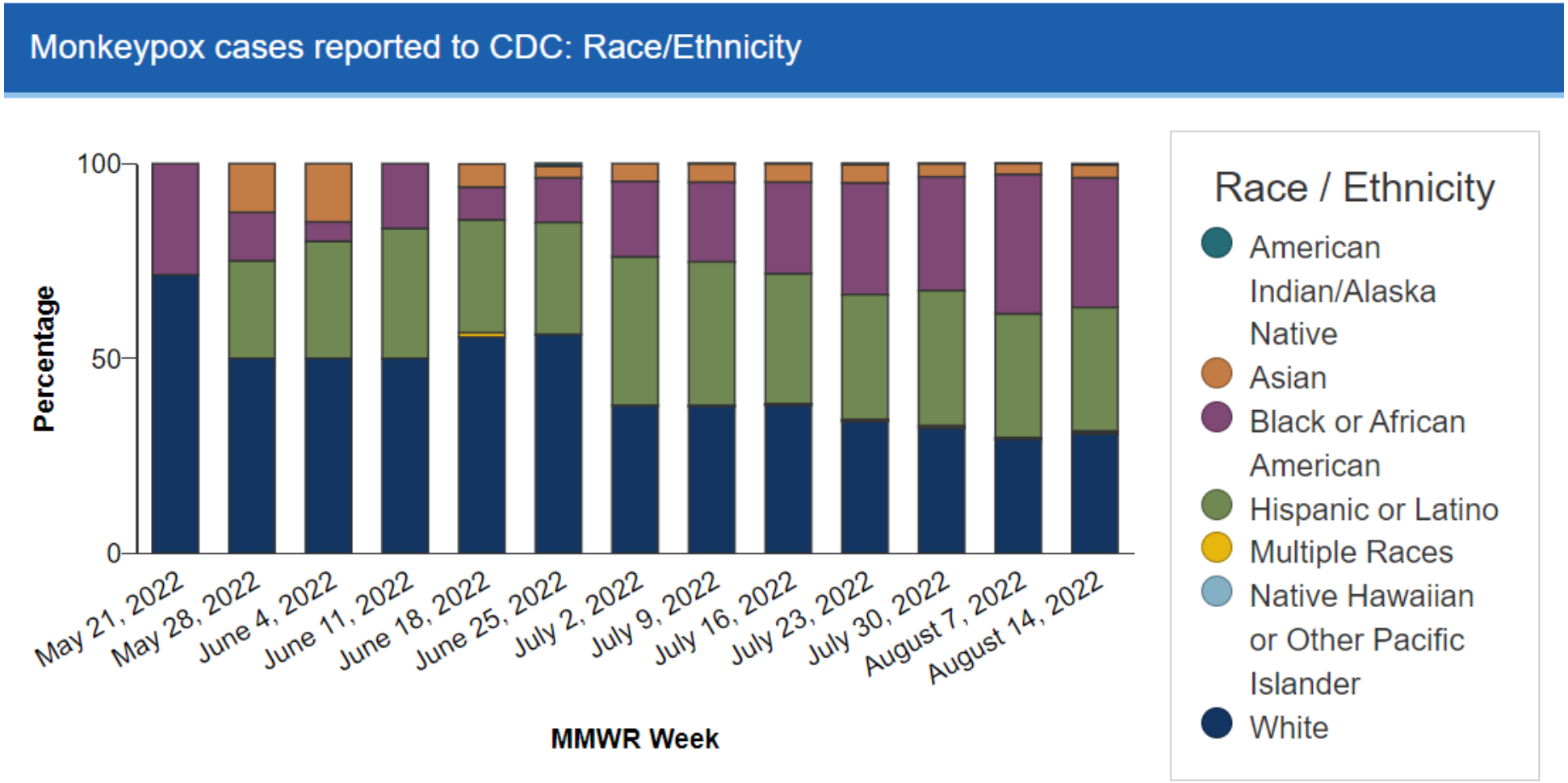
Cisgender men who have sex with men (MSM) are disproportionately affected.



> 90% of people affected are MSM (cisgender and transgender) in multiple series

https://www.cdc.gov/poxvirus/monkeypox/response/2022/demographics.html; Philpott D, MMWR, 2022; Thornhill JP, N Engl J Med, 2022

A majority of recent cases reported to CDC affect Black and Hispanic/Latinx people.



https://www.cdc.gov/poxvirus/monkeypox/response/2022/demographics.html

Clinical presentation

Among 1195 cases reported in the US by July 27, 2022:

- Rash was the initial symptom in 42% (i.e., no prodrome)
- Rash locations included:
  - Genitals in 46%
  - Perianal area in 31%
  - Face in 38%
  - Mouth, lips, or oral mucosa in 25%
  - Palms and/or soles in at least 22%
- Rectal pain was present in 22%
- 8% of people were hospitalized

Lesions may mimic, or co-occur with, sexually transmitted infections such as syphilis and herpes simplex virus (HSV).

