CDC/IDSA Clinician Call

June 5, 2024

Welcome & Introductions

Dana Wollins, DrPH, MGC
Senior Vice President, Strategy
Infectious Diseases Society of America

- About the Clinician Call: Initiated in 2020 as a forum for information sharing among frontline clinicians caring for patients with COVID-19. Now expanded to address timely topics in infectious diseases—all from a clinical perspective.
- The views and opinions expressed here are those of the presenters and do not necessarily reflect the official policy or position of the CDC or IDSA. Involvement of CDC and IDSA should not be viewed as endorsement of any entity or individual involved.
- This webinar is being recorded and can be found online at www.idsociety.org/cliniciancalls.

Clinical Management and Prevention of Clade II Mpox: Plus, HPAI Update

- Jointly hosted with HIVMA

COVID-19 Real-Time Learning Network

Brought to you by CDC and IDSA

hivma

hiv medicine association

1. HPAI - Update

Jay Butler, MD, FIDSA
Deputy Director for Infectious Diseases U.S.
U.S. Centers for Disease Control & Prevention

2. Epidemiology of Clade II Mpox

Agam Rao, MD, FIDSA
CAPT, U.S. Public Health Service
Medical Officer
Poxvirus and Rabies Branch
U.S. Centers for Disease Control & Prevention

3. Update on Mpox Vaccination

Meghan Pennini, PhD
Chief Vaccines and Therapeutics Officer
HHS Coordination Operations and Response Element (H-CORE)
Administration for Strategic Preparedness & Response
U.S. Department of Health & Human Services

4. Update on Tecovirimat EA-IND Eligibility Criteria for Treatment for Mpox

Patty Yu, MPH
Regulatory Health Scientist
U.S. Centers for Disease Control & Prevention

5. Q&A and Discussion – All Presenters Plus:

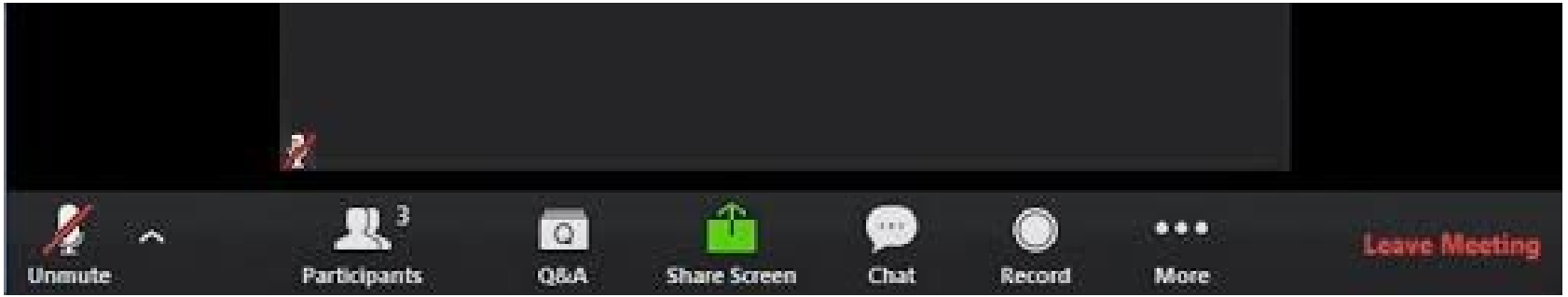
Robert Goldstein, MD, PhD
Commissioner
Massachusetts Department of Public Health

Boghuma K. Titanji, MD, MSc, DTM&H, PhD
Assistant Professor of Medicine
Emory University School of Medicine

Timothy Wilkin, MD
Assistant Dean for Clinical Research Compliance
Weill Cornell Medical College

Question?
Use the “Q&A” Button

Comment?
Use the “Chat” Button



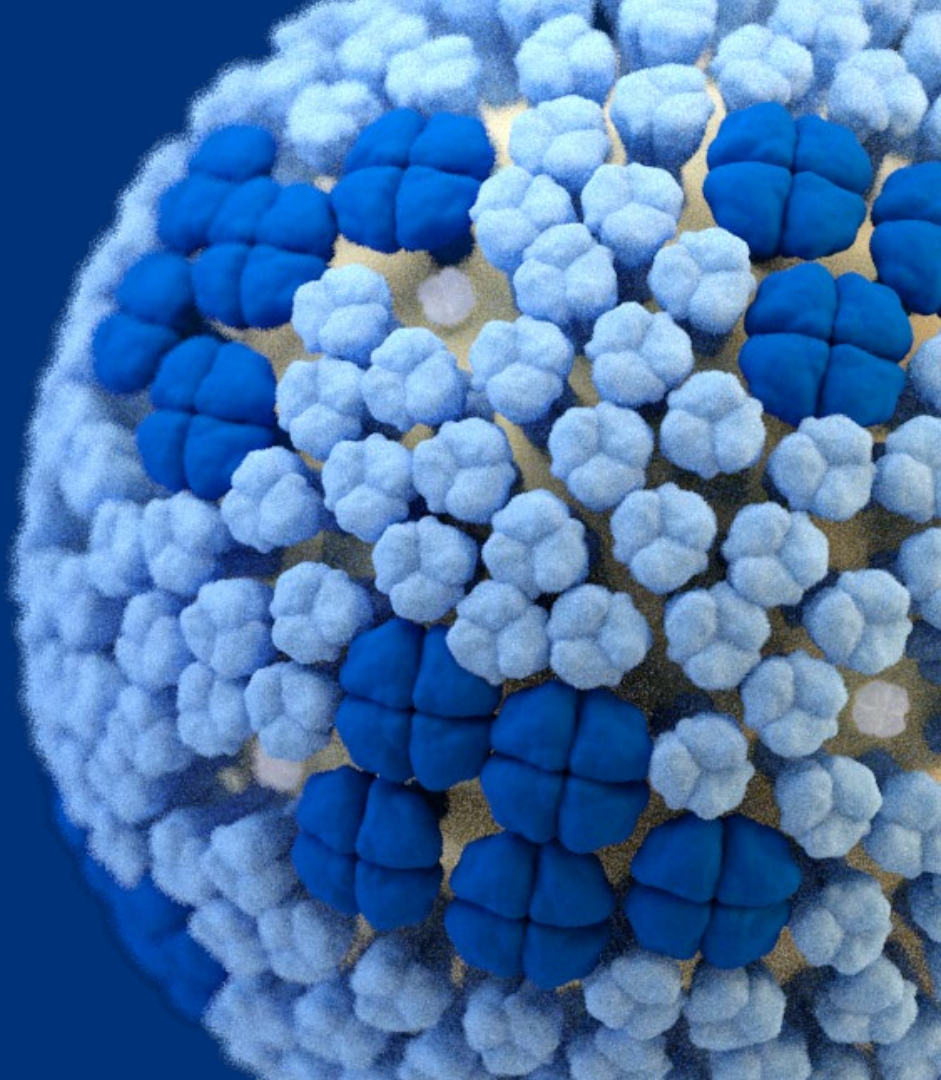
HPAI Update

Jay Butler, MD, FIDSA
Deputy Director for Infectious Diseases U.S. Centers for Disease Control and Prevention

Highly Pathogenic Avian Influenza A(H5N1)

Jay C. Butler, MD, FAAP, MACP, FIDSA
Senior Advisor
2024 Influenza A H5N1 Response
Centers for Disease Control and Prevention

June 5, 2024

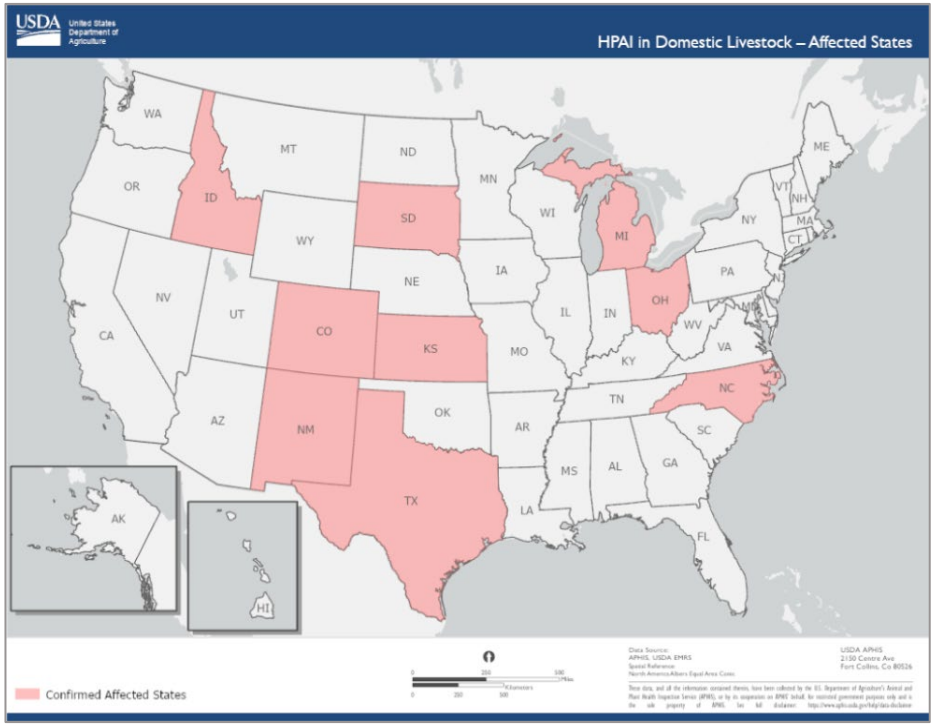


CDC Influenza

H5N1 in Dairy Herds

- USDA has confirmed HPAI in dairy herds in over **75** farms across 9 states:

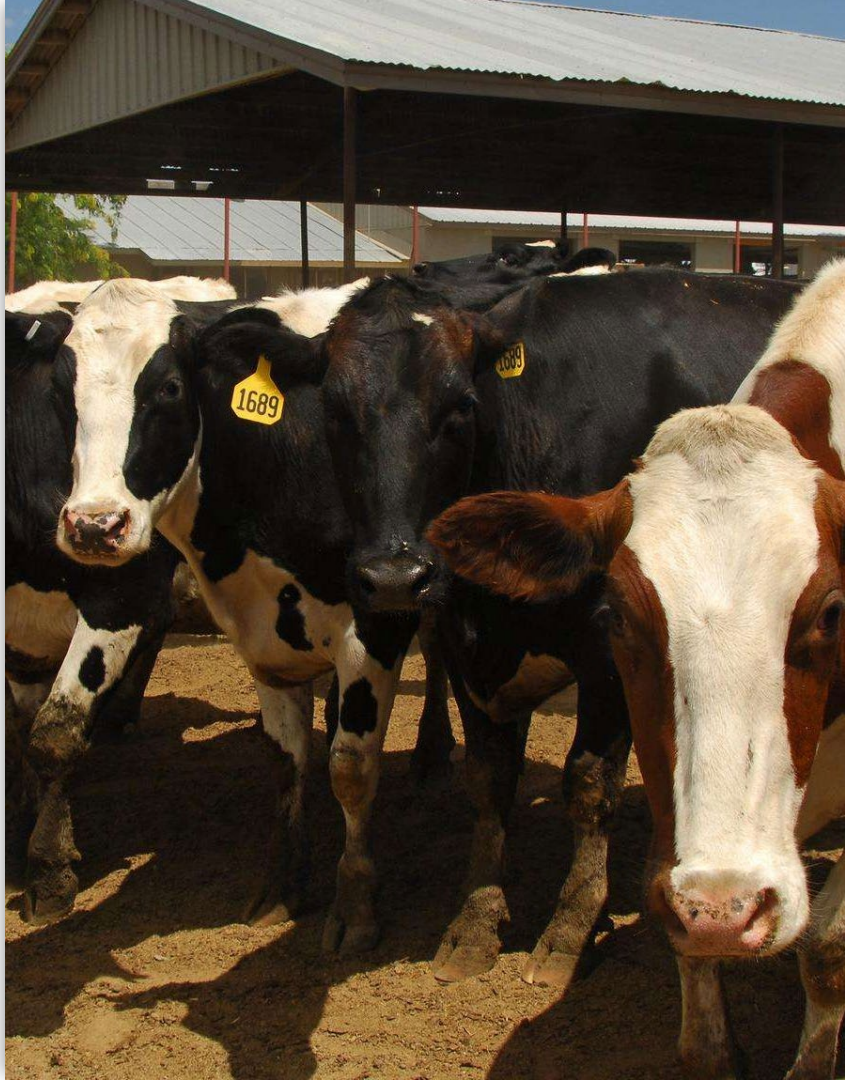
- Other animal species reported: wild birds, cats, racoon, opossums, alpacas



