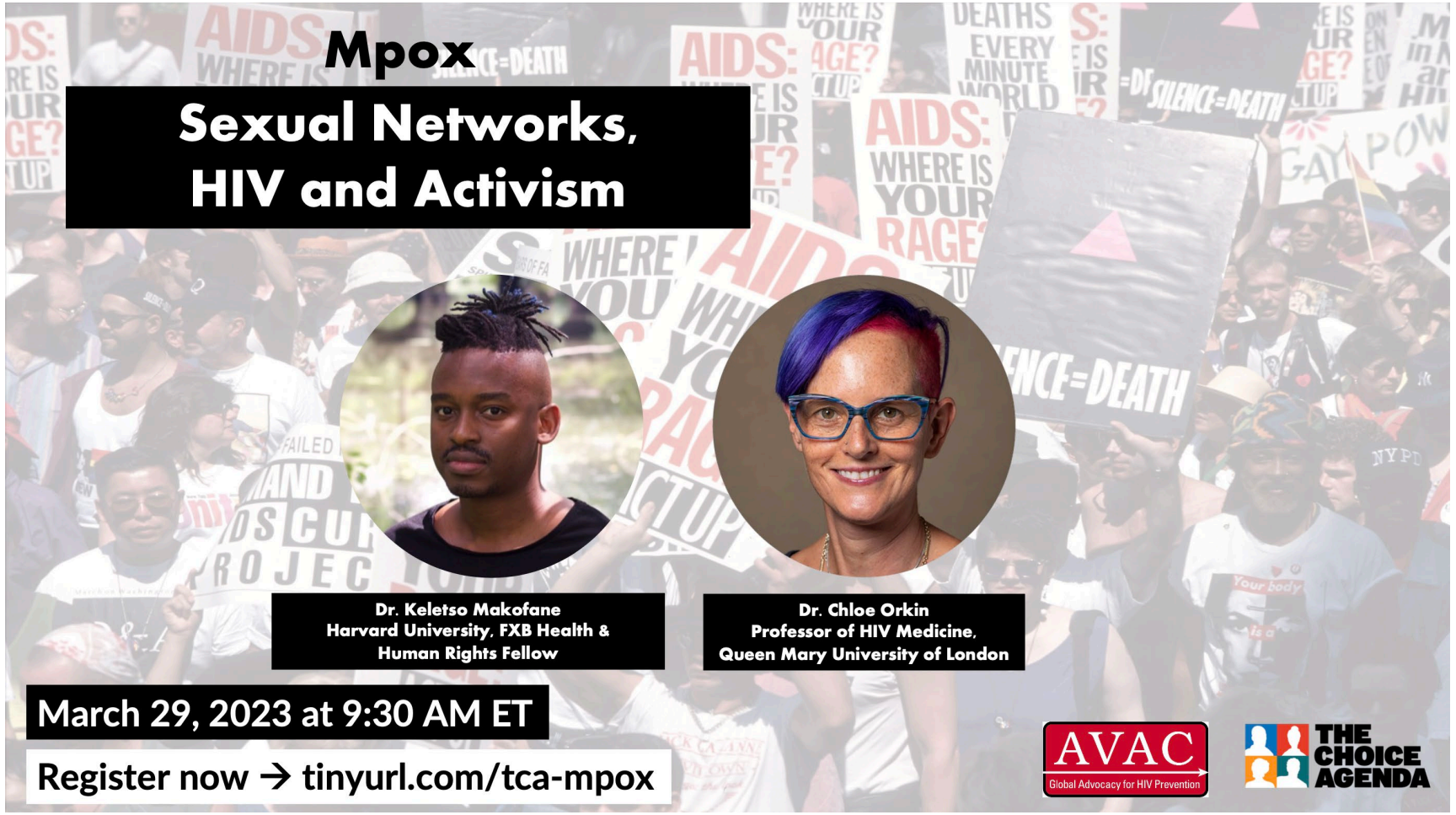
Welcome


Mpox
Sexual Networks, HIV and Activism
Dr. Keletso Makofane
Harvard University, FXB Health & Human Rights Fellow
Dr. Chloe Orkin
Professor of HIV Medicine, Queen Mary University of London
March 29, 2023 at 9:30 AM ET
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Global Advocacy for HIV Prevention
THE CHOICE AGENDA

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Lesotho
Malawi
Mexico
Nigeria
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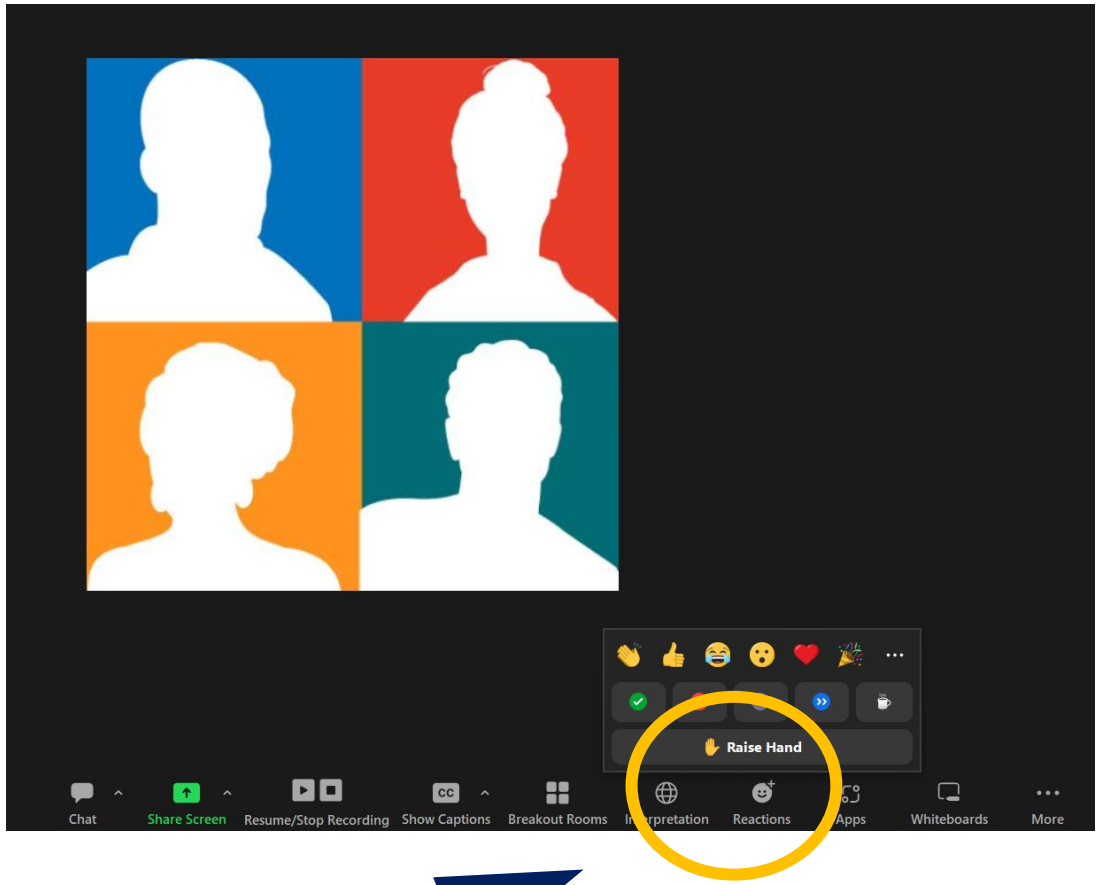
THE CHOICE AGENDA