Philpott D, MMWR, 2022

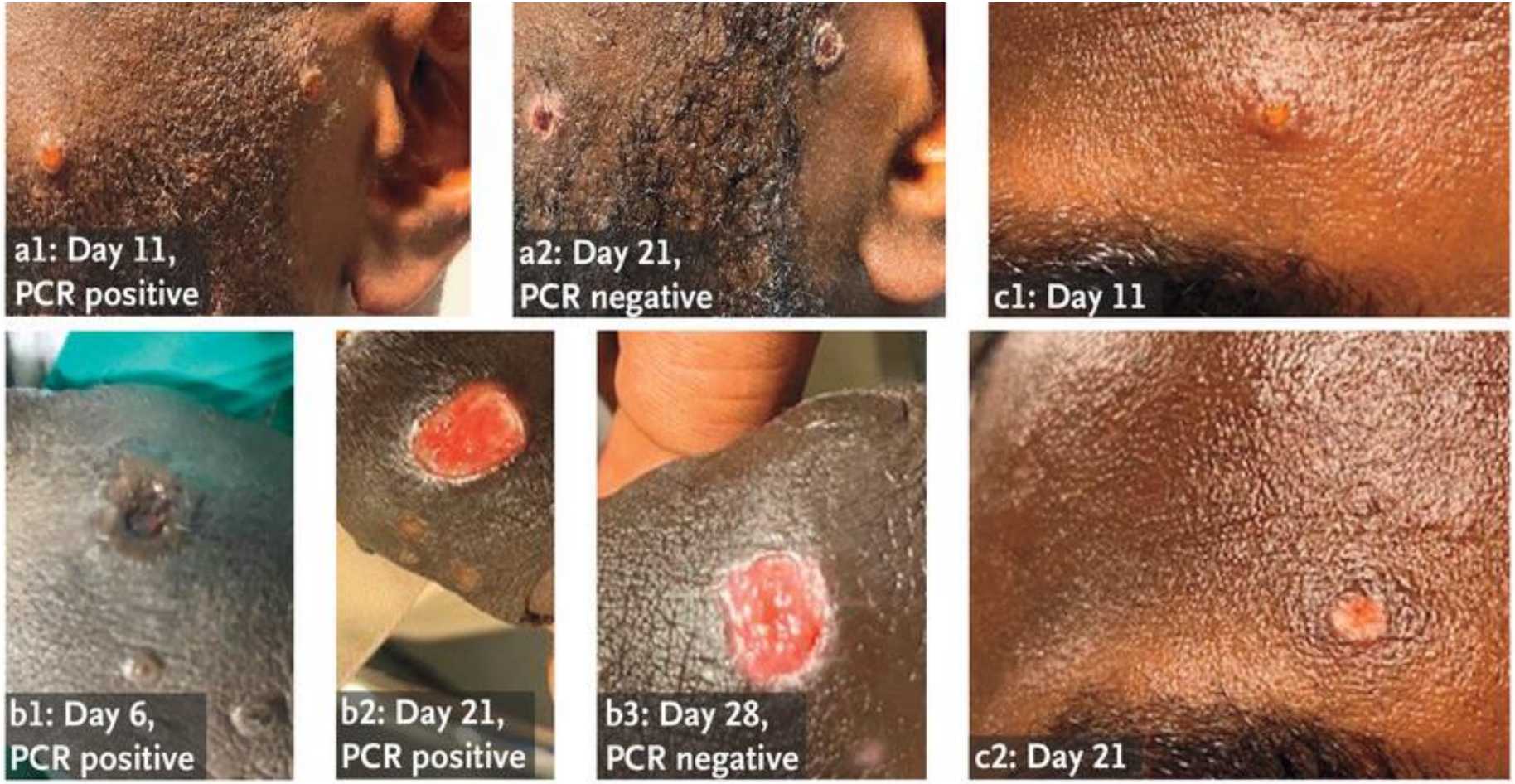
MPX rash features and evolution

Stage	Stage Duration	Characteristics
Enanthem		• Sometimes, lesions first form on the tongue and in the mouth.
Macules	1–2 days	• Macular lesions appear.
Papules	1–2 days	• Lesions typically progress from macular (flat) to papular (raised).
Vesicles	1–2 days	• Lesions then typically become vesicular (raised and filled with clear fluid).
Pustules	5–7 days	• Lesions then typically become pustular (filled with opaque fluid) – sharply raised, usually round, and firm to the touch (deep seated). • Finally, lesions typically develop a depression in the center (umbilication). • The pustules will remain for approximately 5 to 7 days before beginning to crust.
Scabs	7–14 days	• By the end of the second week, pustules have crusted and scabbed over. • Scabs will remain for about a week before beginning to fall off.

- Incubation period 3-17 days
- Lesions are often painful or itchy.
- Lesions are usually, but not always, at the same stage of evolution.
- Most people have fewer than 50 lesions; occasionally, only a single lesion is present.

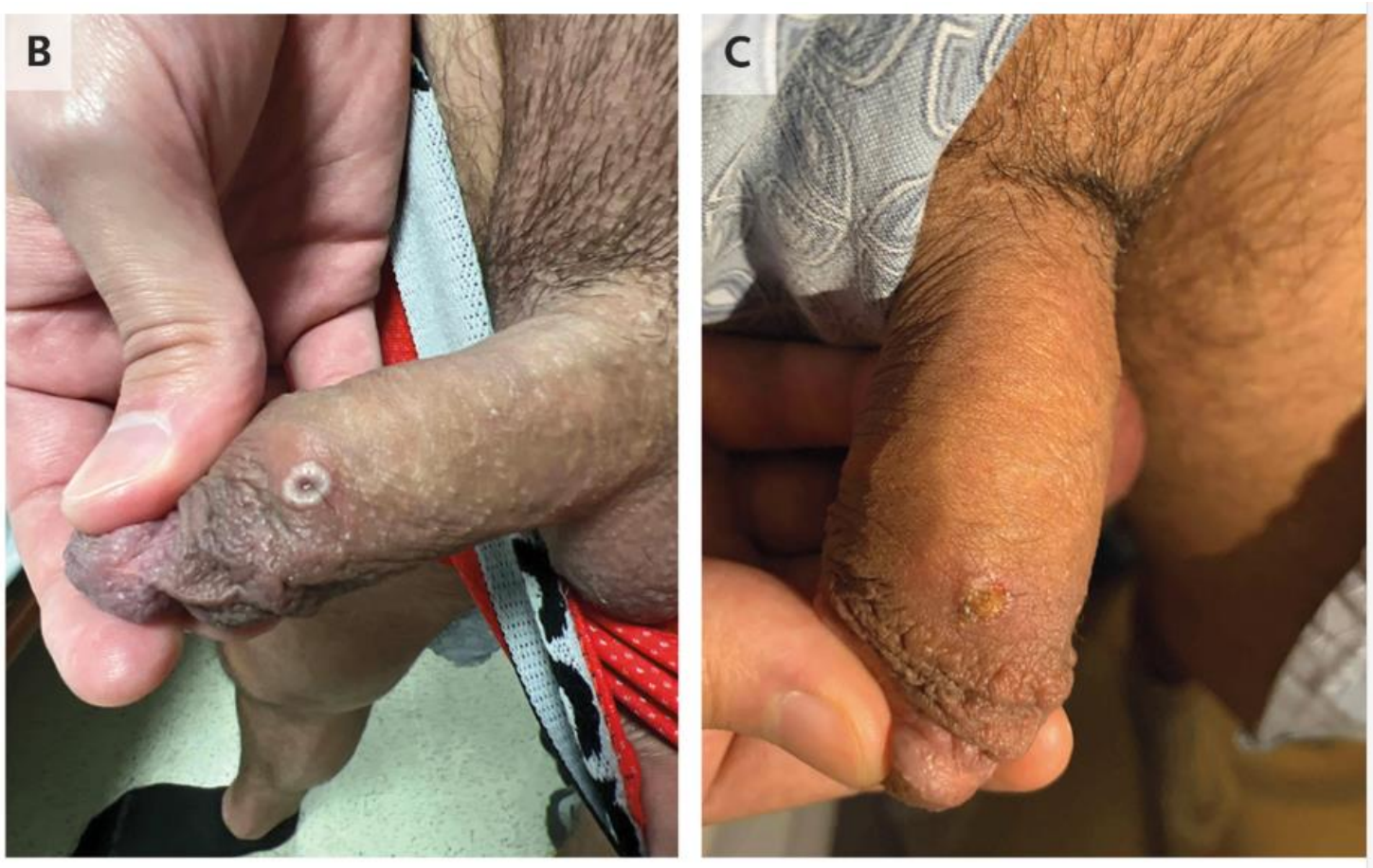
https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html