Highly Pathogenic Avian Influenza (HPAI) Detections in Livestock; WAHIS (woah.org); USDA Support for Producers with Affected Dairy Premises

H5 Human Cases

- Three human cases have been detected related to cattle exposure:
  - April 1 – Texas, farmworker, conjunctivitis
  - May 22 – Michigan, farmworker, conjunctivitis
  - May 30 – Michigan, farmworker, conjunctivitis and upper respiratory symptoms
- Not hospitalized
- Antivirals provided
- Isolation recommended
- No human-to-human transmission

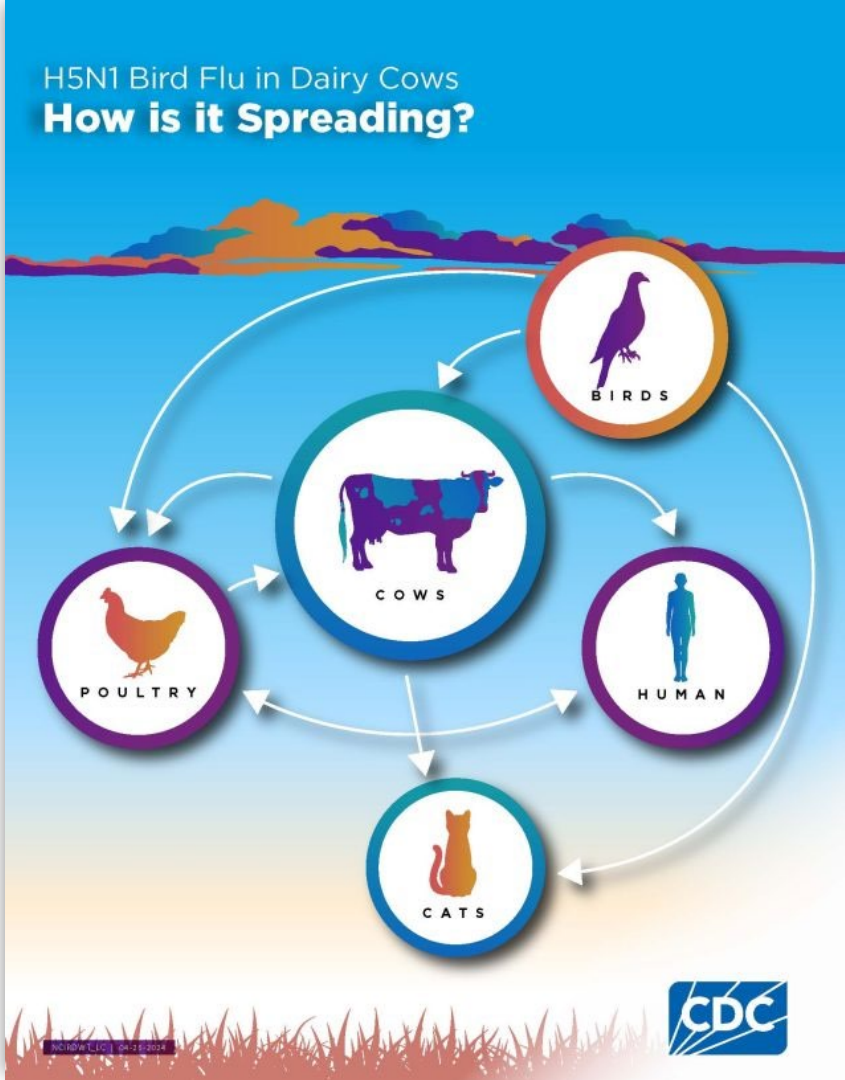


CDC Influenza

Health Alert: First Case of Novel Influenza A (H5N1) in Texas, March 2024 | Texas DSHS

CDC's Priorities

- Supporting and engaging public health and agricultural partners
- Protecting human health and safety
- Understanding risk to people from H5N1 viruses
- Assessing H5N1 viruses for genetic changes



Monitoring, Testing and Treatment

- Human Monitoring and Testing Update
  - Since Mar 24, >390 people monitored from affected farms, >44 tested

- CDC Guidance :
  - Key Public Health Prevention Recommendations for HPAI A(H5N1) | Avian Influenza (Flu) (cdc.gov)

CDC Influenza

Summer Influenza Surveillance Priorities

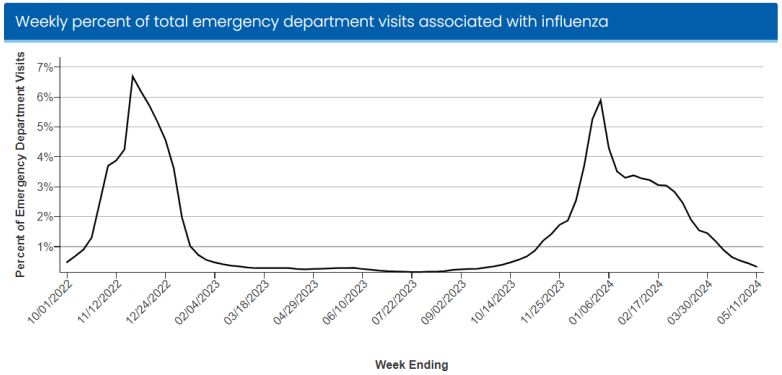
- Implement Enhanced, National Surveillance at Seasonal Influenza Levels

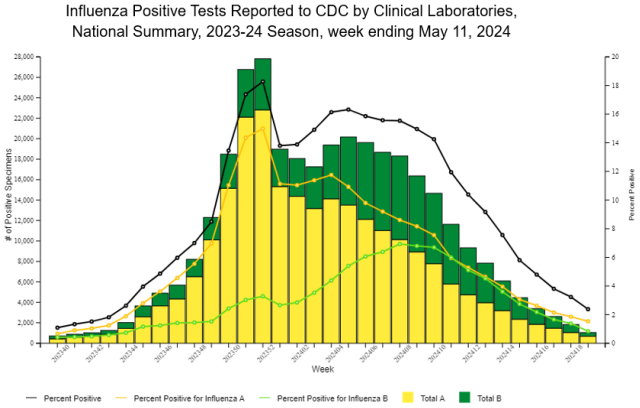
- Help to ensure any cases of A(H5N1) in the community would be detected
- Expand Public Health Lab specimen sources
- Continued follow-up for areas that flag in syndromic and wastewater data
- Continued lab-confirmed influenza associated hospitalization surveillance through FluSurv-NET
- Continued monitoring of workers with recent exposure on A(H5N1) confirmed farms
- Provider outreach to continue influenza testing through summer, particularly for patients with recent history of relevant exposures

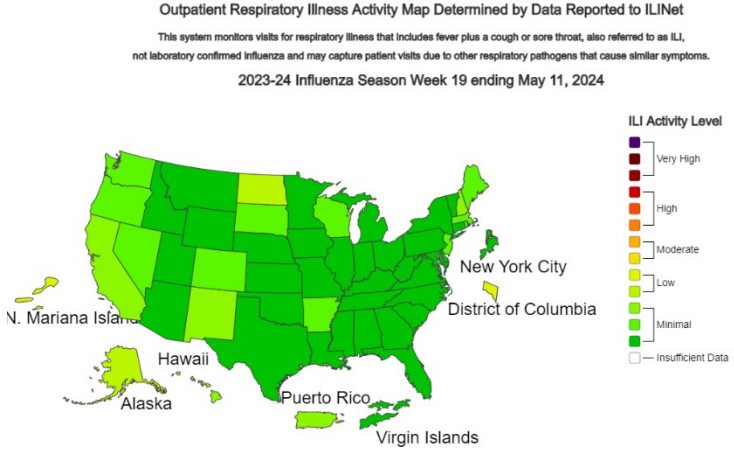
CDC Influenza

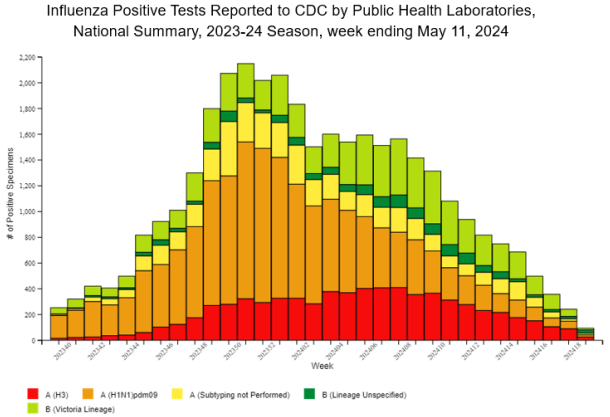
CDC Strategy for Enhanced Summer 2024 Influenza Surveillance | Avian Influenza (Flu)

Influenza Surveillance Systems









CDC Influenza

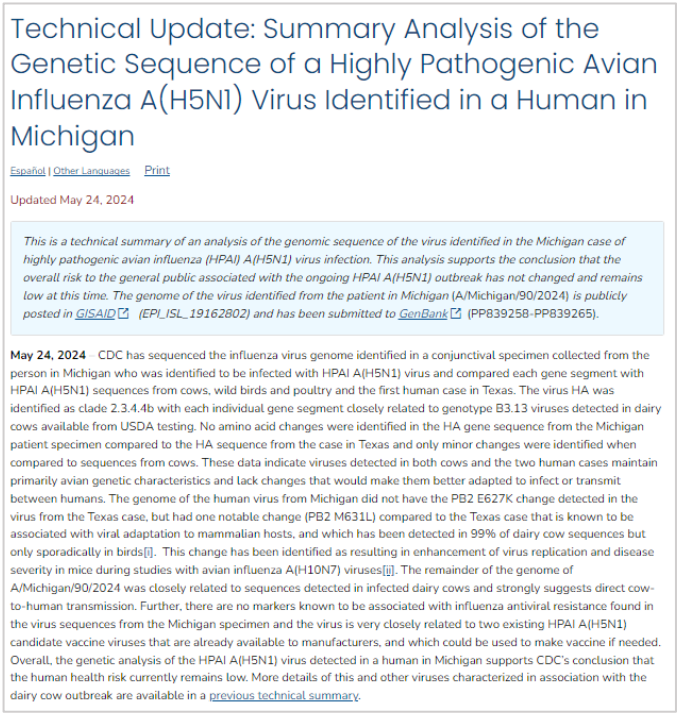
H5N1 Human Case in Texas – Virus Sequence

- **Diagnostics:** No impact to current CDC influenza diagnostic assay's ability to detect A(H5N1) viruses
- **Treatments:** No known markers of resistance to FDA approved antiviral drugs
  - baloxavir
  - oseltamivir, peramivir, and zanamivir
- **Candidate Vaccine Viruses** (CVVs)
  - HA of human influenza virus very closely related to **two available CVVs**
  - CVVs expected to provide good protection against this virus

CDC Influenza

First H5N1 Human Case in Michigan – Virus Sequence

- May 22 case
- CDC sequenced the influenza virus genome from the case in Michigan:
  - Influenza A(H5N1) virus from clade 2.3.4.4b
  - It is 99% identical to the viruses that are circulating in dairy cows
  - Viruses detected in both cows and the two human cases maintain primarily avian genetic characteristics
  - Virus lack changes that would make them better adapted to infect or transmit between humans.