HIV prevention research – a new forum for advocacy on the latest

avac.org/choice-agenda

Webinar Logistics



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HIV Prevention Plus Plus:

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Speakers include:
Ruth Akulu, ICWEA and AVAC fellow
Gregorio Millet, amfAR
Dr. Thesla Palanee-Phillips, Wits RHI

More info, register:

tinyurl.com/hivpreventionplusplus

Let’s start


Dr. Keletso Makofane
Harvard University, FXB Health &
Human Rights Fellow
Dr. Chloe Orkin
Professor of HIV Medicine,
Queen Mary University of London

Mpox (formerly monkeypox) one year on

Prof Chloe Orkin

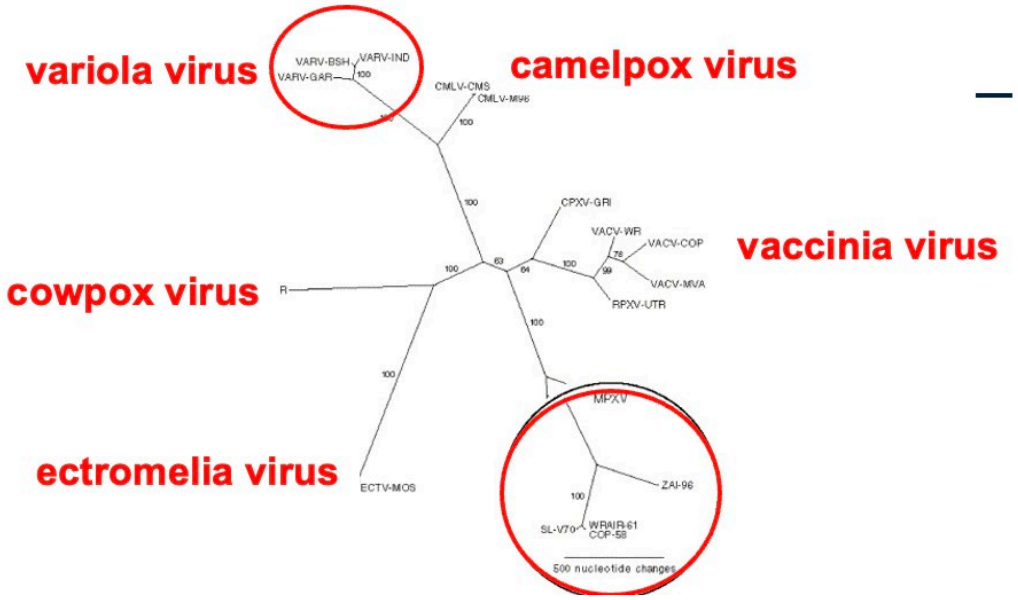