Examples of MPX lesions



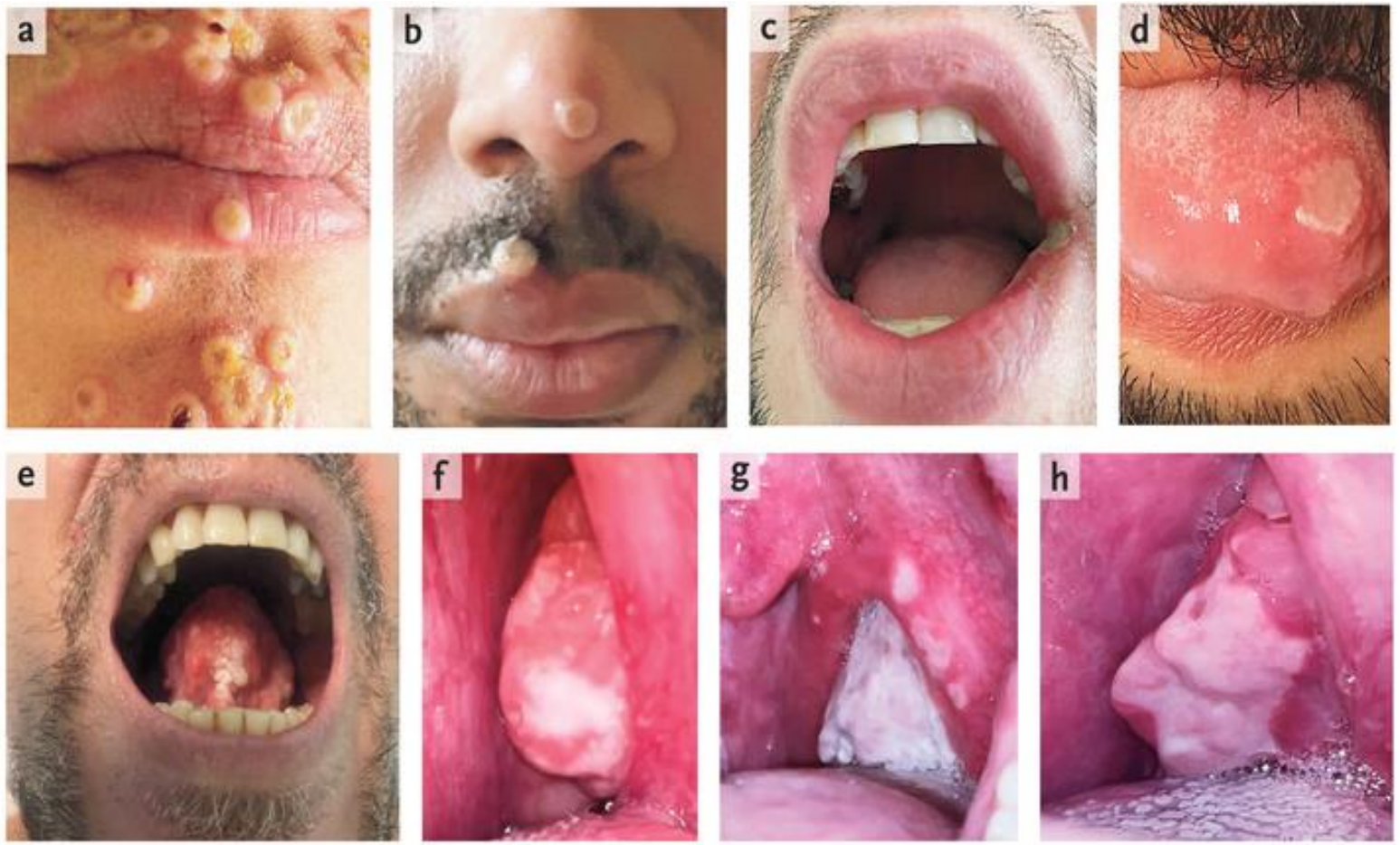
Thornhill JP, N Engl J Med, 2022

Examples of MPX lesions



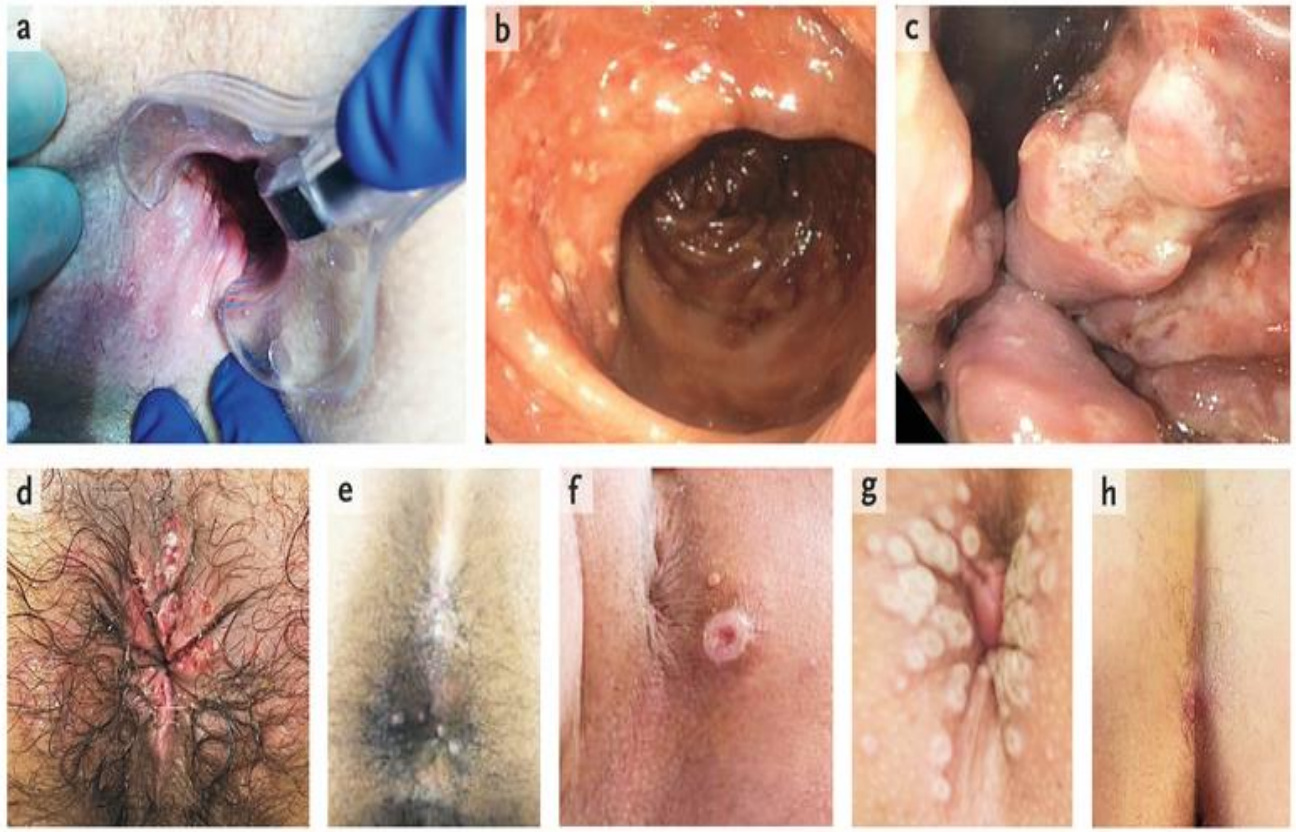
Basgoz N, N Engl J Med, 2022

Examples of MPX lesions



Thornhill JP, N Engl J Med, 2022

Examples of MPX lesions



Thornhill JP, N Engl J Med, 2022

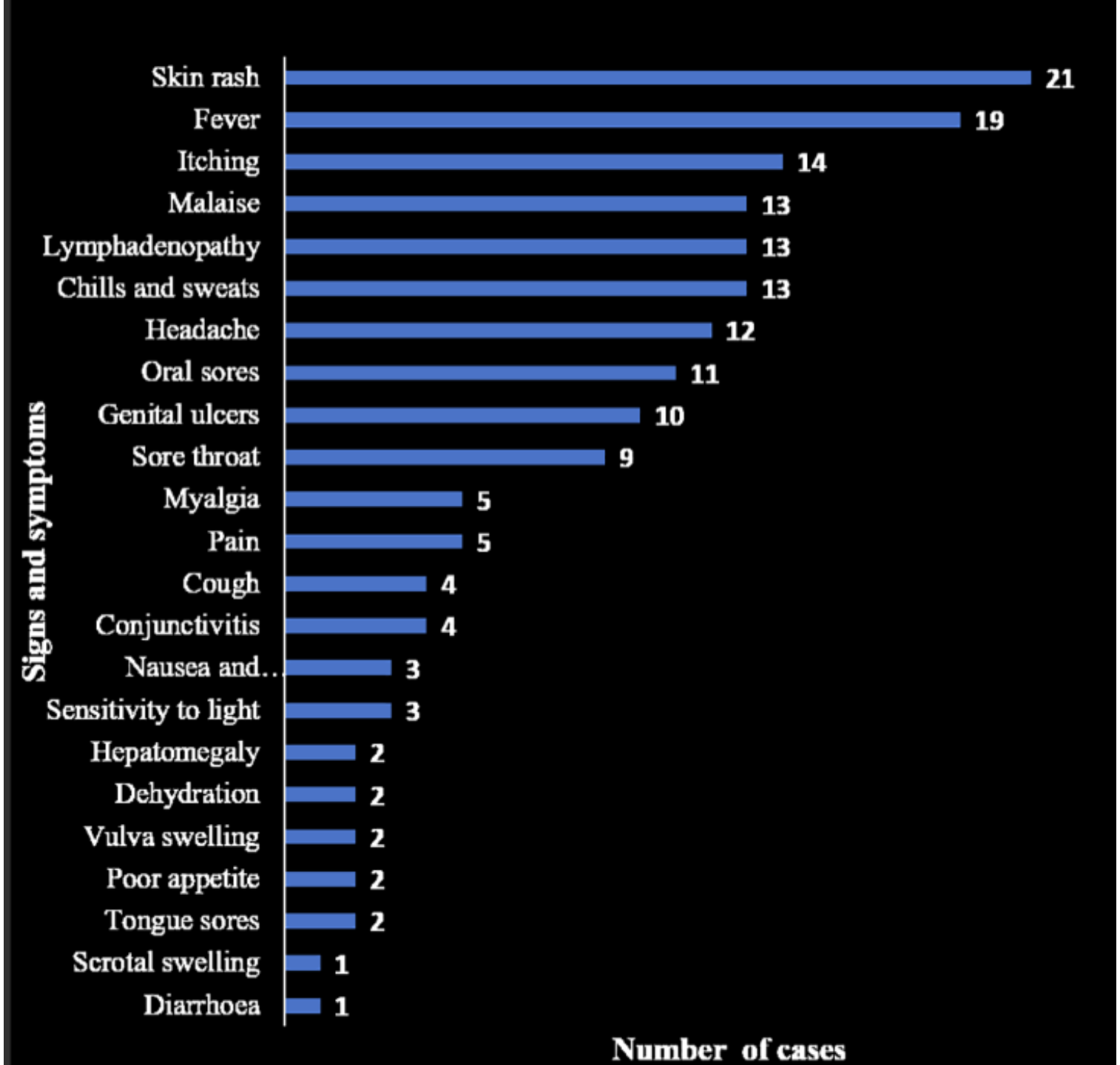
Examples of “atypical” MPX presentations

- A solitary genital lesion, which may be mistaken for a wart or chancre depending on the stage of evolution
- Proctitis with internal and/or external anal lesions, occasionally with a concurrent rectal sexually transmitted infection (STI)
- Whitlow-like lesions on the finger or thumb
- Infection after attendance at a crowded outdoor event, without sexual contact
- Sore throat/pharyngitis, nasal congestion, cough

Karan A, Emerg Infect Dis, 2022; https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html

In a 2017 MPX outbreak in Nigeria:

- 81% of affected people were men
- 48% had genital lesions



Ogoina D, PLoS One, 2019

MPX transmission

1. **Close physical contact, including sex**
2. Contact with objects or surfaces touched by someone with MPX
3. Via respiratory secretions in the setting of prolonged, face-to-face contact
4. From a pregnant person to the fetus through the placenta
5. (Contact with infected animals or animal products)

https://www.cdc.gov/poxvirus/monkeypox/if-sick/transmission.html

Do you think asymptomatic transmission is possible?

Is asymptomatic transmission possible?

Table. Screening for Sexually Transmitted Infections and MPXV Infection in 706 MSM Visiting the Sexual Health Clinic Between 5 June and 11 July 2022

Variable	MSM With No Symptoms of MPXV Infection	MSM With Symptoms Suggesting MPXV Infection
Total number of MSM visiting between 5 June and 11 July 2022	323	383
C trachomatis infections detected on anal swab, *n/N (%)*	32/323 (9.9)	Not tested
N gonorrhoeae infections detected on anal swab, *n/N (%)*	24/323 (7.4)	Not tested
C trachomatis and *N gonorrhoeae* co-infection detected on anal swab, *n/N (%)*	8/323 (2.5)	Not tested
C trachomatis infections detected on first-void urine sample or urethral swab, *n/N (%)*	6/323 (1.9)	Not tested
N gonorrhoeae infections detected on first-void urine sample or urethral swab, *n/N (%)*	3/323 (0.9)	Not tested
C trachomatis and *N gonorrhoeae* co-infection detected on first-void urine sample or urethral swab, *n/N (%)*	1/323 (0.3)	Not tested
MPXV-positive test result, *n/N (%)*	13/200* (6.5)	271/383 (71)

Ferre VM, Ann Intern Med, 2022

Infection control in health care settings