Technical Update: Summary Analysis of the Genetic Sequence of a Highly Pathogenic Avian Influenza A(H5N1) Virus Identified in a Human in Michigan

Español | Other Languages Print

Updated May 24, 2024

This is a technical summary of an analysis of the genomic sequence of the virus identified in the Michigan case of highly pathogenic avian influenza (HPAI) A(H5N1) virus infection. This analysis supports the conclusion that the overall risk to the general public associated with the ongoing HPAI A(H5N1) outbreak has not changed and remains low at this time. The genome of the virus identified from the patient in Michigan (A/Michigan/90/2024) is publicly posted in GISAID (EPI_ISL_19162802) and has been submitted to GenBank (PP839258-PP839265).

May 24, 2024 - CDC has sequenced the influenza virus genome identified in a conjunctival specimen collected from the person in Michigan who was identified to be infected with HPAI A(H5N1) virus and compared each gene segment with HPAI A(H5N1) sequences from cows, wild birds and poultry and the first human case in Texas. The virus HA was identified as clade 2.3.4.4b with each individual gene segment closely related to genotype B3.13 viruses detected in dairy cows available from USDA testing. No amino acid changes were identified in the HA gene sequence from the Michigan patient specimen compared to the HA sequence from the case in Texas and only minor changes were identified when compared to sequences from cows. These data indicate viruses detected in both cows and the two human cases maintain primarily avian genetic characteristics and lack changes that would make them better adapted to infect or transmit between humans. The genome of the human virus from Michigan did not have the PB2 E627K change detected in the virus from the Texas case, but had one notable change (PB2 M631L) compared to the Texas case that is known to be associated with viral adaptation to mammalian hosts, and which has been detected in 99% of dairy cow sequences but only sporadically in birds[i]. This change has been identified as resulting in enhancement of virus replication and disease severity in mice during studies with avian influenza A(H10N7) viruses[ii]. The remainder of the genome of A/Michigan/90/2024 was closely related to sequences detected in infected dairy cows and strongly suggests direct cow-to-human transmission. Further, there are no markers known to be associated with influenza antiviral resistance found in the virus sequences from the Michigan specimen and the virus is very closely related to two existing HPAI A(H5N1) candidate vaccine viruses that are already available to manufacturers, and which could be used to make vaccine if needed. Overall, the genetic analysis of the HPAI A(H5N1) virus detected in a human in Michigan supports CDC's conclusion that the human health risk currently remains low. More details of this and other viruses characterized in association with the dairy cow outbreak are available in a previous technical summary.

https://www.cdc.gov/flu/avianflu/spotlights/2023-2024/h5n1-technical-update-may-24-2024.html

CDC Influenza

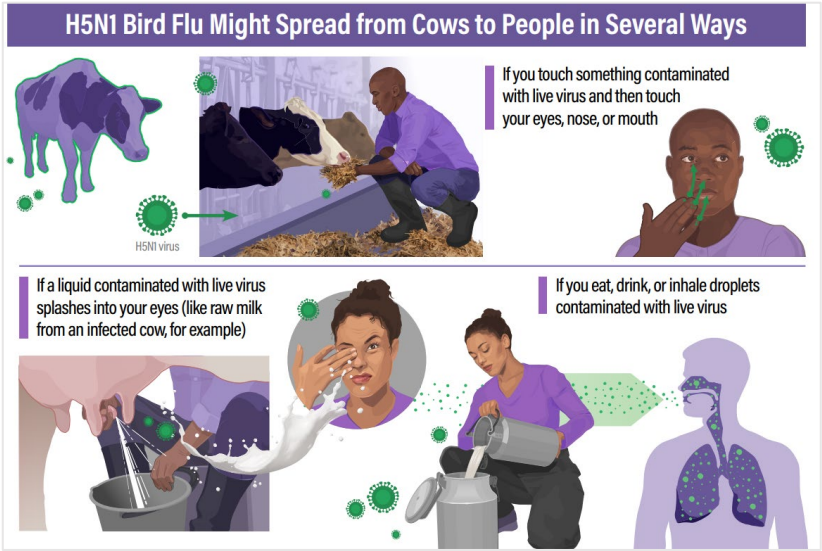
Communications and Resources

—**Situation Updates:**
  —CDC A(H5N1) Bird Flu Response Update | Avian Influenza (Flu)

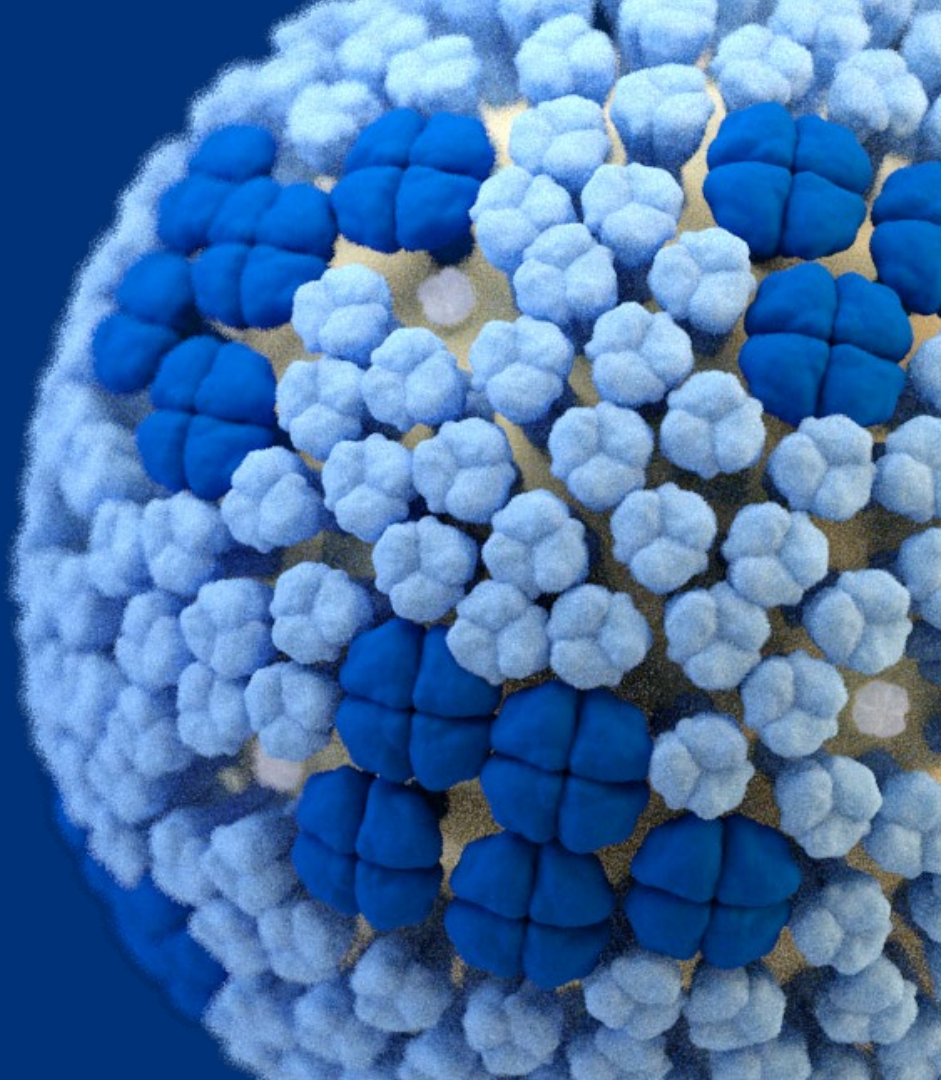
—**Surveillance Updates**
  —How CDC is monitoring influenza data among people to better understand the current avian influenza A (H5N1) situation | Avian Influenza (Flu)

—**Technical Report**
  —Technical Report: Highly Pathogenic Avian Influenza A(H5N1) Viruses | Avian Influenza (Flu) (cdc.gov)

—**Updated Recommendations**
  —Highly Pathogenic Avian Influenza A(H5N1) Virus in Animals: Interim Recommendations for Prevention, Monitoring, and Public Health Investigations
  —Recommendations for Worker Protection and Use of Personal Protective Equipment (PPE) to Reduce Exposure to Novel Influenza A Viruses Associated with Severe Disease in Humans



Thank you

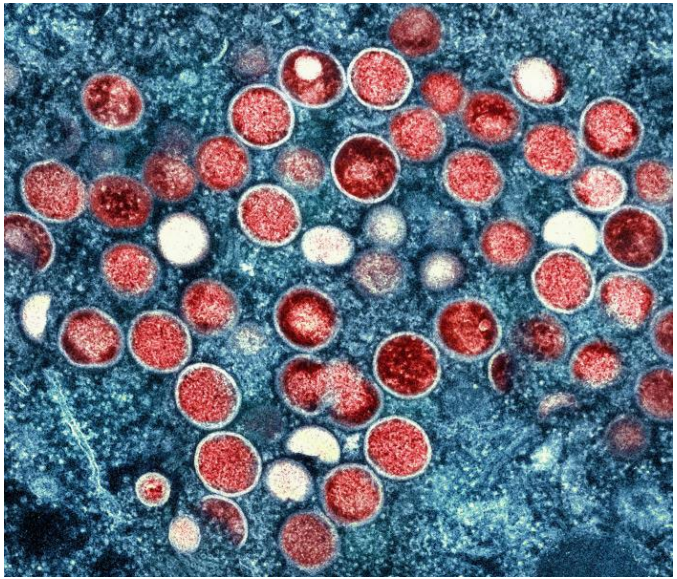


CDC
Influenza

Epidemiology of Clade II Mpox

Agam Rao, MD, FIDSA
CAPT, U.S. Public Health Service
Medical Officer
Poxvirus and Rabies Branch
U.S. Centers for Disease Control & Prevention