Queen Mary University of London

Barts Health NHS Trust

I have no disclosures related to mpox

@profchloeorkin

Mpox is an orthopoxvirus



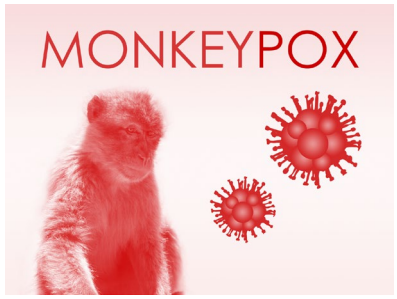
— 500 nucleotide changes

500 nucleotide changes

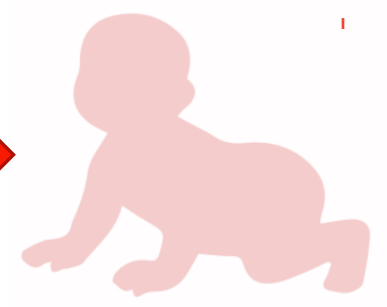
Chen, Virology 2005

Mpox timeline first 50 years

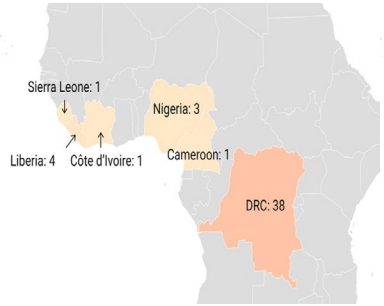
1958 Denmark



1970 Zaire



1970–1979

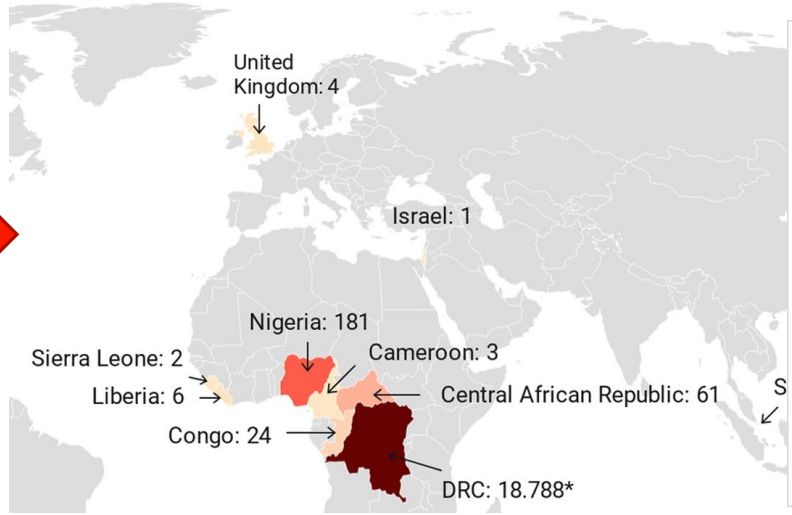


1980–1989

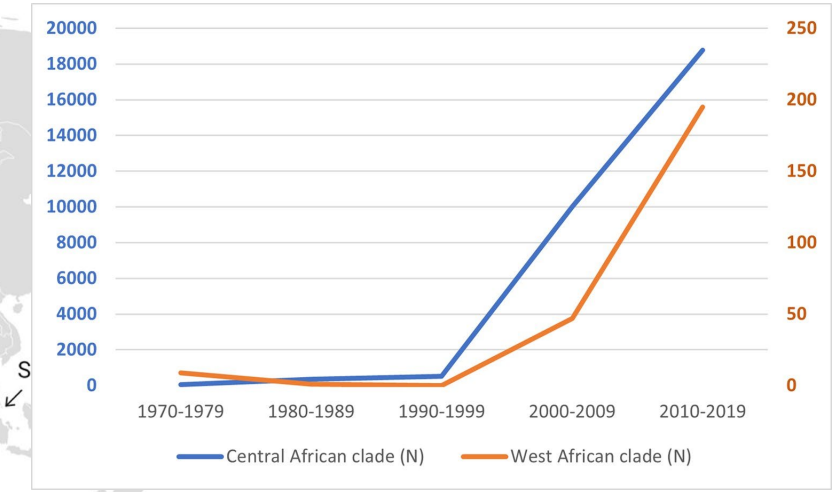
1990–1999

2000-2009

2010-2019

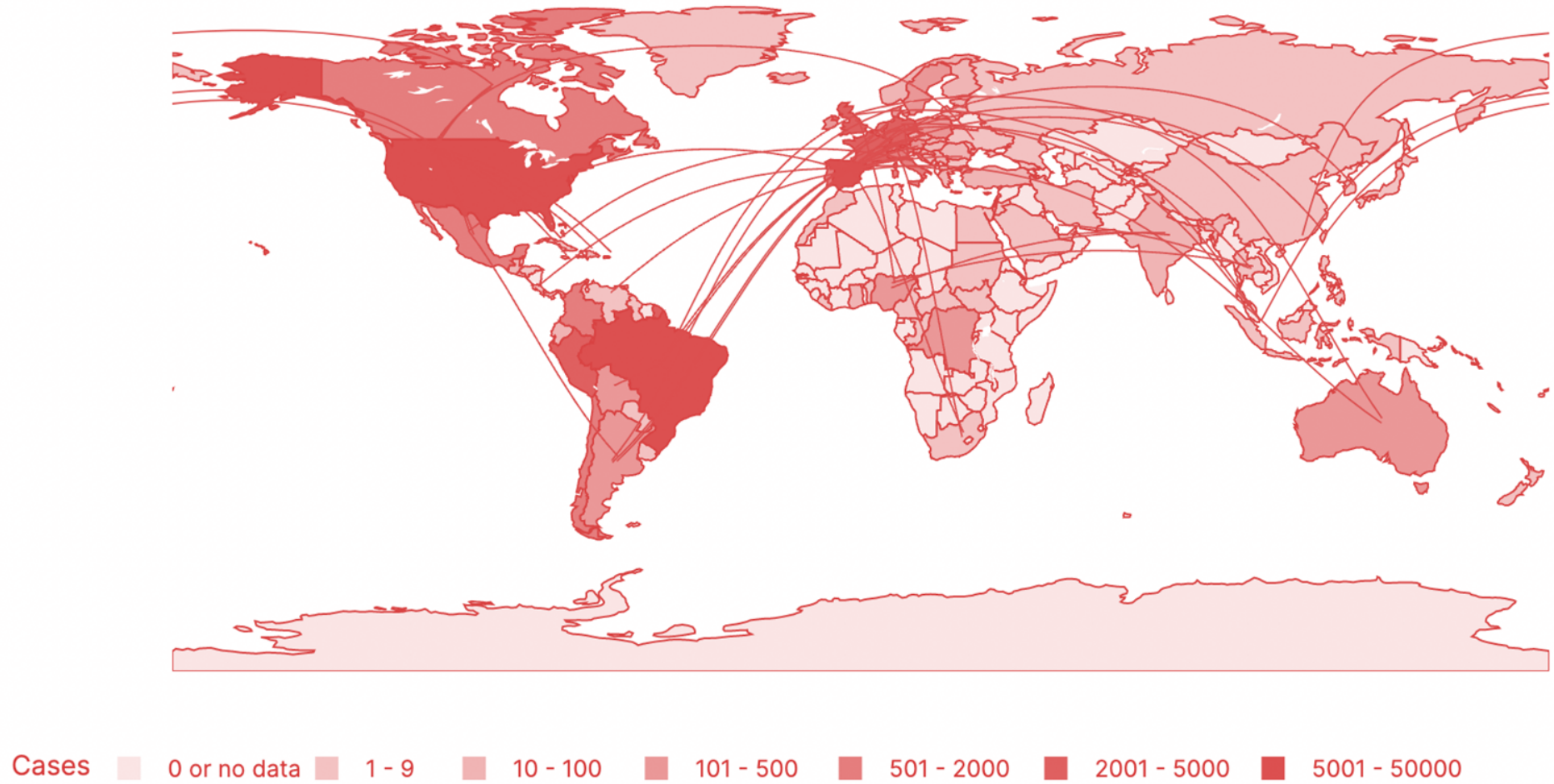


2020



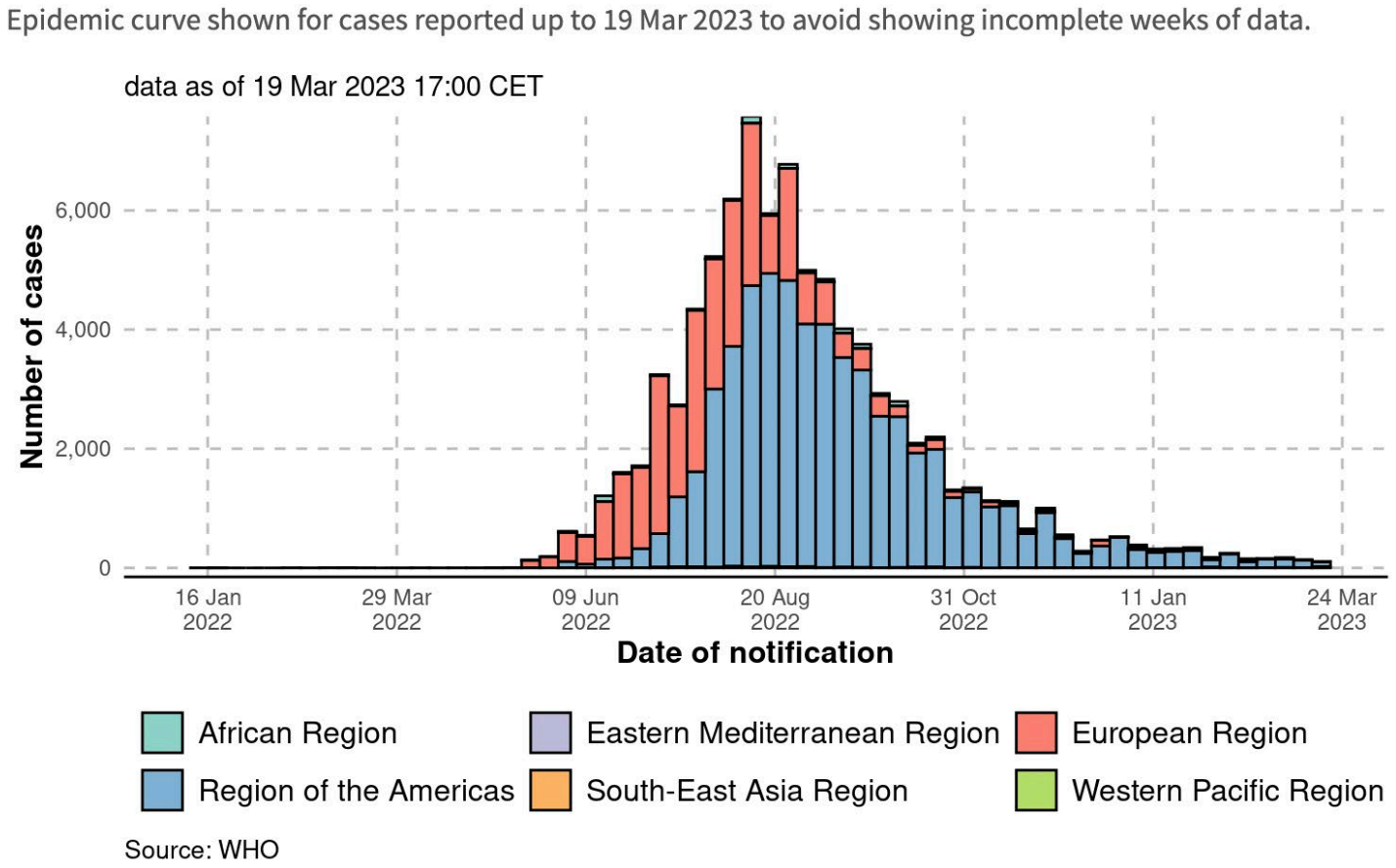
Bunge EM et al. (2022). PLoS Negl Trop Dis