Patient

- Single room, with the door closed if possible
- Surgical mask
- Cover lesions during transport
- Use of airborne isolation if aerosolizing procedures are performed

Health care worker

- Gloves
- Gown
- Goggles or face shield
- N95 mask

https://www.cdc.gov/poxvirus/monkeypox/clinicians/infection-control-healthcare.html#anchor_1660143677200

Testing

- Acceptable specimen types include:
  - Dry swabs of crusts and/or fluid from an open lesion
  - Dry swabs of intact vesicles or pustules
- Obtain samples from different-appearing lesions, if possible.
- Unroofing vesicles or pustules is unnecessary.
- Collect 2 swabs from each lesion.
- Use a synthetic (not cotton) swab.
- Instructions may depend on the laboratory.
- There is no testing option for people prior to the development of rash.

Thornhill JP, N Engl J Med, 2022

MONKEYPOX

Testing Patients for Monkeypox

What lesion specimens to collect

- Collect lesion specimens for initial monkeypox testing at Laboratory Response Network (LRN) laboratories located within your public health department or at authorized commercial laboratories.
  - » Skin lesion material is recommended.
  - » Contact the laboratory (LRN or commercial) fo specifics on acceptable specimen type.
- For further characterization of a specimen at C three types of specimens are accepted.
  - » Dry swabs of lesion material
  - » Swabs of lesion material in viral transport me (VTM)
  - » Lesion crusts

MONKEYPOX

Tips for Adequate Collection of a Lesion Specimen from a Suspect Monkeypox Virus Case

Vigorous swabbing of lesion specimens maximizes the probability of achieving accurate diagnostic results. **Specimens that do not contain enough human DNA may lead to inconclusive PCR test results, with no positive or negative result.** Inconclusive results necessitate patients being sampled again which can delay diagnosis. Follow the instructions below to make sure your specimens are adequate for testing. While vigorous swabbing on the surface of a lesion should collect enough viral DNA, more viral DNA can be found in crusts when present. Recommended infection prevention and control practices, including the use of personal protective equipment (PPE), for caring for a patient with suspected or confirmed monkeypox infection should be used during specimen collection: What Healthcare Professionals Should Know. Unroofing or aspiration of lesions (or otherwise using sharp instruments for monkeypox testing) is **not necessary, nor recommended due to the risk for sharps injury.**

Swabbing of Lesion Surface:

1. Use sterile, synthetic swabs. Do not use cotton swabs.

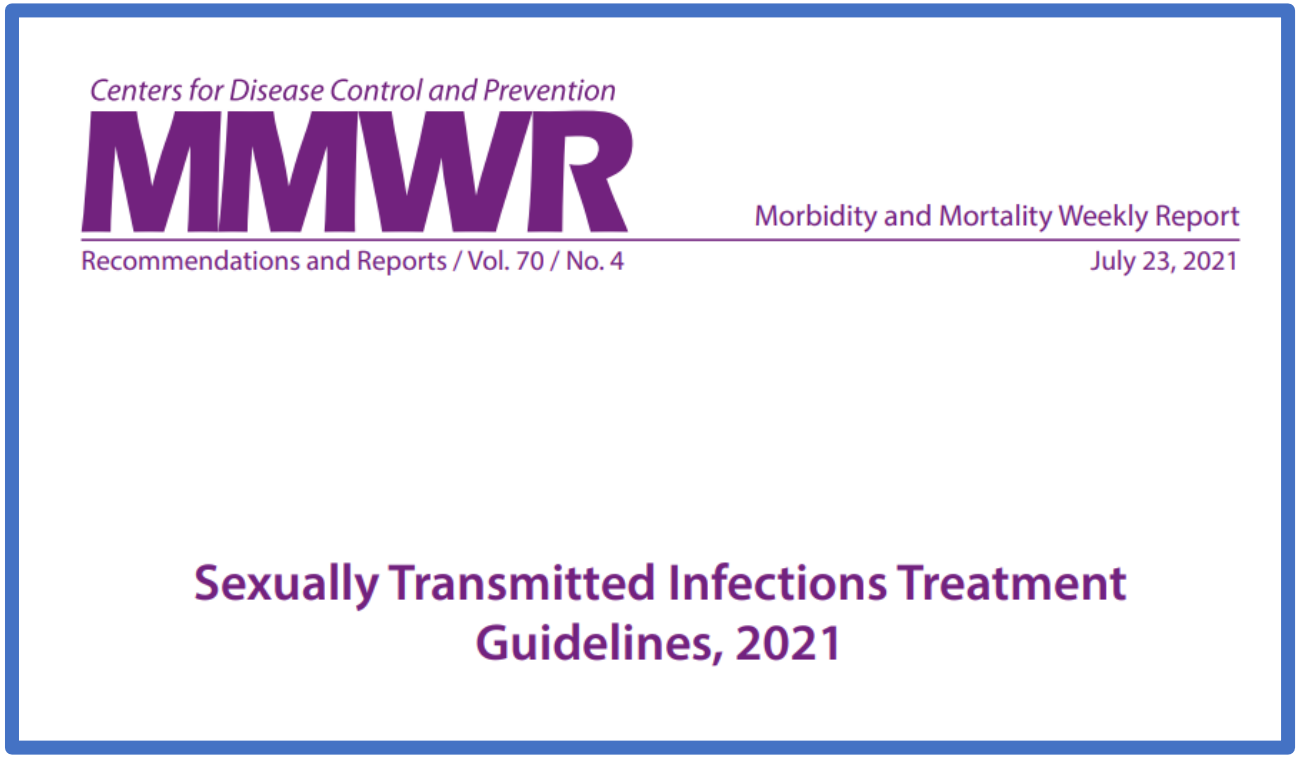
Collection of crusts from healing lesions:

Crusts are not accepted by all

https://www.cdc.gov/poxvirus/monkeypox/clinicians/prep-collection-specimens.html

Clinical management

- Consider, and test for, other STIs, such as syphilis, HSV, gonorrhea, chlamydia
  - Co-occurring infections present in 29% of cases.
  - HSV/VZV testing and bacterial cultures from potential lesions may be held until MPX testing is complete; consider empiric treatment.
  - Refer to the 2021 STI Treatment Guidelines for recommended empiric regimens.



Thornhill JP, N Engl J Med, 2022; 2021 STI Treatment Guidelines, CDC, 2021

Address pain

- Topical and systemic treatments (sitz baths, topical lidocaine, NSAIDs, opioids if necessary)

- Pain may be an indication for tecovirimat.

CDC recommends the following:

- Assess pain in all patients with monkeypox virus infection.
- Recognize that substantial pain may exist from mucosal lesions not evident on physical exam; validation of the pain experience can build trust in the care provider and care plan.
- Use topical and systemic strategies to manage pain. These can include sitz baths and salt-water gargles, topical steroids and lidocaine, over-the-counter pain relievers (e.g., non-steroidal anti-inflammatory drugs, acetaminophen), and ultimately prescription pain relievers (e.g., gabapentin, opioids) as indicated by need for pain control.
- Seek consultation with pain specialists for refractory cases.
- Use stool softeners for proctitis, especially if opioid analgesia is prescribed.
- Stay in contact with patients to regularly assess their pain control and adjust pain management as indicated.
- Monkeypox treatment[6] may be indicated for pain control.

We have much to learn about the novel clinical presentations of monkeypox in the 2022 outbreak. The experiences of healthcare providers on the front lines are critical for building the evidence base to inform optimal approaches to pain management. To this end, CDC encourages providers and researchers to document and report the patient pain experience to determine the incidence of pain, predictive factors for developing pain, and successful methods to control pain associated with monkeypox.

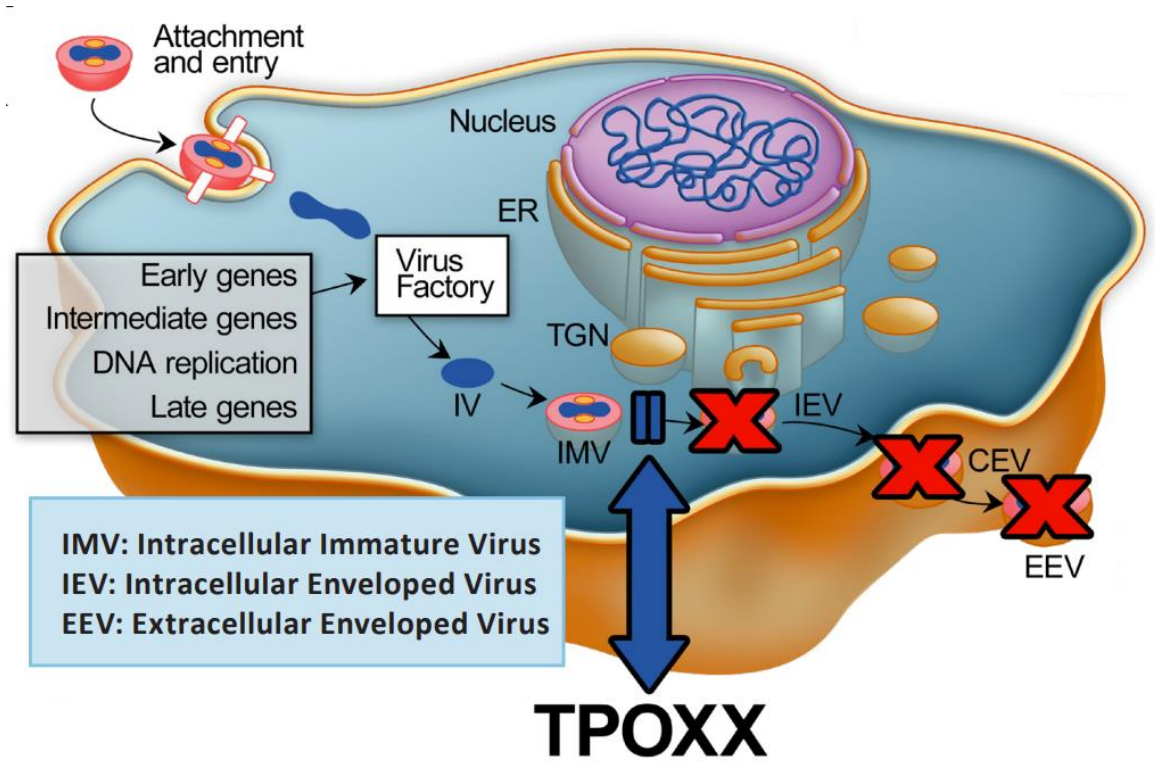
We look forward to working with you to provide the guidance necessary for healthcare providers and clinicians to address this outbreak. No single group can do this alone, and we thank each of you for your effort and commitment to effective patient care.