Epidemiology and Prevention of Monkeypox virus in the United States—An Update



Agam Rao, MD FIDSA

CAPT, US Public Health Service

Poxvirus and Rabies Branch

Centers for Disease Control and Prevention

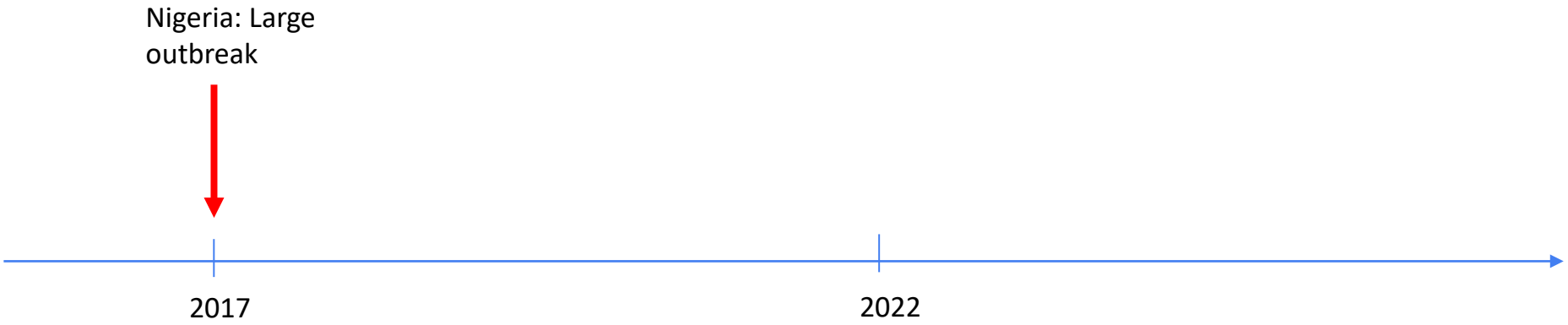
CDC/IDSA Clinician Call

June 5, 2024

Clade II MPXV: Countries historically known to be endemic

Nigeria, Sierra Leone, Liberia, Cameroon, Cote D'Ivoire

Historical context: Global clade II Monkeypox virus (MPXV) outbreak



Historical context: Global clade II Monkeypox virus (MPXV) outbreak

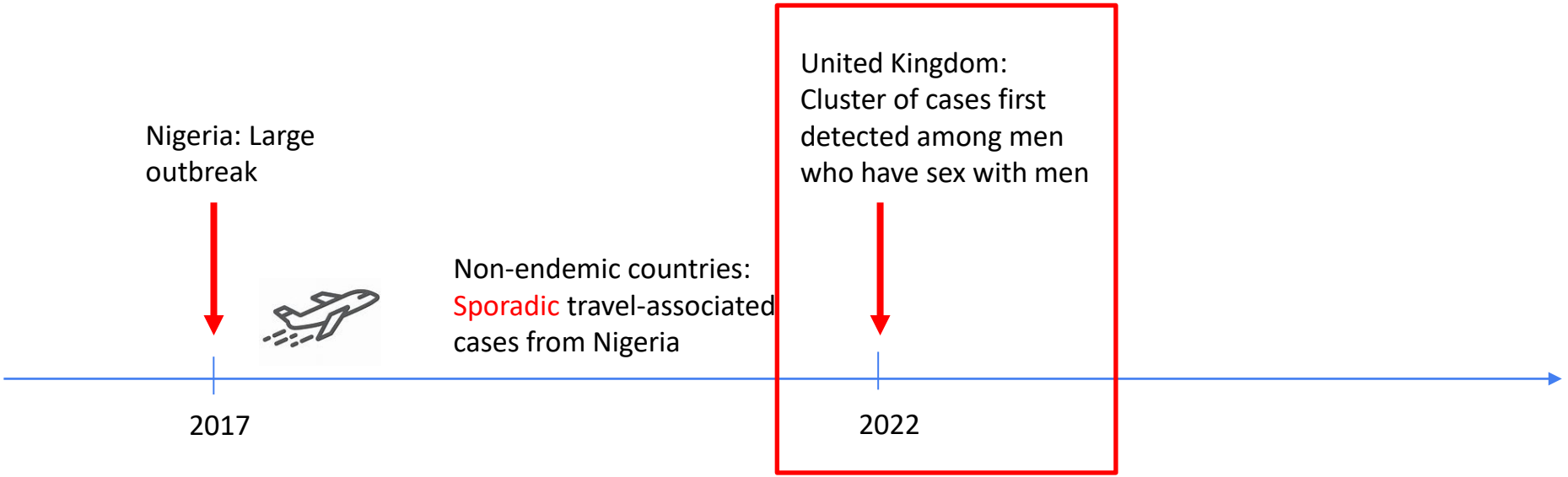
Nigeria: Large outbreak

Non-endemic countries: Sporadic travel-associated cases from Nigeria

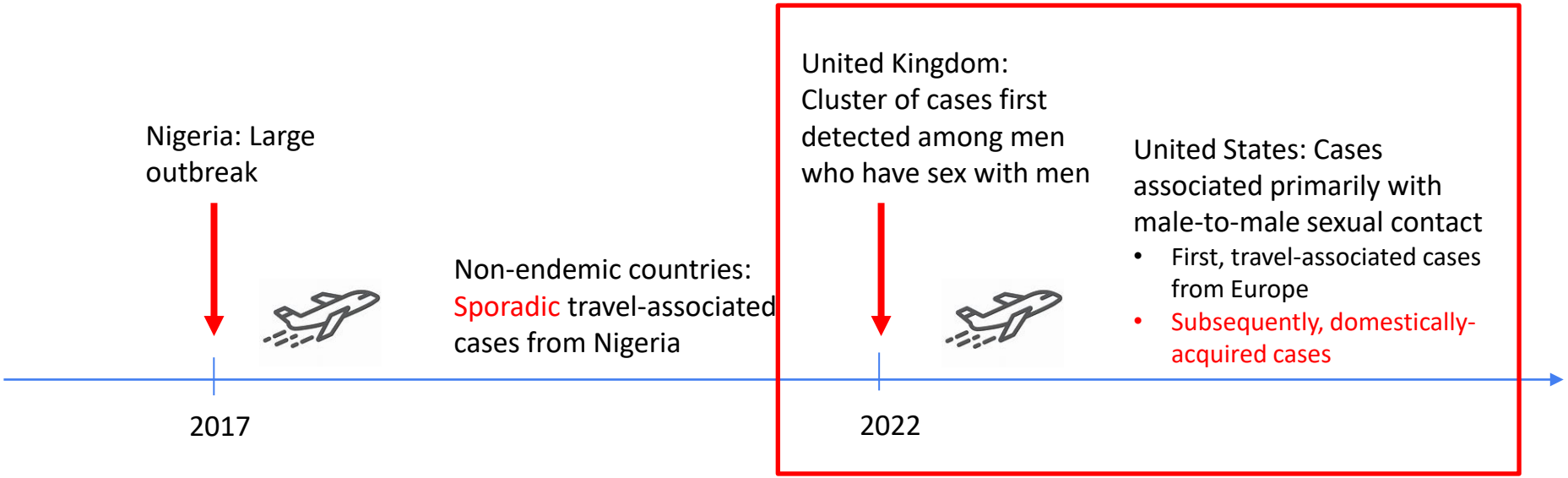
2017

2022

Historical context: Global clade II Monkeypox virus (MPXV) outbreak



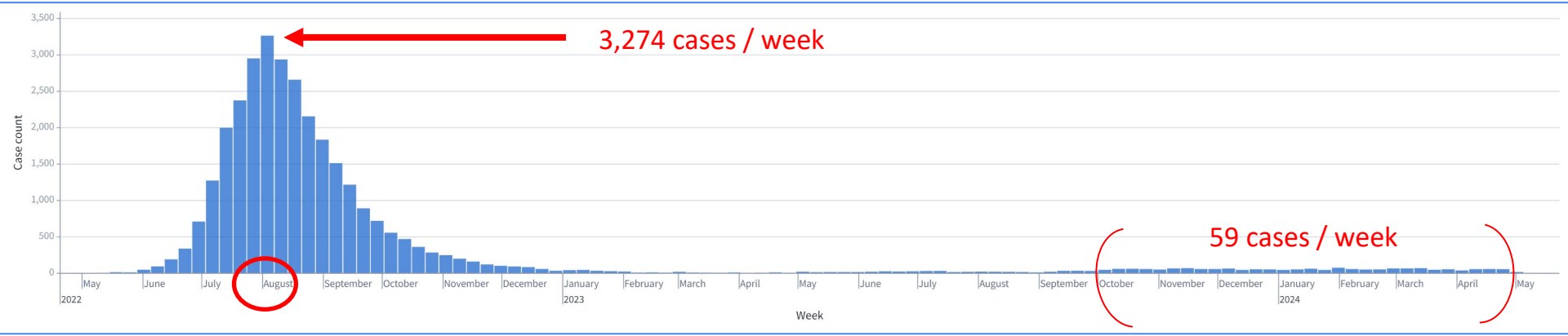
Historical context: Global clade II Monkeypox virus (MPXV) outbreak



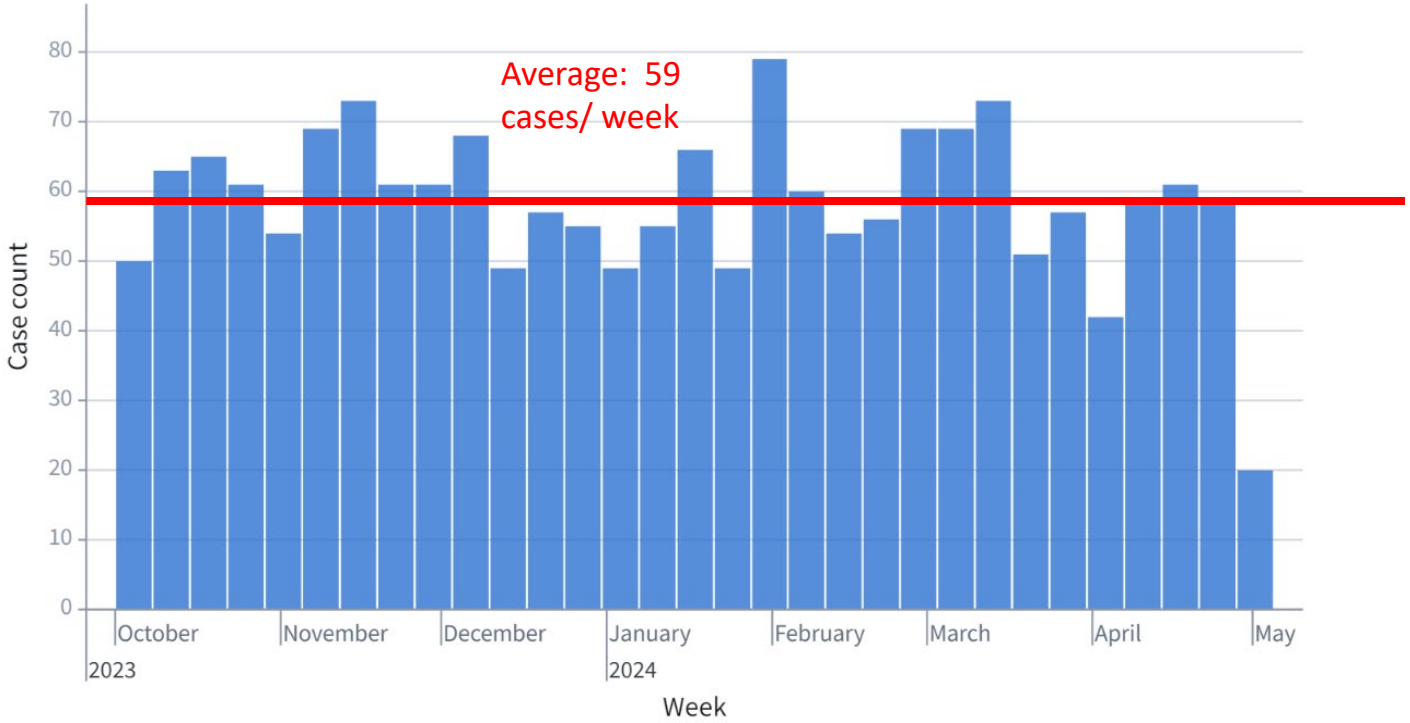
- Men who have sex with men (MSM) most affected

What has happened since May 2022?