August 2022: Mpox global outbreaks



https://www.monkeypox.global.health/

Current epidemiology



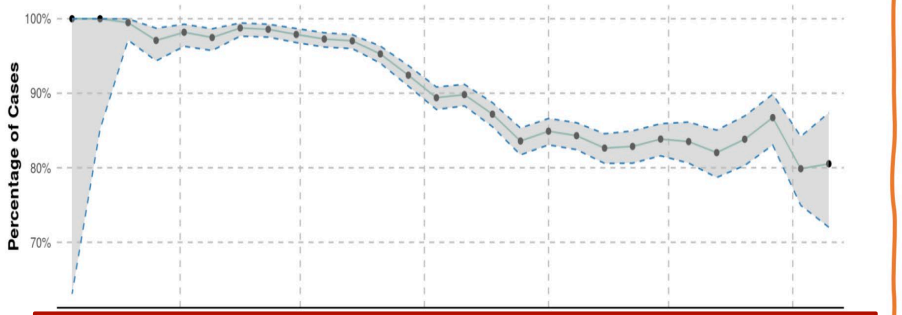
94 deaths in newly-affected countries, 18 in Africa in 2022-23

106 cases globally last week, mainly Americas

https://worldhealthorg.shinyapps.io/mpx_global/

Who is/was affected?

Proportion who are MSM



May to November 2022

- ~86K cases globally
- 110 countries
- 96.5% men (85% GBMSM)
- Global case series:
  - In women, mainly acquired through sexual contact
  - ~25% of cisgender women acquired mpox non-sexually
  - Children in homes of ~25%, only 2 got MPOX

https://worldhealthorg.shinyapps.io/mpx_global/

Thornhill Lancet 17 November 2022 (epub)

Why and how?

- Host immunity?
- Viral evolution?
- Human behaviour?

Host immunity

- Smallpox eradicated in 1980
- Vax campaigns discontinued, people <50 not vaccinated
- Increasing susceptibility with global waning of immunity

Jezeck et col Am J Epidemiol 1987
Fine et col Int J Epidemiol 1987
Hobson et col Eurosurveillance 2021
Adler et col Lancet Inf dis 2022

Viral evolution

- 2 Clades (formerly W and C African)
- Renamed Clade 1 and 2
- Previous estimates of the substitution rate for orthopoxviridae:
  -1-2 substitutions per genome/year

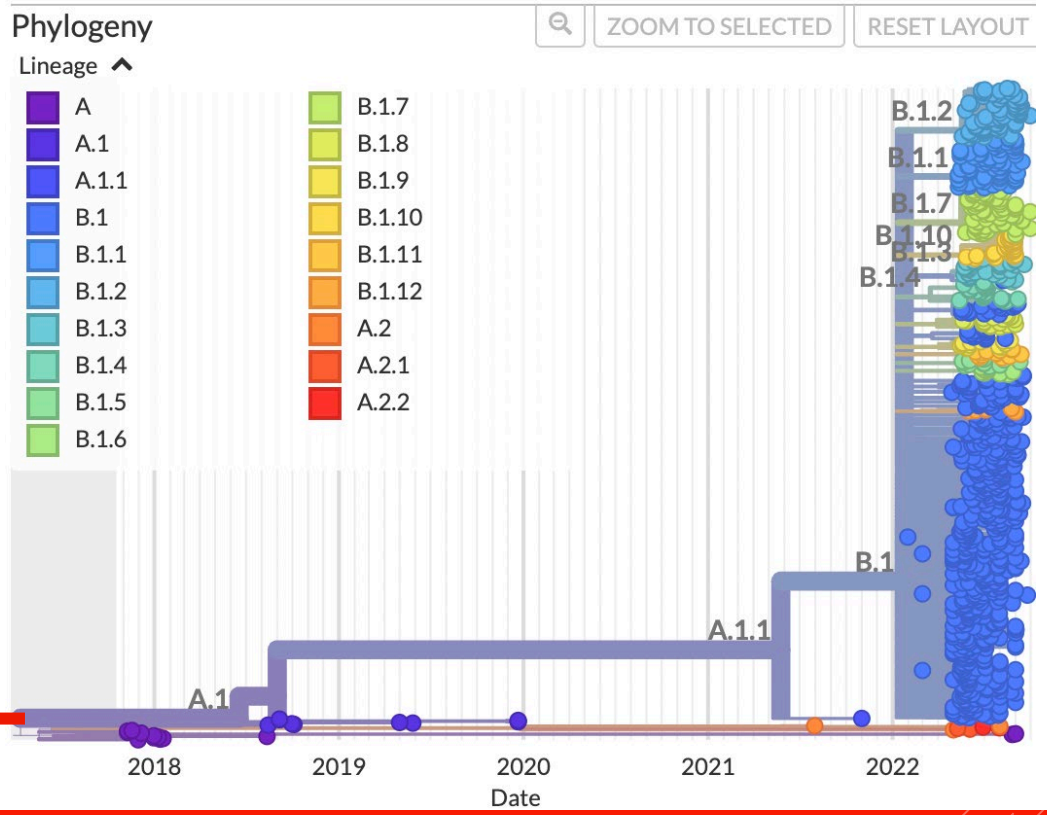
https://nextstrain.org/monkeypox/hmpxv1?d=tree,map&p=grid

Viral evolution

- 2 Clades (formerly W and C African)
- Renamed Clade 1 and 2
- Previous estimates of the substitution rate for orthopoxviridae:
  -1-2 substitutions per genome/year
- Clade 2b : ~50 single-nucleotide polymorphisms (SNPs)
- 6 to 12-fold more than expected
- APOBEC-3 associated adaptive immunity