Sincerely,

Rochelle P. Walensky, MD, MPH
Director, CDC

Tecovirimat (TPOXX)

- Mechanism of action: Blocking secondary viral envelope formation
- FDA approved (under the “Animal Rule”) for the treatment of smallpox in adults and children
- Not FDA approved for monkeypox or other orthopoxviruses
- Available during this outbreak through an expanded access IND



https://www.siga.com/wp-content/themes/sigahba/TPOXX-Fact-Sheet.pdf

CDC’s treatment considerations

1. Severe disease (e.g., confluent lesions, sepsis, encephalitis, hospitalization)
2. Increased risk for severe disease
   - Immunocompromise
   - People < 8 years of age
   - Pregnant or breastfeeding people
   - Atopic dermatitis or other active exfoliative skin conditions
   - One or more complications (e.g., secondary infection, gastroenteritis, dehydration)
3. Infections involving the eyes, mouth, or other anatomic locations (genitals, anus) where infection might constitute a “special hazard”

Tecovirimat, continued

Forms

- **Oral:** 200 mg capsules, best absorbed with a fatty meal (600 calories, 25 grams of fat)
- **Intravenous:** Not for use in people with CrCl < 30 mL/minute and to be used with caution in people with CrCl of 30-80 mL/minute

Dosing and duration

- 40-119 kg: 600 mg (3 capsules) by mouth twice daily for 14 days
- ≥ 120 kg: 600 mg by mouth three times daily for 14 days

Tecovirimat, continued

Adverse reactions:

- Headache (12%) and nausea (5%) with the oral formulation
- Injection site reactions (>70%) and headache (15%) with the IV formulation

Drug-drug interactions:

- Repaglinide -> Hypoglycemia
- Midazolam -> Decreased effect of midazolam
- Rilpivirine, maraviroc -> Decreased drug concentrations (uncertain significance)

Pregnancy and breastfeeding

- Pregnancy and breastfeeding are on the list of CDC’s treatment considerations.
- No human data are available to address safety or efficacy.
- No teratogenic effects were observed in mice or rabbits.

Note: Treatment can be started pending monkepox test results

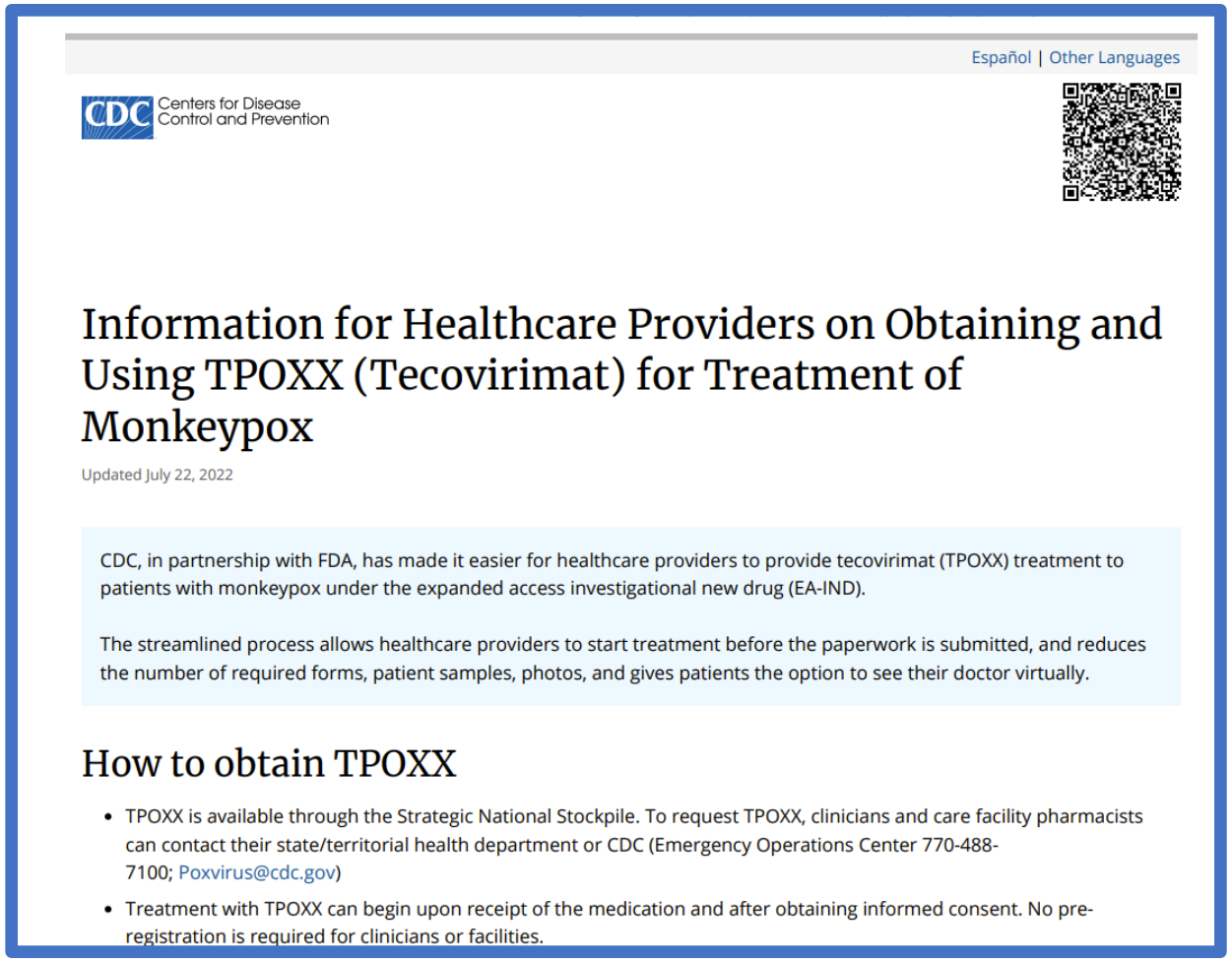
Table 4. Summary of Clinical Assessment and Monitoring Parameters

Parameters \ Days	Pre-Tecovirimat Treatment [a]	Post Completion of Tecovirimat Treatment [a]
	Patient Intake Form (Attachment 2 -A)	Optional Clinical Outcome Form (Attachment 2 -B)
	Prior to first dose of Tecovirimat (≤ 24 hours)	Outpatients: 3-14 Days after treatment completion
Sign Informed Consent	x	N/A
Inclusion/Exclusion Criteria	x	N/A
Baseline clinical assessment Give patient the Diary form[c]	x	N/A
Clinical progress	N/A	x
Serious Adverse Events[d]	N/A	Report if SAEs occur
Lesion Photos[b]	Optional	Optional
Hematology, chemistry, urinalysis	Optional	Optional
Lesion samples	Optional	Optional (for any new lesions post-treatment)
PK samples	Optional	

https://www.cdc.gov/poxvirus/monkeypox/pdf/Tecovirimat-IND-Protocol-CDC-IRB.pdf

Treatment logistics

- Tecovirimat for monkeypox is only available under IND.
- To prescribe tecovirimat, a facility must have a signed FDA Form 1572 filed with CDC, and each prescriber must be listed on the form.
- The medication is not available at retail pharmacies.



Español | Other Languages

CDC Centers for Disease Control and Prevention

Information for Healthcare Providers on Obtaining and Using TPOXX (Tecovirimat) for Treatment of Monkeypox

Updated July 22, 2022

CDC, in partnership with FDA, has made it easier for healthcare providers to provide tecovirimat (TPOXX) treatment to patients with monkeypox under the expanded access investigational new drug (EA-IND).