Mpox clade II epic-curve—United States, May 2022-May 2024, N= 32,798



U.S. Clade II cases steady during October 1, 2023-April 30, 2024, n= 1802



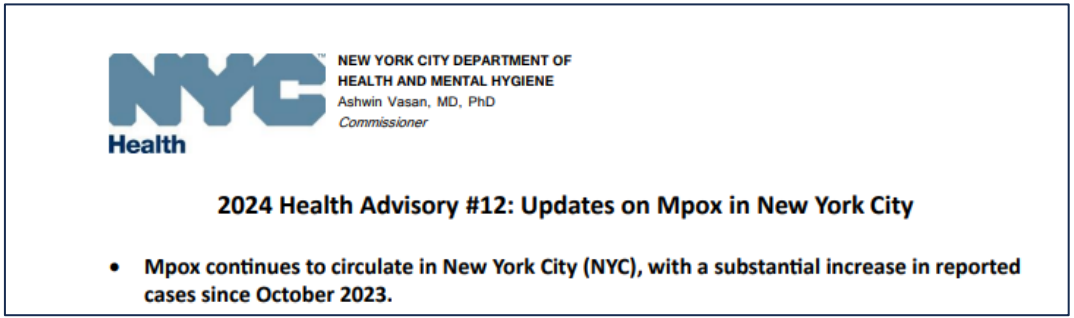
National epidemiology overall unchanged—October 1, 2023-April 30, 2024

- Cisgender men: 94%
- Persons identifying as gay or bisexual: 90%
- Few cases among children
  - Cases among persons <18 years of age: 6
  - Cases include adolescents with sexual behaviors consistent with those of adult cases and young children with exposure via household contact
- Persons with HIV+ status: 48%
- Race and ethnicity
  - 34% Hispanic, 32% White, 25% Black, 3% Asian, 2% multiracial, 4% other race

- Deaths still occurring among people with severe immunocompromise

Case counts in states and counties—October 2023–present

- Asynchronous clusters nationally, particularly in metropolitan cities
- Most have had fluctuating case counts resulting in national numbers that are steady
- Reasons for occasional increases in some national jurisdictions may differ by jurisdiction
  - Low vaccine coverage?
  - Increased opportunities for exposure?
  - Other reasons?
- NYC with sustained elevation


NEW YORK CITY DEPARTMENT OF HEALTH AND MENTAL HYGIENE
Ashwin Vasan, MD, PhD
Commissioner

Health

2024 Health Advisory #12: Updates on Mpox in New York City

- **Mpox continues to circulate in New York City (NYC), with a substantial increase in reported cases since October 2023.**

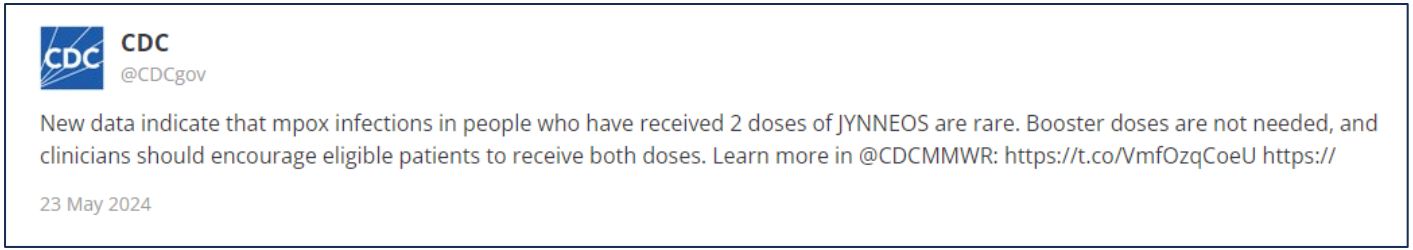
https://www.nyc.gov/assets/doh/downloads/pdf/han/advisory/2024/han-advisory-12-mpox.pdf

Long-term immunity: Being monitored

- Reports to CDC of mpox reinfection are few: Protection after illness resolution appears robust at this time
- Real-world observations*: Infections after 2 JYNNEOS doses
  - Rare (<1% of nationally reported mpox cases§)
  - Occurring at disparate time intervals
  - Less severe than infections among unvaccinated persons
- Vaccine immunity remains durable at this time
  - Clinical significance of waning antibody levels uncertain; cell-mediated immunity and innate immunity likely important to protection

*https://www.cdc.gov/mmwr/volumes/73/wr/mm7320a3.htm?s_cid=mm7320a3_w

§ Cases for which vaccination data reported to CDC



Mpox cases among fully vaccinated persons

- Reason for these cases not clear
- Possibly “due to frequent behaviors associated with mpox transmission, even with relatively high vaccine effectiveness and vaccine coverage”*

Clinical Infectious Diseases

MAJOR ARTICLE

Investigation of an Mpox Outbreak Affecting Many Vaccinated Persons in Chicago, Illinois—March 2023–June 2023

Emily A. G. Faherty,[1,2,a,©] Taylor Holly,[2,a] Yasmin P. Ogale,[1] Hillary Spencer,[1,2] Ashley M. Becht,[2] Gordon Crisler,[2] Michael Wasz,[2] Patrick Stonehouse,[2] Hannah J. Barbian,[3] Christy Zelinski,[2] Alyse Kittner,[2] Dorothy Foulkes,[2] Kendall W. Anderson,[2] Tiffany Evans,[2] Lavinia Nicolae,[4] Amber Staton,[5] Carla Hardnett,[4] Michael B. Townsend,[6] William C. Carson,[6] Panayampalli S. Satheshkumar,[6] Christina L. Hutson,[6] Crystal M. Gigante,[6] Laura A. S. Quilter,[4] Susan Gorman,[7] Brian Borah,[2] Stephanie R. Black,[2] Massimo Pacilli,[2,©] David Kern,[2] Janna Kerins,[2] Andrea M. McCollum,[6] Agam K. Rao,[6,b,©] and Irina Tabidze[2,b]

[1]Epidemic Intelligence Service, Centers for Disease Control and Prevention, Atlanta, Georgia, USA; [2]Chicago Department of Public Health, Chicago, Illinois, USA; [3]Departments of Internal Medicine, Rush University Medical Center, Chicago, Illinois, USA; [4]National Center for HIV, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia, USA; [5]Office of the Chief Operating Officer, Centers for Disease Control and Prevention, Atlanta, Georgia, USA; [6]National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA; and [7]Department of Health and Human Services, Office of Strategic National Stockpile, Atlanta, Georgia, USA

*https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciae181/7639496?login=true

Recommendations unchanged at this time

- Mpox vaccinations not recommended
  - For persons who recovered from mpox
  - For persons who already received the recommended 2 JYNNEOS doses

- Emphasis should be on
  - Vaccinating those for whom vaccine is recommended but who have not yet received 1 or both JYNNEOS doses
  - Counseling patients about other prevention strategies

Populations for whom mpox vaccine recommended

ACIP (as of October 2024) recommends vaccination with the 2-dose JYNNEOS vaccine series for persons aged 18 years and older at risk for mpox¶

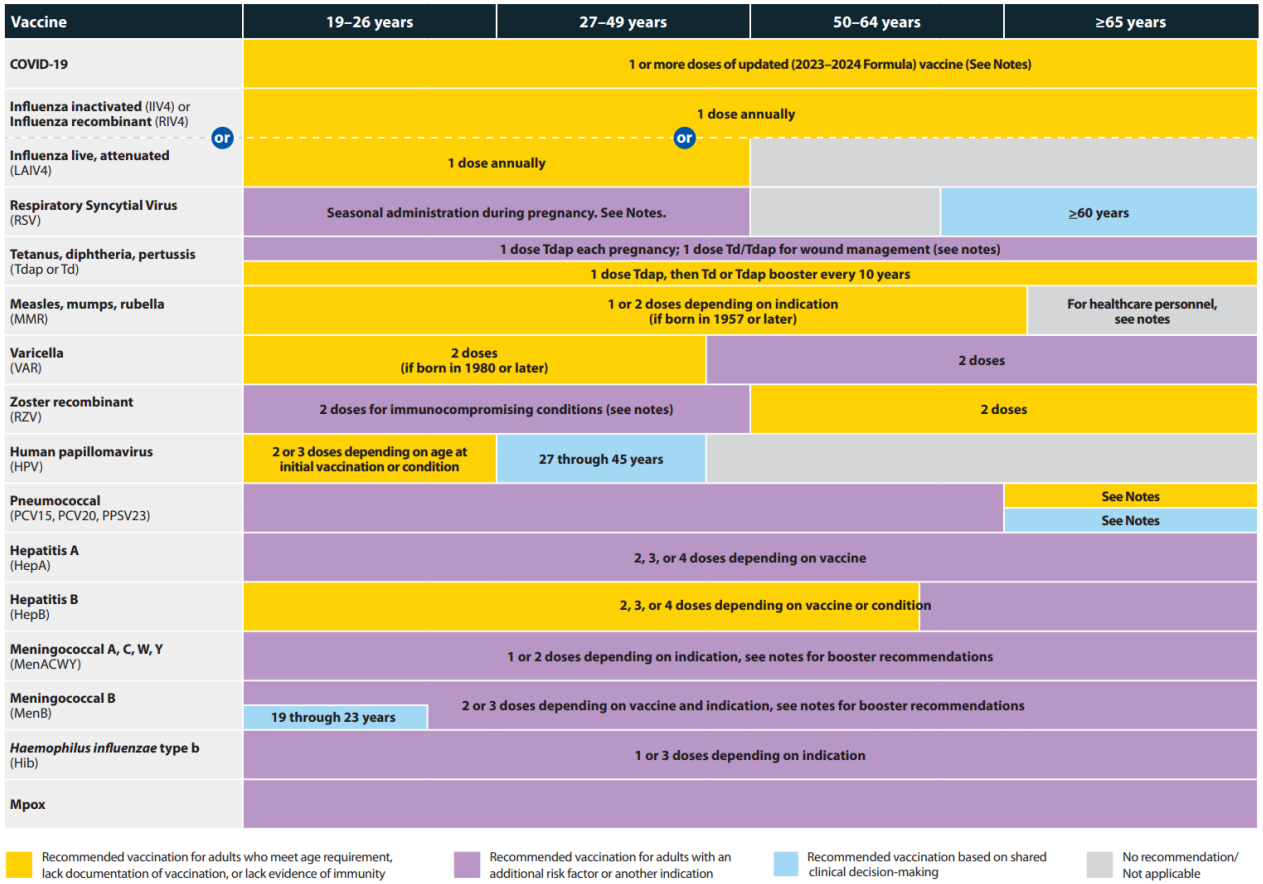
¶Persons at risk

- 1. Gay, bisexual, and other men who have sex with men, 2. transgender people or 3. nonbinary people who, in the past 6 months, have had one of the following
  - New diagnosis of ≥ 1 sexually transmitted disease
  - More than one sex partner
  - Sex at a commercial venue
  - Sex in association with a large public event in a geographic area where mpox transmission is occurring
- Sexual partners of persons with the risks described above
- Persons who anticipate experiencing any of the above

https://www.cdc.gov/poxvirus/mpox/vaccines/vaccine-recommendations.html

Mpox vaccine on routine immunization schedule

Table 1 Recommended Adult Immunization Schedule by Age Group, United States, 2024



Mpox vaccination

Special situations

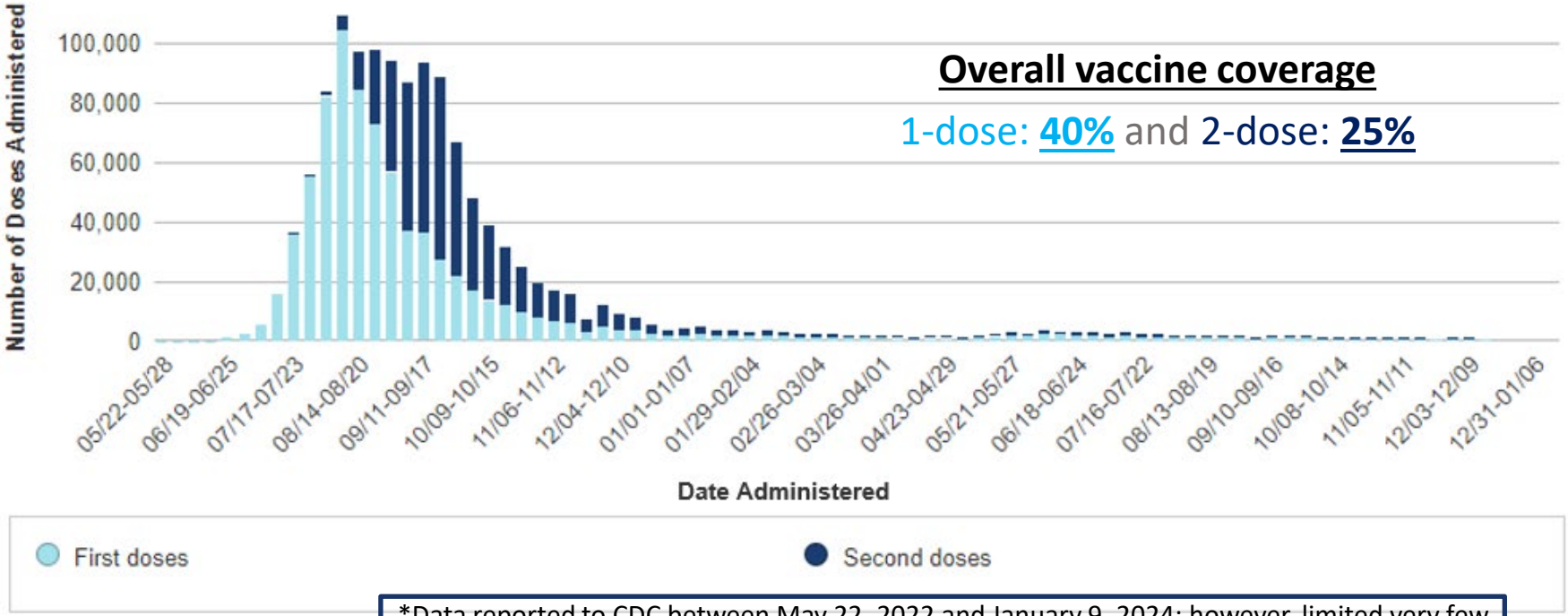
- **Any person at risk for Mpox infection:** 2-dose series, 28 days apart.