Clade 1

Clade 2



https://nextstrain.org/monkeypox/hmpxv1?d=tree,map&p=grid

Isidro, Nat Med 2022

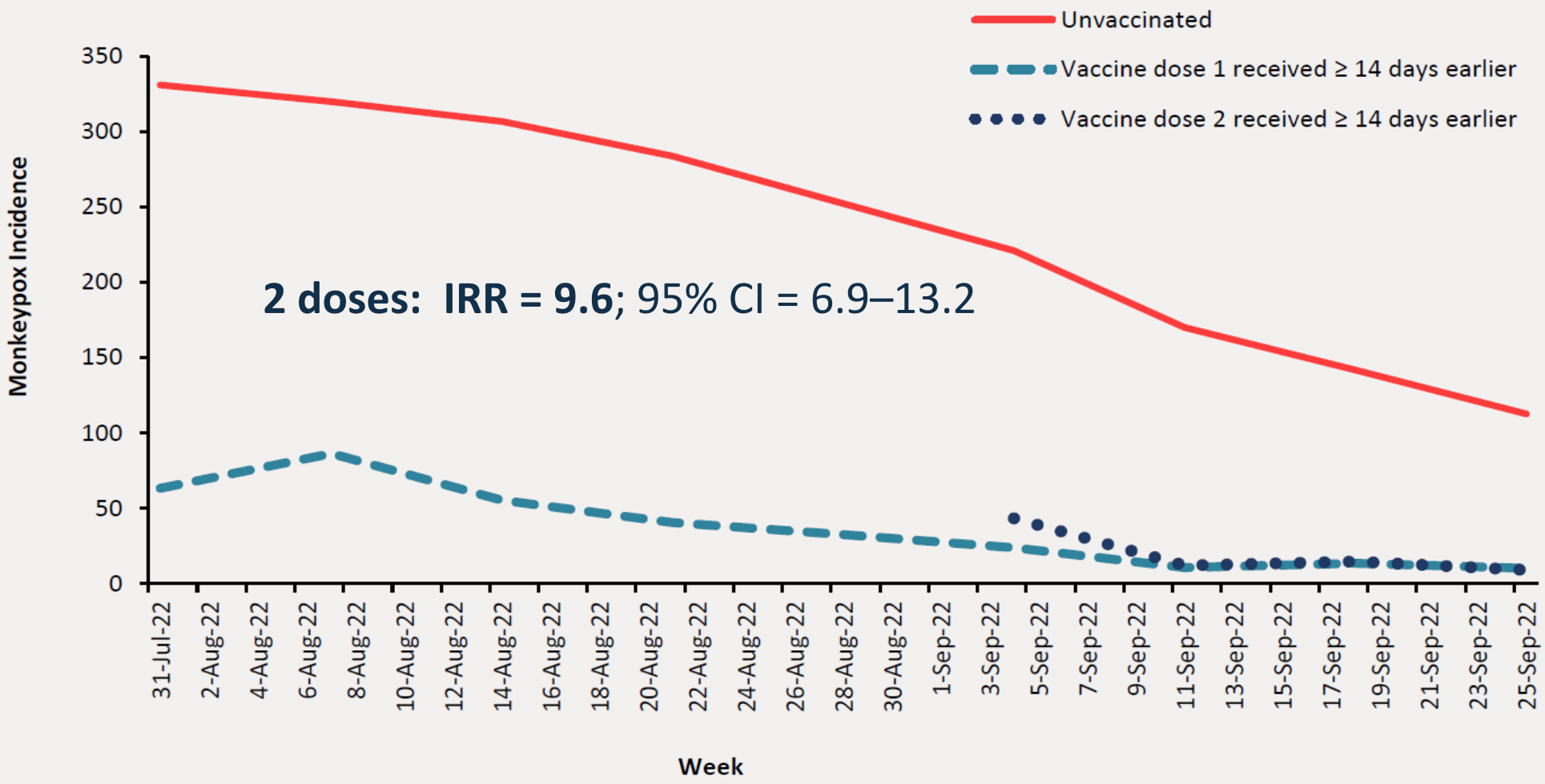
Epidemiological associations based on case series and early WHO reports

The NEW ENGLAND JOURNAL of MEDICINE | THE LANCET Infectious Diseases | thebmj | THE LANCET | World Health Organization

1.Girometti N , Lancet Infect Dis 2022 Sep;22(9):1321-1328; 2. Thornhill J N Engl J Med 2022; 387:679-691;3. Patel A; BMJ 2022 378; :e072410; 4. Tarin-Vicente E, Lancet 2022 Aug 27;400(10353):661-669

Vaccination with JYNNEOS prevents infection*

Weekly mpox incidence among vaccine-eligible men aged 18–49 years, by vaccination status
43 U.S. jurisdictions, July 31– October 1, 2022



Source: Payne *et al*. MMWR 2022. IRR = incidence rate ratio. *modified vaccinia Ankara-Bavarian Nordic (MVA-BN)

International Case Definitions May 2022

- Expanded to specify **sexually active** gay and bisexual men-who-have-sex-with-men (GBMSM)

https://www.gov.uk/guidance/monkeypox-case-definitions ;https://www.cdc.gov/poxvirus/monkeypox/clinicians/case-definition.html ;https://www.who.int/publications/i/item/WHO-MPX-Surveillance-2022.2; https://www.ecdc.europa.eu/en/news-events/epidemiological-update-monkeypox-multi-country-outbreak-15-june

But is it an STI?

- Depends who you ask….. but my view is yes.