The streamlined process allows healthcare providers to start treatment before the paperwork is submitted, and reduces the number of required forms, patient samples, photos, and gives patients the option to see their doctor virtually.

How to obtain TPOXX

- TPOXX is available through the Strategic National Stockpile. To request TPOXX, clinicians and care facility pharmacists can contact their state/territorial health department or CDC (Emergency Operations Center 770-488-7100; Poxvirus@cdc.gov)
- Treatment with TPOXX can begin upon receipt of the medication and after obtaining informed consent. No pre-registration is required for clinicians or facilities.

https://www.cdc.gov/poxvirus/monkeypox/clinicians/obtaining-tecovirimat.html#print

Vaccination with JYNNEOS

- Replication-deficient *Vaccinia* virus
- Licensed as a series of two subcutaneous injections, 4 weeks apart
- Recommended by the Advisory Committee on Immunization Practices as pre-exposure prophylaxis for laboratory and other personnel with occupational exposure to orthopoxviruses
- Booster doses recommended every 2 years for those with exposure to monkeypox
- The only contraindication is severe allergy to a vaccine component (ciprofloxacin, gentamicin, egg).
- Side effects include injection site reactions; serious side effects are rare.
- The vaccine can be given to people with HIV and immunocompromising conditions.

Rao AK, MMWR, 2022

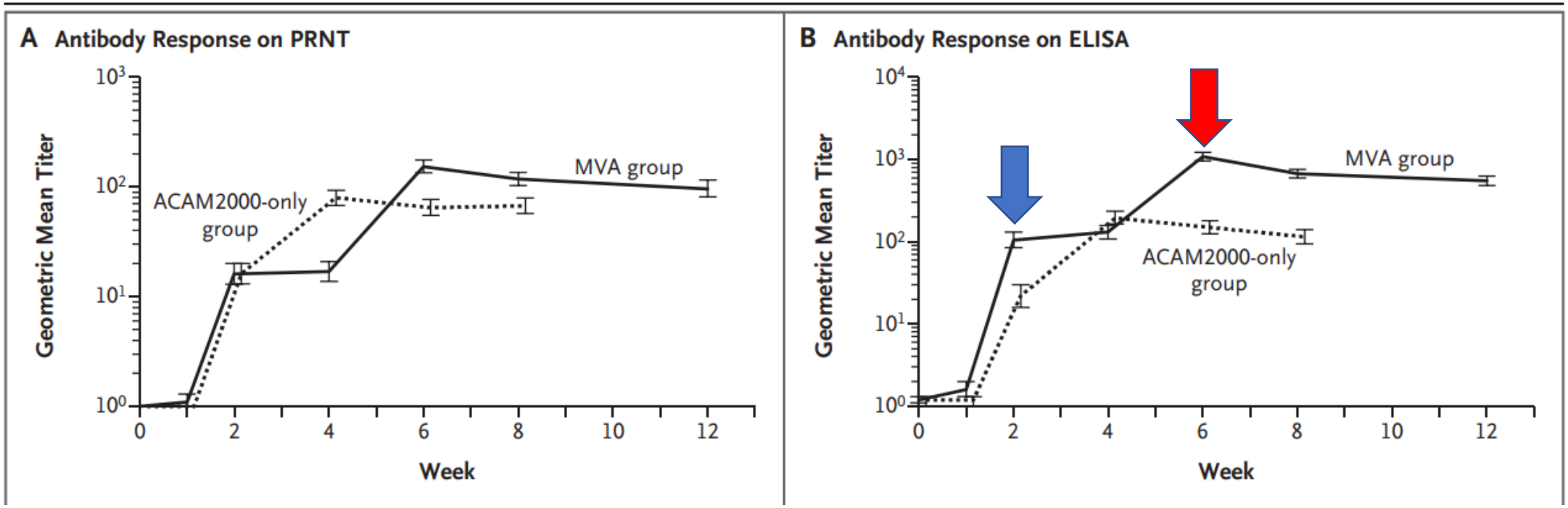
ACAM2000 is available but more problematic than JYNNEOS.

TABLE 3. Contraindication to administration of ACAM2000 and JYNNEOS to recipients or their household contacts with certain conditions — United States, 2022

Clinical characteristic	Contraindication to receipt of ACAM2000			Contraindication to receipt of JYNNEOS
	Vaccine recipient with condition		Household contact with condition*	
	Primary vaccination	Revaccination		
History or presence of atopic dermatitis	Y	Y	Y	—
Other active exfoliative skin conditions†	Y	Y	Y	—
Immunosuppression§	Y	Y	Y	—
Pregnancy¶	Y	Y	Y	—
Age <1 year**	Y	Y	Y	—
Breastfeeding††	Y	Y	—	—
Serious vaccine component allergy	Y	Y	—	Y
Known underlying heart disease (e.g., coronary artery disease or cardiomyopathy)	Y	Y	—	—
≥3 known major cardiac risk factors§§	Y	—	—	—

Rao AK, MMWR, 2022

Antibody response with JYNNEOS are non-inferior to those with ACAM2000.



Antibody titers at 2 weeks (ie, after a single dose) are similar between JYNNEOS and ACAM2000.

Peak antibody titers are achieved at 6 weeks (ie, 2 weeks after the second dose).

Pittman PR, N Engl J Med, 2019

Post-exposure (PEP) vaccination strategies

- There are no efficacy data on PEP with JYNNEOS for the current outbreak.
- Vaccination may:
  - Prevent disease if given within 4 days of exposure
  - Reduce disease severity if given between 4-14 days of exposure
- 2 related strategies:
  - **PEP** for people with a confirmed exposure to MPX through public health investigation, contact tracing, or risk exposure assessments
  - **PEP++** for people with presumed exposure to MPX
    - Know a sexual partner within the past 14 days was diagnosed with MPX
    - Have had multiple sex partners in the past 14 days in an area with MPX
    - MSM or transgender or gender diverse person having sex with men who in the past 14 days has:
      - Had sex at a commercial venue
      - Had sex at an event or venue where monkeypox transmission is occurring

https://www.cdc.gov/poxvirus/monkeypox/vaccines/vaccine-basics.html

A shift to intradermal dosing to increase vaccine supply

FDA NEWS RELEASE

Monkeypox Update: FDA Authorizes Emergency Use of JYNNEOS Vaccine to Increase Vaccine Supply

For Immediate Release:

August 09, 2022

https://www.fda.gov/news-events/press-announcements/monkeypox-update-fda-authorizes-emergency-use-jynneos-vaccine-increase-vaccine-supply

Rationale for intradermal dosing

- Antibody responses to intradermal dosing are non-inferior to those of subcutaneous dosing
- Intradermal administration requires 1/5th of the subcutaneous dose
- Local redness and induration are more common with intradermal than subcutaneous dosing