Risk factors for Mpox infection include:

- Persons who are gay, bisexual, and other MSM, transgender or nonbinary people who in the past 6 months have had:
  - A new diagnosis of at least 1 sexually transmitted disease
  - More than 1 sex partner
  - Sex at a commercial sex venue
  - Sex in association with a large public event in a geographic area where Mpox transmission is occurring
- Persons who are sexual partners of the persons described above
- Persons who anticipate experiencing any of the situations described above

www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf

Vaccinations: U.S. JYNNEOS Administration Data, 2022-2024*



Overall vaccine coverage

1-dose: **40%** and 2-dose: **25%**

*Data reported to CDC between May 22, 2022 and January 9, 2024; however, limited very few requests for JYNNEOS since then

Additional prevention strategies: Counseling patients

- Patients can speak with sex partners about any mpox signs and symptoms and be aware of any unexplained rashes or lesions on a partner’s body
- Avoid close or intimate contact if they or a sex partner become sick with mpox or experience mpox-like rash

Clade I MPXV

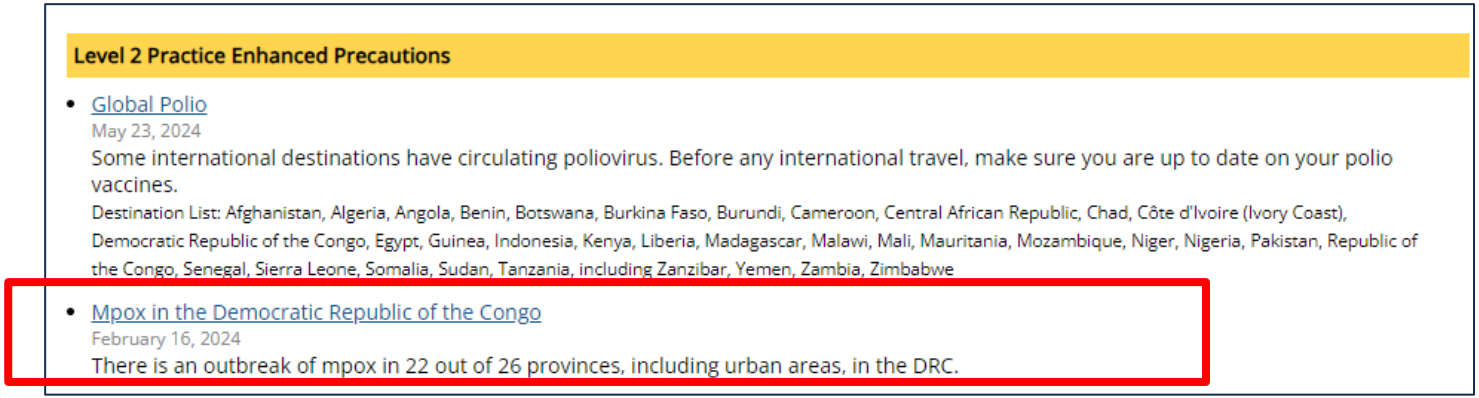
At this time, NO clade I cases identified outside of countries known to be endemic for this MPXV clade

Clade I MPXV: Countries historically known to be endemic

Democratic Republic of Congo, Central African Republic, Republic of Congo, Cameroon, Gabon

If clade I cases occur in the United States…

- Similar to clade IIb spread, travel from other countries could be source of earliest infections
- Global outbreak showed that sexual exposures were efficient means of mpox spread



Level 2 Practice Enhanced Precautions

- Global Polio
  May 23, 2024
  Some international destinations have circulating poliovirus. Before any international travel, make sure you are up to date on your polio vaccines.
  Destination List: Afghanistan, Algeria, Angola, Benin, Botswana, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Côte d'Ivoire (Ivory Coast), Democratic Republic of the Congo, Egypt, Guinea, Indonesia, Kenya, Liberia, Madagascar, Malawi, Mali, Mauritania, Mozambique, Niger, Nigeria, Pakistan, Republic of the Congo, Senegal, Sierra Leone, Somalia, Sudan, Tanzania, including Zanzibar, Yemen, Zambia, Zimbabwe
- Mpox in the Democratic Republic of the Congo
  February 16, 2024
  There is an outbreak of mpox in 22 out of 26 provinces, including urban areas, in the DRC.

https://wwwnc.cdc.gov/travel/destinations/traveler/none/democratic-republic-of-congo#:~:text=Malaria-,Recommendations,during%20and%20after%20your%20trip.

CDC messaging

- For patients with suspected mpox and a history of recent travel to DRC, contact public health authorities as soon as possible so that Clade specific testing can be expedited
- Regardless, clade specific testing is occurring for positive specimens in the United States; CDC is collaborating with many private and public health laboratories
- CDC interim guidance previously presented during CDC-IDSA clinician call*
- CDC Preparedness and Response to Increasing clade I mpox cases in DRC published in MMWR§

*https://www.idsociety.org/globalassets/idsa/multimedia/clinician-call-slides--qa/3-14-2024-clinician-call.pdf

§ https://www.cdc.gov/mmwr/volumes/73/wr/mm7319a3.htm?s_cid=mm7319a3_w

Take-home messages about mpox epidemiology

- Clade II
  - Continues to circulate
  - Nationally, clade II MPXV case counts stable since October 2023
  - Regionally, clusters have occurred; differing reasons may explain these cases but waning immunity is an unlikely reason
  - Increasing 2-dose vaccination coverage and counseling patients about other prevention strategies are best ways for clinicians to prevent cases
- Clade I
  - At this time, no clade I mpox cases have occurred outside of endemic countries
  - Clinicians should contact public health authorities if they suspect Clade I in a patient with recent travel to DRC

Thank you

poxvirus@cdc.gov

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.

Update on Mpox Vaccination

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ASPR Administration for Strategic Preparedness & Response

Jynneos Transition to Commercial Availability

U.S. Department of Health and Human Services (HHS)

Meghan Pennini, PhD
Chief Science Officer
HHS Coordination Operations and Response Element (H-CORE)
Administration for Strategic Preparedness & Response (ASPR)

05 June 2024

Mpox in the United States – Where are We?

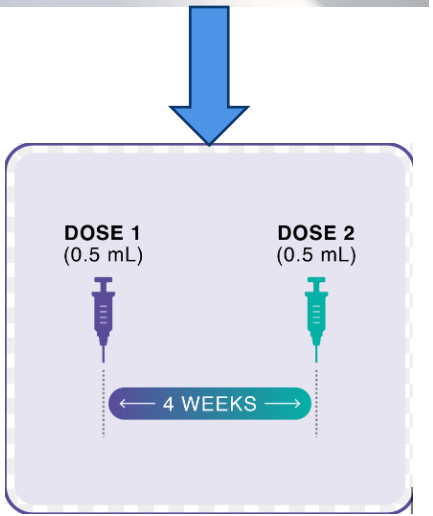
- As of 3/24, weekly case counts remain low

CDC. 2022-2023 outbreak cases and data. Accessed January 10, 2024. https://www.cdc.gov/poxvirus/mpox/response/2022/index.html

Jynneos Commercialization Transition

- Jynneos is FDA approved for prevention of smallpox and mpox disease in adults 18 years and older at high risk for infection
  - Currently on the ACIP routine immunization schedule for certain individuals
- Jynneos has an EUA for active immunization by subcutaneous injection for prevention of mpox disease in individuals younger than 18 years of age determined to be at high risk for mpox infection

- Jynneos should be administered as two injections (two-dose series)
  - The two doses should be given 28 days apart (range 24-35 days)



Jynneos Transition Timeline

- Beginning in May 2022, HHS has made Jynneos available from the Strategic National Stockpile under the National Mpox Vaccination Strategy

- **February 2023**: ACIP recommendation for at risk adults during an outbreak
- **October 2023**: ACIP recommendation for routine vaccination of adults at risk of mpox infection
- **April 1, 2024**: Bavarian Nordic made Jynneos available for commercial purchase
- **April 30, 2024**: Distribution of HHS supplied Jynneos transitioned to request only as commercial market ramped up
  - Providers should use any remaining HHS-supplied inventory that was previously distributed, especially to support access for under or uninsured
  - Additional ordering is only to support access in circumstances where commercial supply is not yet accessible
- **On or near August 1, 2024**: Full transition of Jynneos to usual commercial workflow

Sustained Access through Commercial Availability

- Medicaid & Medicare
  - Full coverage for all beneficiaries within ACIP recommended populations
- Commercial Insurance
  - Expect private insurance plans to fully cover within ACIP recommendations
  - Plans obligated to cover first plan year that begins one year after the ACIP recommendation
- CDC 317 & Vaccine For Children (VFC) Programs
  - Access for under/uninsured individuals within ACIP recommendation (currently 18+, high risk)
    - 18 years: VFC provides vaccines for uninsured (and underinsured when served in FQHCs/RHCs)
    - 19+ years: 317 program used by jurisdictional partners to serve some adults
  - Ordering expected to open on or near August 1, 2024
- Ryan White & other HRSA-supported clinics
  - Access for under and uninsured populations
  - HRSA grant and Ryan White HIV/AIDS Program (RWHAP) funding may be used to purchase and administer Jynneos vaccine www.hrsa.gov/mpox-faqs
  - 340B Prime Vendor Program offers reduced price to eligible provider sites (e.g., FQHCs)
- Retail Pharmacies
  - Appointments now available at several pharmacy chains (e.g., CVS, Rite Aid) in states that allow pharmacist administration

Update on Tecovirimat EA-IND Eligibility Criteria for Treatment for Mpox

Patty Yu, MPH
Regulatory Health Scientist
U.S. Centers for Disease Control & Prevention

Update on Tecovirimat Expanded Access Investigational New Drug (EA-IND) Protocol Eligibility Criteria for Treatment of Mpox