Found in semen and vaginal fluid

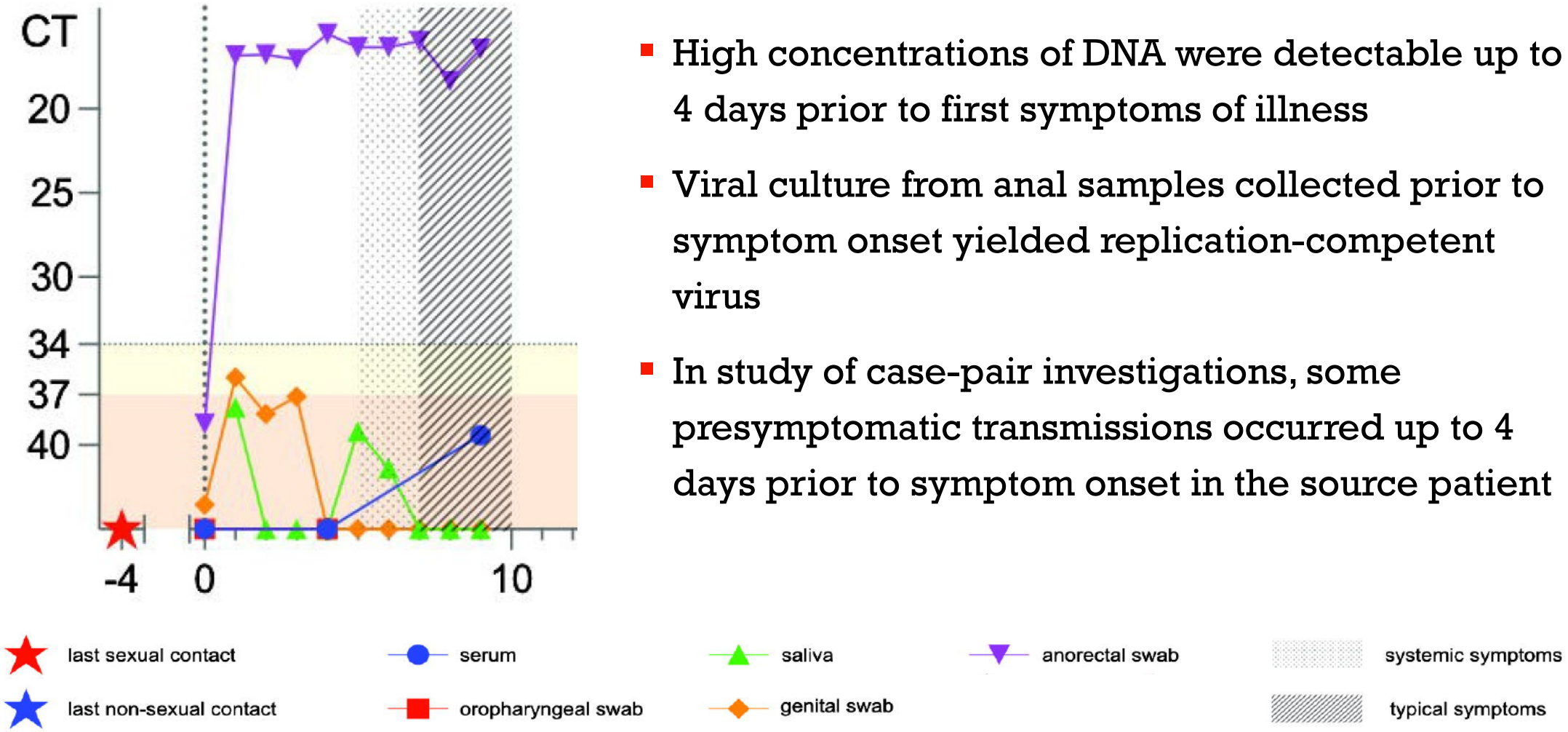
- Found in 29/32 of samples tested (global series)
- Viable virus isolated from anal & urethral swabs
- Found in 100% (14/14) vaginal swabs (global series)

Thornhill J N Engl J Med 2022; 387:679-69;
Antinori A et al, Euro Survellance 2022;27(22):2200421;
Moschese D et al, Euro Surveillance 2022; 27 (26);2200675
Thornhill Lancet 17/November 2022 (epub)

Evidence for STI

- Exposure to skin and anorectum carries greatest risk of transmission
- Evidence for asymptomatic carriage (asymptomatic rectal swabs in June/July 2022)
- 6.5% (13/200) MSM swabbed MPXV pcr +

Source: Paran et al. Euro Surveill 2022. *Palich et al. Lancet Infect Dis 2022*
Ward T, BMJ 2022 *Férré V, Annals of Internal Medicine 2022De Baetselier, Nature Medicine 2022*



- High concentrations of DNA were detectable up to 4 days prior to first symptoms of illness
- Viral culture from anal samples collected prior to symptom onset yielded replication-competent virus
- In study of case-pair investigations, some presymptomatic transmissions occurred up to 4 days prior to symptom onset in the source patient

Source: Brosius et al. medRxiv 2022. Miura et al. medRxiv
Source: Paran et al. Euro Surveill 2022. Palich et al. Lancet Infect Dis 2022
Source: Ward T, BMJ 2022 Férré V, Annals of Internal Medicine 2022De Baetselier, Nature Medicine 2022

The NEW ENGLAND JOURNAL of MEDICINE

THE LANCET Infectious Diseases

thebmj

THE LANCET

How Is MPXV presenting clinically in the global outbreaks?

ORIGINAL ARTICLE

Monkeypox Virus Infection in Humans across 16 Countries — April–June 2022

J.P. Thornhill, S. Barkati, S. Walmsley, J. Rockstroh, A. Antinori, L.B. Harrison, R. Palich, A. Nori, I. Reeves, M.S. Habibi, V. Apea, C. Boesecke, L. Vandekerckhove, M. Yakubovsky, E. Sendagorta, J.L. Blanco, E. Florence, D. Moschese, F.M. Maltez, A. Goorhuis, V. Pourcher, P. Migaud, S. Noe, C. Pintado, F. Maggi, A.-B.E. Hansen, C. Hoffmann, J.I. Lezama, C. Mussini, A.M. Cattelan, K. Makofane, D. Tan, S. Nozza, J. Nemeth, M.B. Klein, and C.M. Orkin, for the SHARE-net Clinical Group*

Clinical features and novel presentations of human monkeypox in a central London centre during the 2022 outbreak: descriptive case series

Aatish Patel, Julia Bilinska, Jerry C H Tam, Dayana Da Silva Fontoura, Claire Y Mason, Anna Daunt, Luke B Snell, Jamie Murphy, Jack Potter, Cecilia Tuudah, Rohan Sundramoorthi, Movin Abeywickrema, Caitlin Pley, Vasanth Naidu, Gaia Nebbia, Emma Aarons, Alina Botgros, Sam T Douthwaite, Claire van Nispen tot Pannerden, Helen Winslow, Aisling Brown, Daniella Chilton, Achyuta Nori

Clinical presentation and virological assessment of confirmed human monkeypox virus cases in Spain: a prospective observational cohort study

Eloy José Tarín-Vicente, Andrea Alemany, Manuel Agud-Dios, Maria Ubals, Clara Suñer, Andrés Antón, Maider Arando, Jorge Arroyo-Andrés, Lorena Calderón-Lozano, Cristina Casañ, José Miguel Cabrera, Pep Coll, Vicente Descalzo, María Dolores Folgueira, Jorge N García-Pérez, Elena Gil-Cruz, Borja González-Rodríguez, Christian Gutiérrez-Collar, Águeda Hernández-Rodríguez, Paula López-Roa, María de los Ángeles Meléndez, Julia Montero-Menárguez, Irene Muñoz-Gallego, Sara Isabel Palencia-Pérez, Roger Paredes, Alfredo Pérez-Rivilla, María Piñana, Nuria Prat, Aída Ramírez, Ángel Rivero, Carmen Alejandra Rubio-Muñiz, Martí Vall, Kevin Stephen Acosta-Velásquez, An Wang, Cristina Galván-Casas, Michael Marks*, Pablo L Ortiz-Romero*, Oriol Mitjà**