Frey SA, Vaccine, 2015

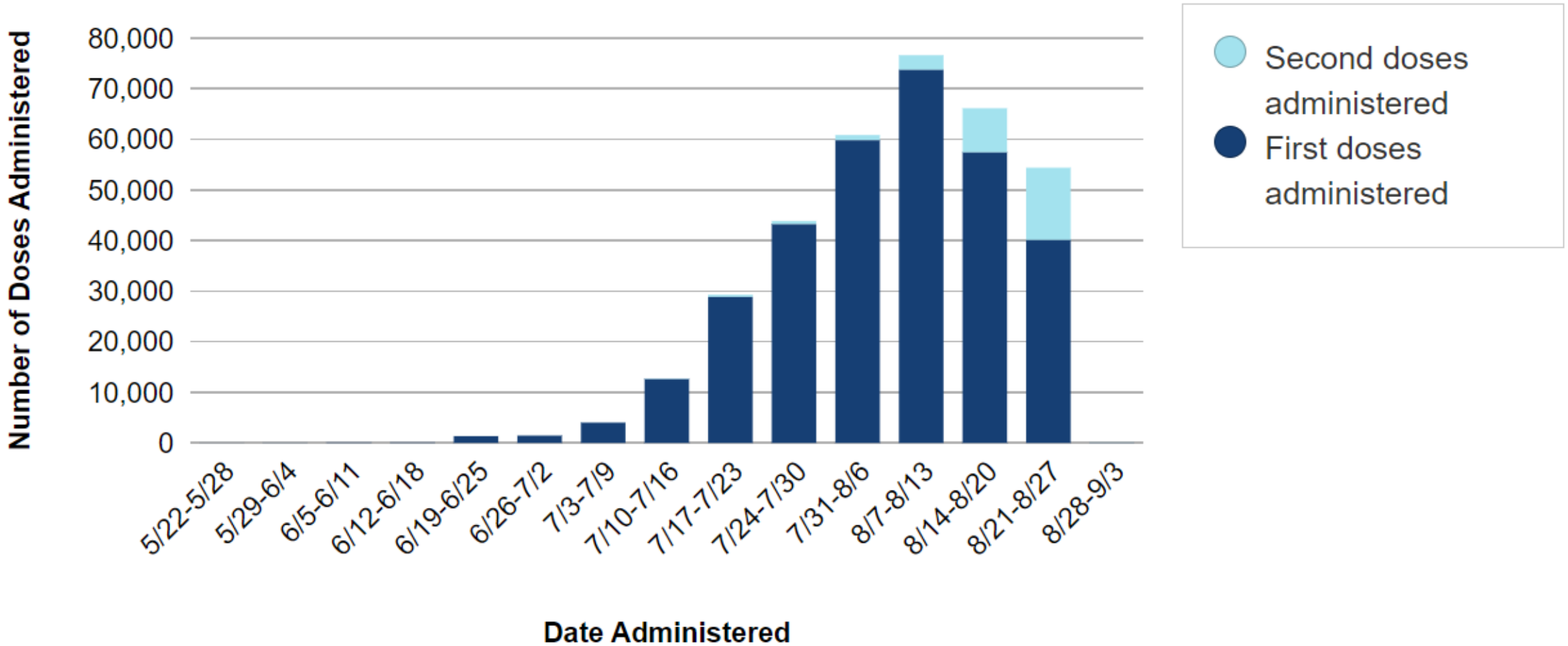
Vaccine strategies

Table 2. Vaccination Schedule and Dosing Regimens for JYNNEOS Vaccine

JYNNEOS vaccine regimen	Route of administration	Injection volume	Recommended number of doses	Recommended interval between 1st and 2nd dose
Alternative regimen				
People age ≥18 years	ID	0.1 mL	2	28 days
Standard regimen				
People age <18 years	Subcut	0.5 mL	2	28 days
People of any age who have a history of developing keloid scars	Subcut	0.5 mL	2	28 days

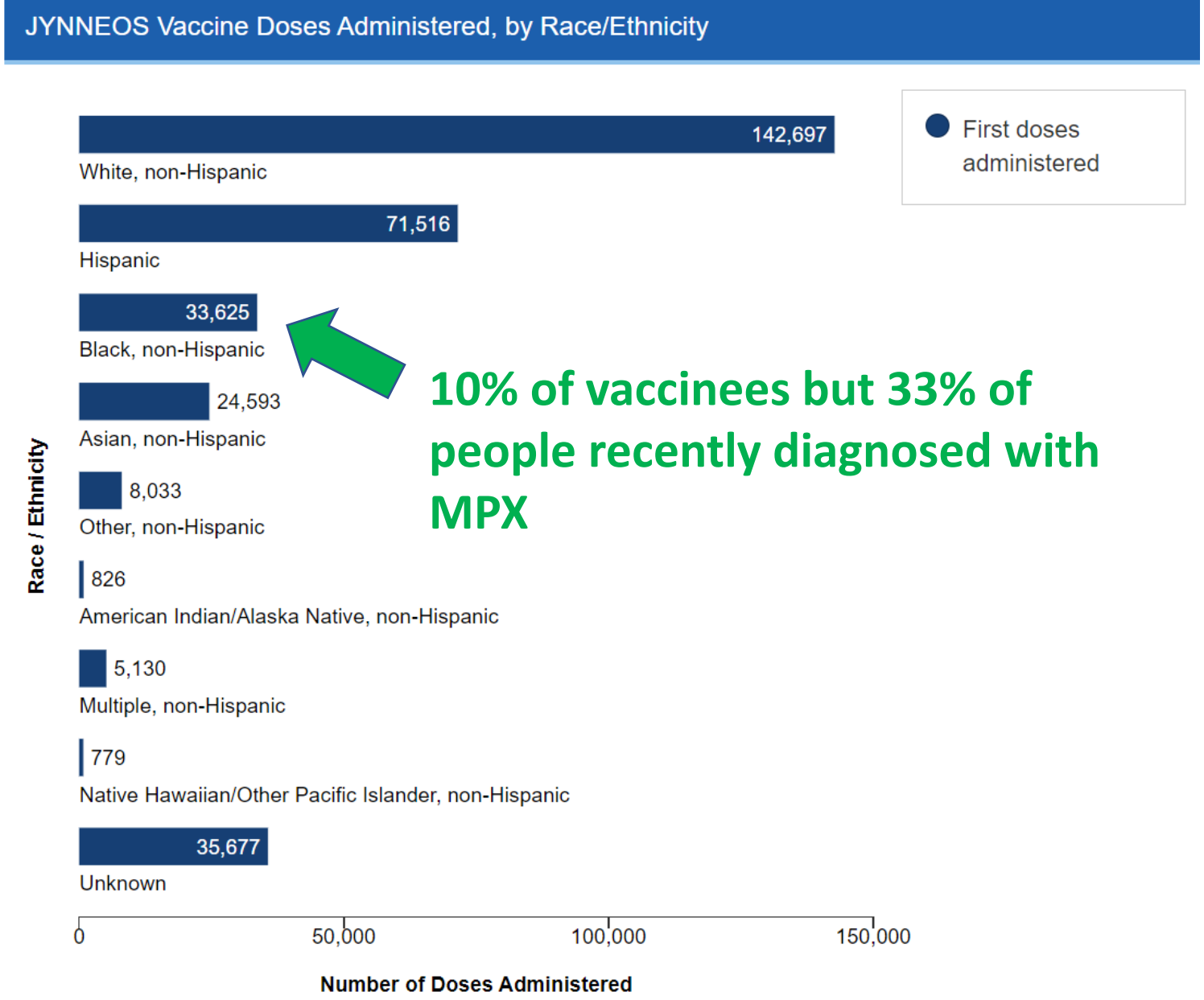
https://www.cdc.gov/poxvirus/monkeypox/interim-considerations/jynneos-vaccine.html#print

Total JYNNEOS Vaccine Doses Administered and Reported to CDC



https://www.cdc.gov/poxvirus/monkeypox/response/2022/vaccines_data.html

The distribution of administered vaccines by race/ethnicity does not match current case epidemiology.



https://www.cdc.gov/poxvirus/monkeypox/response/2022/vaccines_data.html

Summary

- The clinical presentation of monkeypox in this outbreak often differs from classic descriptions and varies among patients and over the course of the illness.
- Treatment with tecovirimat is indicated under IND for those with or at risk for severe disease and/or those with lesions in sensitive anatomic areas.
- Post-exposure vaccination may prevent or reduce the severity of infection; administering the vaccine intradermally will increase vaccine supply.