CDC/IDSA Clinician Call

June 5, 2024

Patty Yu, MPH

Medical Countermeasures Regulatory Support Team

Office of Readiness and Response

Disclaimer

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Background

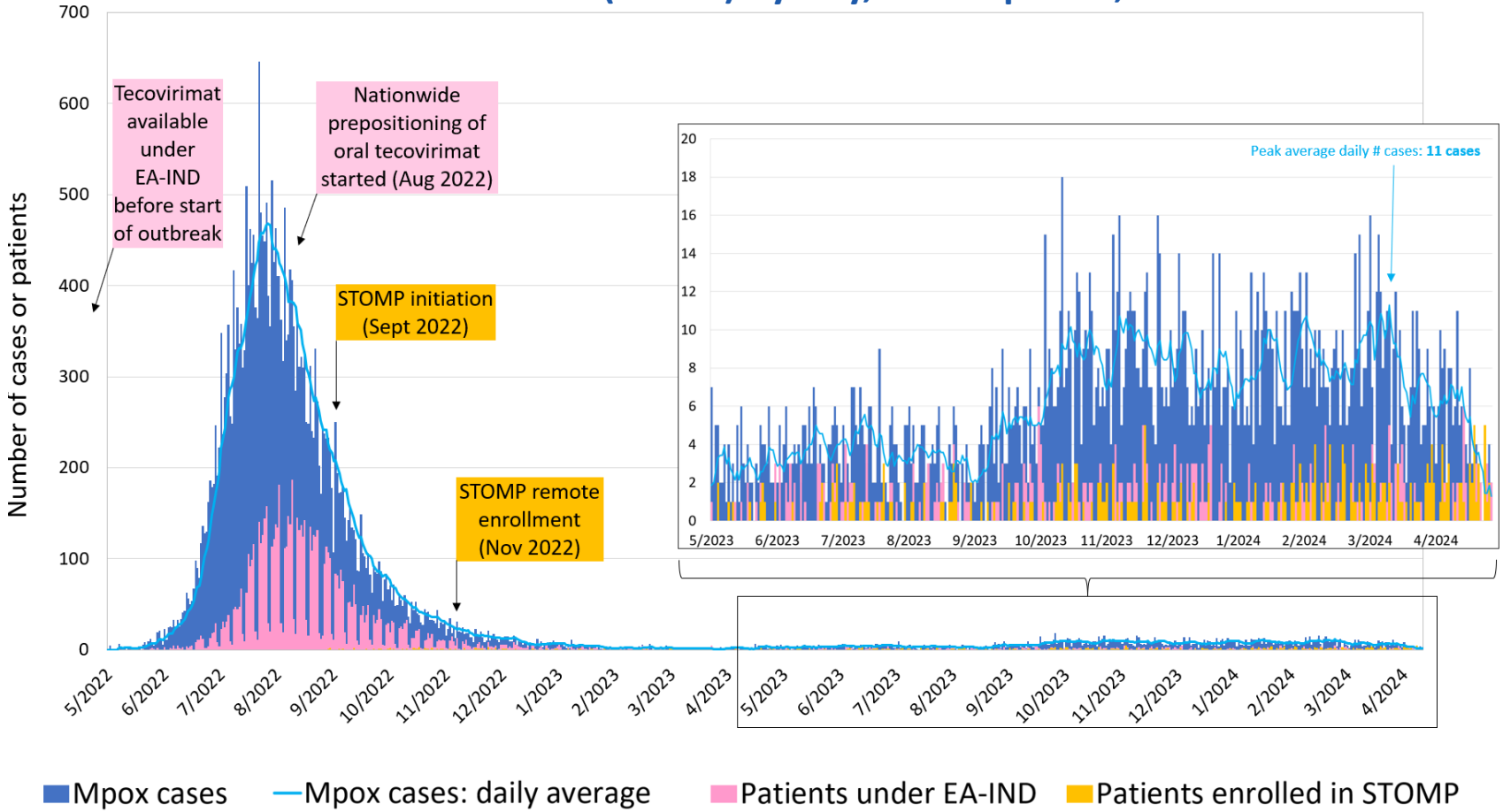
- Tecovirimat is FDA-approved only for treatment of smallpox based on animal efficacy data; not FDA-approved for mpox
  - No established human efficacy of tecovirimat for treatment of orthopoxvirus infection
- EA-INDs intended for compassionate use for treatment of **serious** or **life-threatening** disease/condition and no comparable or satisfactory alternative therapy
  - Not designed to determine efficacy in humans
- U.S. government made stockpiled tecovirimat available under EA-IND at the start of the outbreak given the emerging situation at the time and unknown severity of mpox in the affected population

Background, continued

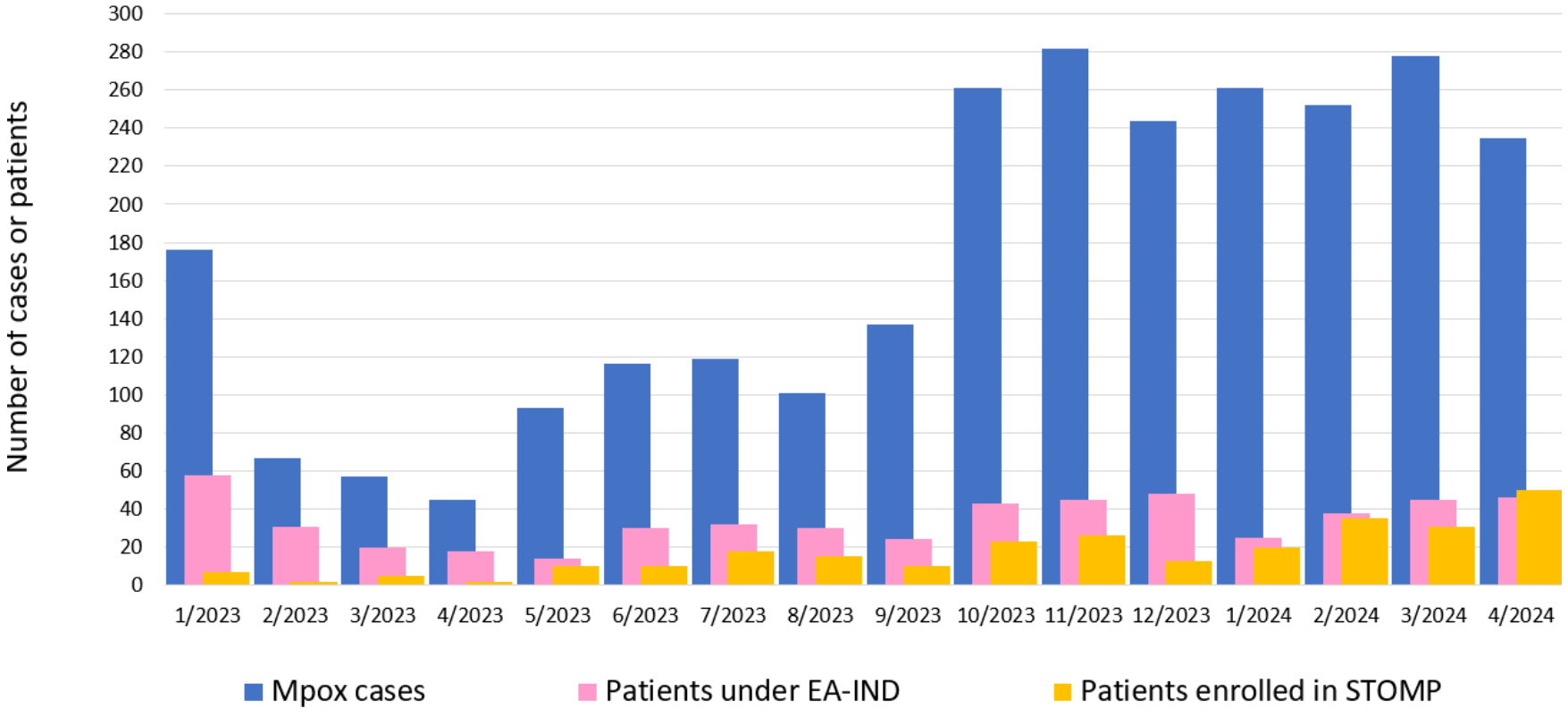
- Over 7,000 patients prescribed tecovirimat with returned EA-IND baseline intake forms
  - Most treated as outpatients with mild to moderate illness
  - Reasons for tecovirimat reported by providers: lesions in sensitive anatomic areas; pain, including pain alone
- NIH's Study of Tecovirimat for Mpox (STOMP) launched in Sept 2022
- EA-IND use **cannot interfere** with the conduct or completion of **clinical investigations** that could **support marketing approval** of the product
- Tecovirimat resistance
  - Resistance in > 50 patients with mpox who received tecovirimat during their illness[1] and a new cluster of tecovirimat resistance
  - A cluster of tecovirimat-resistant monkeypox virus infections was identified among 11 tecovirimat-naïve individuals[2]

[1] Smith et al., 2023
[2] Garrigues et al., 2023

Mpox Cases (n=32,797), Patients Prescribed Tecovirimat under EA-IND (n=7,618), and Patients Enrolled in STOMP (n=332) by Day, as of April 30, 2024



Number of Mpox Cases, Patients Prescribed Tecovirimat under EA-IND, and Patients Enrolled in STOMP, by Month, as of April 30, 2024



Alignment of EA-IND Eligibility with STOMP's Open-Label Treatment Arm

Revised Tecovirimat EA-IND Eligibility To Be Implemented

Severe immunocompromise

STOMP Open-label Treatment Arm	Revised EA-IND Eligibility Criteria (ver6.4)
Patients with severe immunocompromise: • HIV with CD4 < 200 cells/mm^3 or plasma HIV-1 RNA > 1,000 copies/mL • Leukemia or lymphoma • Generalized malignancy • Solid organ transplantation • Therapy with alkylating agents within 180 days prior to study entry • Antimetabolites within 180 days prior to study entry • Radiation therapy within 180 days prior to study entry • Tumor necrosis factor inhibitors within 180 days prior to study entry • High-dose corticosteroids (equivalent of 20 mg or greater of prednisone for at least 14 days) within 90 days prior to study entry • Being a recipient with hematopoietic stem cell transplant <24 months post-transplant or ≥24 months but with graft-versus-host disease or disease relapse, or having autoimmune disease with immunodeficiency as a clinical component	**Patients with severe immunocompromise:** • HIV with CD4 < 200 cells/mm^3 • Leukemia or lymphoma • Generalized malignancy • Solid organ transplantation • Therapy with alkylating agents within 180 days prior to mpox illness onset • Antimetabolites within 180 days prior to mpox illness onset • Radiation therapy within 180 days prior to mpox illness onset • Tumor necrosis factor inhibitors within 180 days prior to mpox illness onset • High-dose corticosteroids (equivalent of 20 mg or greater of prednisone for at least 14 days) within 90 days prior to mpox illness onset • Being a recipient with hematopoietic stem cell transplant < 24 months post-transplant or ≥ 24 months but with graft-versus-host disease or disease relapse, or having autoimmune disease with immunodeficiency as a clinical component • Other comparable severe immunocompromising condition

Differences in EA-IND Eligibility Criteria To Be Implemented Compared to EA-IND Version 6.3

Revised Tecovirimat EA-IND Eligibility To Be Implemented

Disease severity and at-risk patients

Eligibility Criteria (ver6.3)	Revised Eligibility Criteria (ver6.4)
Patients who are at high risk for ~~severe disease~~: • People with a condition affecting skin integrity — conditions such as atopic dermatitis, eczema, burns, impetigo, varicella zoster virus infection, herpes simplex virus infection, severe acne, severe diaper dermatitis with extensive areas of denuded skin, psoriasis, or Darier disease (keratosis follicularis) • Pregnant or breastfeeding people • Pediatric populations, particularly patients younger than 1 year of age	**Patients in the following categories who might be at high risk for protracted or life-threatening manifestations of mpox based on prior experience from other orthopoxvirus infections in humans:** • Persons with active skin conditions placing the person at higher risk for disseminated infection defined as: atopic dermatitis; active exfoliative skin condition(s) such as eczema, burns, impetigo, active varicella zoster virus infection, psoriasis, or Darier disease (keratosis follicularis) • Pregnant or lactating individuals regardless of illness severity or underlying comorbidities at presentation • Children (< 18 years) regardless of illness severity or underlying comorbidities at presentation