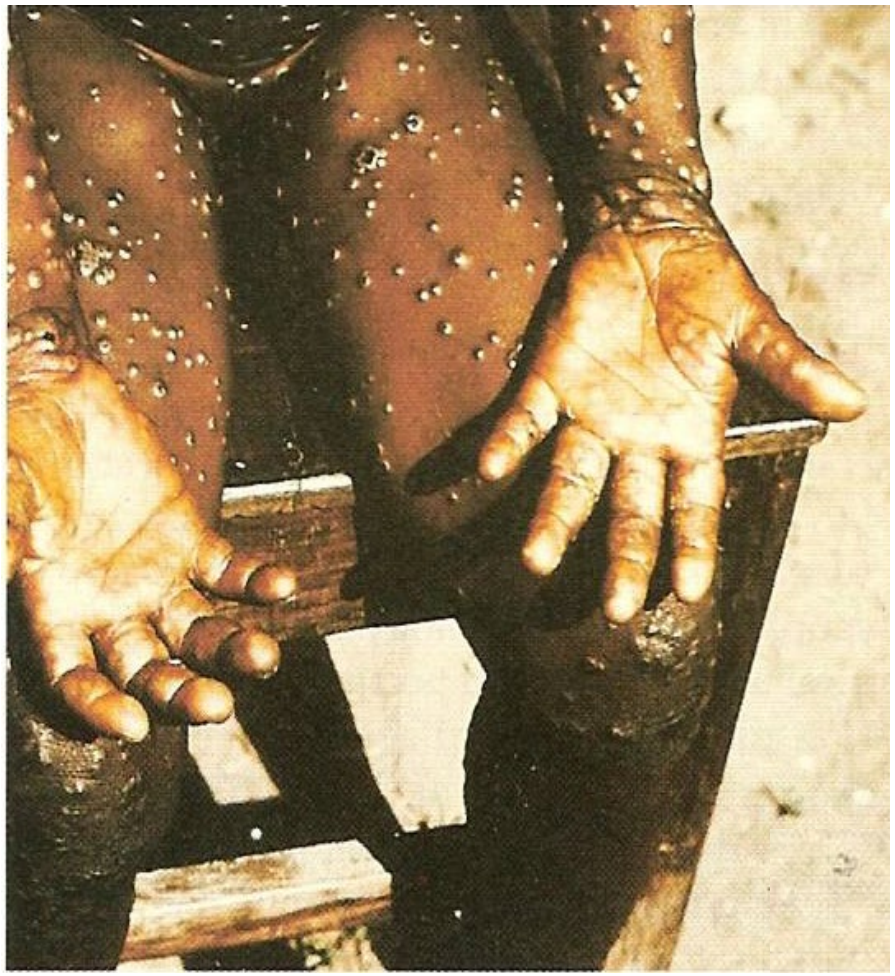
Epidemiologic and Clinical Characteristics of Monkeypox Cases — United States, May 17–July 22, 2022

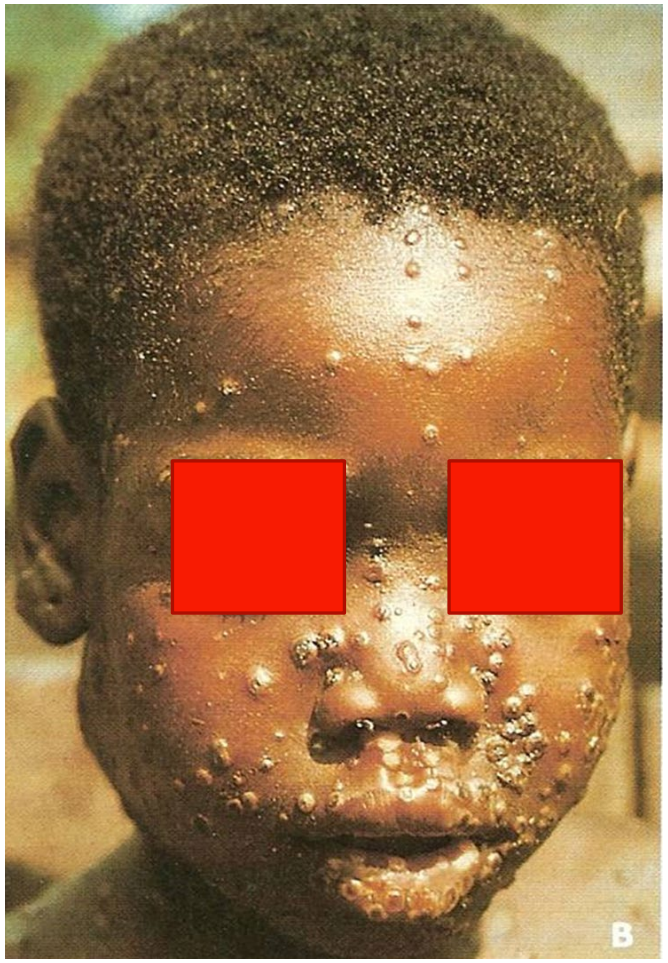
Weekly / August 12, 2022 / 71(32);1018-1022

On August 5, 2022, this report was posted online as an MMWR *Early Release.*

David Philpott, MD[1,2]; Christine M. Hughes, MPH[2]; Karen A. Alroy, DVM[3]; Janna L. Kerins, VMD[4]; Jessica Pavlick, DrPH[5]; Lenore Asbel, MD[6]; Addie Crawley, MPH[3]; Alexandra P. Newman, DVM[7]; Hillary Spencer, MD[1,4]; Amanda Feldpausch, DVM[5]; Kelly Cogswell, MPH[8]; Kenneth R. Davis, MPH[9]; Jinlene Chen, MD[10]; Tiffany Henderson, MPH[11]; Katherine Murphy, MPH[12]; Meghan Barnes, MSPH[13]; Brandi Hopkins, MPH[14]; Mary-Margaret A. Fill, MD[15]; Anil T. Mangla, PhD[16]; Dana Perella, MPH[6]; Arti Barnes, MD[17]; Scott Hughes, PhD[3]; Jayne Griffith, MPH[18]; Abby L. Berns, MPH[19]; Lauren Milroy, MPH[20]; Haley Blake, MPH[21]; Maria M. Sievers, MPH[22]; Melissa Marzan-Rodriguez, DrPH[23]; Marco Tori, MD[1,24]; Stephanie R. Black, MD[4]; Erik Kopping, PhD[3,25]; Irene Ruberto, PhD[26]; Angela Maxted, DVM, PhD[27]; Anuj Sharma, MPH[5]; Kara Tarter, MPH[28]; Sydney A. Jones, PhD[29,30]; Brooklyn White, MPH[31]; Ryan Chatelain, MPH[32]; Mia Russo; Sarah Gillani, MPH[16]; Ethan Bornstein, MD[1,8]; Stephen L. White, PhD[9]; Shannon A. Johnson, MPH[11]; Emma Ortega, MPHTM[12]; Lori Saathoff-Huber, MPH[17]; Anam Syed, MPH[5]; Aprielle Wills, MPH[3]; Bridget J. Anderson, PhD[7]; Alexandra M. Oster, MD[2]; Athalia Christie, DrPH[2]; Jennifer McQuiston, DVM[2]; Andrea M. McCollum, PhD[2]; Agam K. Rao, MD[2,*]; María E. Negrón, DVM, PhD[2,*]; CDC Multinational Monkeypox Response Team (View author affiliations)