Revised Tecovirimat EA-IND Eligibility To Be Implemented

Disease severity

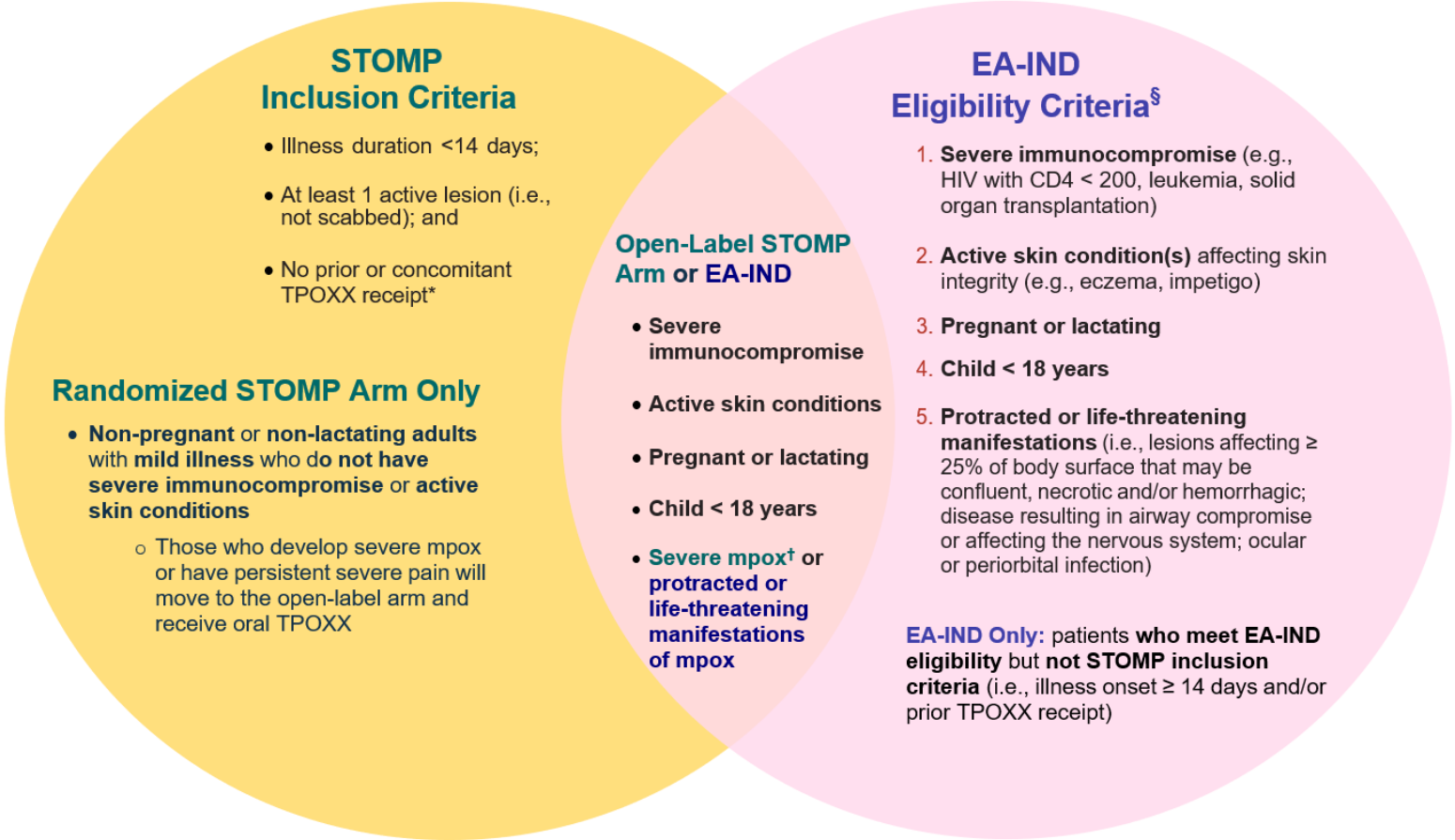
Eligibility Criteria (ver6.3)	Revised Eligibility Criteria (ver6.4)
Patients with ~~severe disease~~ such as: • Hemorrhagic disease • A large number of lesions such that they are confluent; necrotic lesions • Severe lymphadenopathy that can be necrotizing or obstructing (such as in airways) • Involvement of multiple organ systems and associated comorbidities (for example, pulmonary involvement with nodular lesions; sepsis; encephalitis; myocarditis; ocular or periorbital infections) • ~~Other conditions requiring hospitalization~~	**Patients with protracted or life-threatening manifestations of mpox at presentation as defined by one of the following:** • Lesions affecting ≥ 25% of body surface that may be confluent, necrotic, and/or hemorrhagic in appearance or cause sepsis • Disease resulting in airway compromise or affecting the nervous system • Cardiac (e.g., myocarditis) and or neurologic disease (e.g., encephalitis) which might occur in a small number of patients with mpox • Ocular or periorbital infection, regardless of the time since infection onset

Revised Tecovirimat EA-IND Eligibility To Be Implemented

Lesions in certain anatomic areas

Eligibility Criteria (ver6.3)	Revised Eligibility Criteria (ver6.4)
~~**Involvement of anatomic areas which might result in serious sequelae that include scarring or strictures including:**~~ • ~~Lesions directly involving the pharynx causing dysphagia~~ • ~~Inability to control secretions, or need for parenteral feeding;~~ • ~~Penile foreskin, vulva, vagina, urethra, or anorectum with the potential for causing strictures or requiring catheterization;~~ • ~~Anorectal lesions interfering with bowel movements (for example, severe pain)~~ • ~~Severe infections (including secondary bacterial skin infections), especially those that require surgical intervention such as debridement~~	Tecovirimat may be considered on a **case-by-case basis** for an unusual situation wherein CDC consult team and/or CDC Principal Investigator in discussion with the treating clinician deem treatment under the EA-IND may potentially be beneficial; such consideration is expected to be rare and intended for unusual situations associated with disease that could result in clear long-term sequelae (e.g., urethral stricture)

Oral Tecovirimat via NIH's STOMP vs. CDC's EA-IND Protocol



* <18 years and pregnant and/or lactating persons may have received up to 3 days of TPOXX immediately prior to enrollment
† STOMP severe mpox definition (e.g., ocular involvement; facial lesions on the malar, nose, or eyelid; confluent facial lesions; hospitalization due to monkeypox virus infection) broader than the EA-IND's protracted or life-threating manifestations
§ as defined in **Section 2.1** of the EA-IND protocol

Q&A/ Discussion

Selected Resources

Program Links:

- This webinar is being recorded and can be found with the slides online at https://www.idsociety.org/cliniciancalls
- COVID-19 Real-Time Learning Network: https://www.idsociety.org/covid-19-real-time-learning-network/
- Vaccine FAQ: https://www.idsociety.org/covid-19-real-time-learning-network/vaccines/vaccines-information--faq/

Dr. Butler

- https://www.aphis.usda.gov/livestock-poultry-disease/avian/avian-influenza/hpai-detections/livestock
- WAHIS (woah.org); USDA Support for Producers with Affected Dairy Premises
- https://www.dshs.texas.gov/news-alerts/health-alert-first-case-novel-influenza-h5n1-texas-march-2024
- https://www.cdc.gov/flu/avianflu/hpai/hpai-health-recommendations.html
- https://www.cdc.gov/flu/avianflu/strategy-enhanced-surveillance.htm
- https://www.cdc.gov/flu/avianflu/spotlights/2023-2024/h5n1-technical-update-may-24-2024.html
  - —Situation Updates: https://www.cdc.gov/flu/avianflu/spotlights/2023-2024/avian-situation-update-05032024.htm
  - —Surveillance Updates: https://www.cdc.gov/flu/avianflu/h5-monitoring.html
  - —Technical Report: https://www.cdc.gov/flu/avianflu/spotlights/2023-2024/h5n1-technical-report_april-2024.htm
  - —Updated Recommendations: https://www.cdc.gov/flu/avianflu/hpai/hpai-interim-recommendations.html
  - https://www.cdc.gov/flu/avianflu/h5/worker-protection-ppe.htm

Dr. Rao

- https://www.nyc.gov/assets/doh/downloads/pdf/han/advisory/2024/han-advisory-12-mpox.pdf
- https://www.cdc.gov/mmwr/volumes/73/wr/mm7320a3.htm?s_cid=mm7320a3_w
- https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciae181/7639496?login=true
- https://www.cdc.gov/poxvirus/mpox/vaccines/vaccine-recommendations.html

Selected Resources

Dr. Rao continued:

- www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf
- https://www.idsociety.org/globalassets/idsa/multimedia/clinician-call-slides--qa/3-14-2024-clinician-call.pdf
- https://www.cdc.gov/mmwr/volumes/73/wr/mm7319a3.htm?s_cid=mm7319a3_w

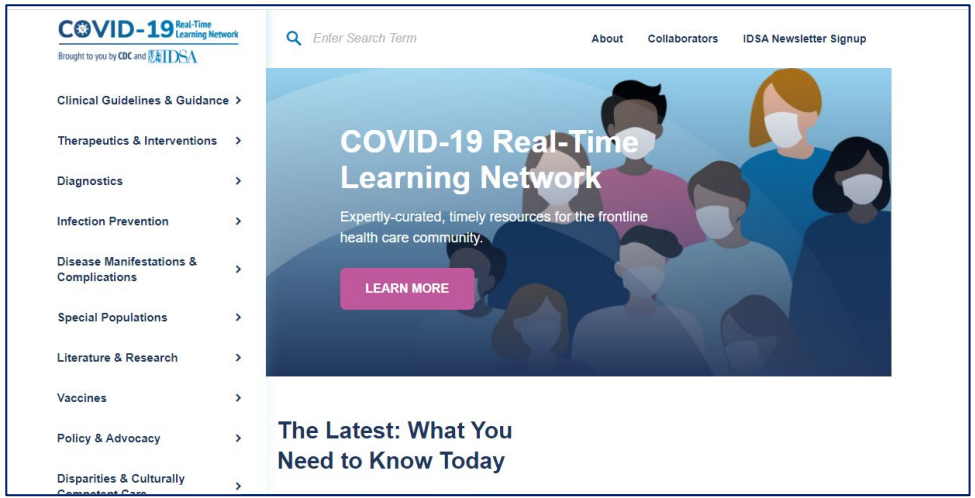
Dr. Pennini:

- https://www.cdc.gov/poxvirus/mpox/response/2022/index.html
- https://www.hrsa.gov/mpox-faqs

COVID-19 Real-Time Learning Network

Brought to you by CDC and IDSA

An online community bringing together information and opportunities for discussion on latest research, guidelines, tools and resources from a variety of medical subspecialties around the world.



Specialty Society Collaborators

American Academy of Family Physicians
American Academy of Pediatrics
American College of Emergency Physicians
American College of Obstetricians and Gynecologists
American College of Physicians
American Geriatrics Society
American Thoracic Society
Pediatric Infectious Diseases Society
Society for Critical Care Medicine
Society for Healthcare Epidemiology of America
Society of Hospital Medicine
Society of Infectious Diseases Pharmacists

www.COVID19LearningNetwork.org
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THANK YOU

We want to hear from you!

Please complete the post-call survey.

A recording of this call, slides and the answered Q&A will be posted at
www.idsociety.org/cliniciancalls

-- library of all past calls available --

Contact Us:

Dana Wollins (dwollins@idsociety.org)
Deirdre Lewis (dlewis@idsociety.org)