Mpox clinical presentation prior to 2022





CDC Public health library

Clinical case definitions in May 2022 - **derived from historical literature**[26]

	World Health Organization	ecdc EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL	CDC	UK Health Security Agency
Rash description	An unexplained acute rash or one or more acute skin lesions	An unexplained rash on any part of the body	Deep-seated, well-circumscribed lesion… progression through macules, papules, vesicles, pustules, scabs	An unexplained rash on any part of their body
Fever	>38.3°C (101°F)	Fever (usually > 38.5°C)	Not mentioned	>38.5°C
Lymphadenopathy	Lymphadenopathy	Generalised or localised	Not mentioned	Lymphadenopathy
Other	intense headache, back pain, myalgia and intense asthenia	headache, backache, and fatigue	Not mentioned	Chills, headache, exhaustion, Myalgia, back pain Asthenia

https://www.gov.uk/guidance/monkeypox-case-definitions ;https://www.cdc.gov/poxvirus/monkeypox/clinicians/case-definition.html ;https://www.who.int/publications/i/item/WHO-MPX-Surveillance-2022.2; https://www.ecdc.europa.eu/en/news-events/epidemiological-update-monkeypox-multi-country-outbreak-15-june

Genital and Mucosal Lesions not specified or mentioned

	WHO			UKHSA
Rash description	An unexplair one or more lesions		ircumscribed lication; lesion h specific macules, ustules, scabs	An unexplained rash on any part of their body
Fever	>38.3ºC (101			>38.5°C
Lymphadenopathy	Lymphadeno			Lymphadenopathy
Other	intense head myalgia and			chills, headache, exhaustion, Myalgia Back pain Asthenia

https://www.gov.uk/guidance/monkeypox-case-definitions ;https://www.cdc.gov/poxvirus/monkeypox/clinicians/case-definition.html ;https://www.who.int/publications/i/item/WHO-MPX-Surveillance-2022.2; https://www.ecdc.europa.eu/en/news-events/epidemiological-update-monkeypox-multi-country-outbreak-15-june

Clinical Presentation

The NEW ENGLAND JOURNAL of MEDICINE

Monkeypox Virus Infection in Humans across 16 Countries — April–June 2022

Thornhill JP et al. DOI: 10.1056/NEJMoa2207323

CLINICAL PROBLEM

Sporadic outbreaks of monkeypox virus infection in humans have been reported for decades in Africa, but until recently, secondary spread and travel-associated cases were limited. In the spring of 2022, cases increased rapidly worldwide; risk factors, transmission routes, clinical presentation, and outcomes were poorly understood.

OBSERVATIONAL STUDY

Design: A global collaborative research group contributed to a convenience-sample case series to better describe human monkeypox infection.

Methods: 528 persons with polymerase-chain-reaction–confirmed infection diagnosed in 16 countries on 5 continents between late April and late June 2022 were assessed for potential exposures, demographic characteristics, clinical findings, and outcomes.

RESULTS

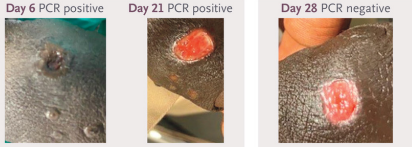
Among the persons with infection in this case series, 98% were gay or bisexual men, 75% were White, and 41% had HIV infection (largely well controlled). Skin lesions, most often in the anogenital area, trunk or limbs, or face, were noted in 95%; mucosal lesions were observed in 41%. Common systemic features included fever, lymphadenopathy, lethargy, myalgia, and headache. Sexual close contact was the suspected route of transmission in 95% of patients, although sexual transmission could not be confirmed. The median incubation period, determined on the basis of data from 23 persons, was 7 days. Overall, 13% of the persons with infection were hospitalized, most often for pain management. No deaths were reported.

LIMITATIONS AND REMAINING QUESTIONS

- This was a convenience sample based on persons who presented with symptoms, largely to sexual health clinics, with limited standardization of prospective data collection.
- Monkeypox virus DNA was found in the semen of 29 of 32 persons who were tested, but whether this DNA was replication competent is unknown.
- The duration of potentially infectious viral shedding after lesion clearance is uncertain.

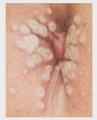
Links: Full Article | NEJM Quick Take | Editorial

Evolution of Cutaneous (Penile) Lesions



Perioral and Oral Lesions

Perianal Lesions



Characteristic	All Persons (N=528)
Site of positive monkeypox viral PCR — no. (%)	
Skin or anogenital lesion	512 (97)
Nose or throat swab	138 (26)
Blood	35 (7)
Urine	14 (3)
Semen	29 (5)
Site of skin lesions — no. (%)	
Anogenital area	383 (73)
Face	134 (25)
Trunk or limbs	292 (55)
Palms or soles	51 (10)
Site of mucosal lesions — no./total no. (%)	
Anogenital only	148/217 (68)
Oropharyngeal only	50/217 (23)
Anogenital and oral	16/217 (7)
Nasal and eye	3/217 (1)

CONCLUSIONS

In an international convenience sample of monkeypox virus infections, nearly all the persons with infection were gay or bisexual men. Skin lesions were the most common presenting symptom, and the prognosis was good, with no deaths reported.

- Global case series
- 16 countries; 528 people, all men
- 95% presented with a rash **to a wide variety of clinical settings.**
- **Where:**
  - 73% genital and/or anal lesions
- **How many lesions?**
  - Two thirds had < 10 lesions
  - 10% had a single genital lesion
- **What does rash look like:**
  - Lesions in multiple phases of evolution.
  - 58% had vesiculo-pustular lesions

Thornhill J N Engl J Med 2022; 387:679-69

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New mucosal presentations

- Lesions occur close to site of sexual contact
- **In the male global series: 41%** had mucosal lesions
- Mucosal **primary** presentations were common
- In the women's global case series:
- Presents similarly in men and women
  - Misdiagnosis more common in women than men
  - Women with non-genital routes of acquisition were less likely to have genital lesions

Thornhill J N Engl J Med 2022; 387:679-69; Patel A; BMJ 2022 378; :e072410; Tarin-Vicente E, Lancet 2022 Aug 27;400(10353):661-669
Thornhill Lancet 17/November 2022 (epub)

Complications

- **Local:**
  - Superinfection: cellulitis, abscess
  - Anorectal pain, ulcers, perforation
  - Paraphymosis, urinary retention
  - Oropharyngeal: tonsillitis, odynophagia, epiglottitis
  - Ocular: keratitis, peri-orbital cellulitis
- **Systemic**
  - Encephalitis, seizure, confusion, headache, depression (2%)
  - Myocarditis
  - Dehydration, acute renal injury

Girometti N , Lancet Infect Dis 2022 Sep;22(9):1321-1328; Thornhill J N Engl J Med 2022; 387:679-691;
Patel A; BMJ 2022 378; :e072410; Tarin-Vicente E, Lancet 2022 Aug 27;400(10353):661-669;Badenoch Lancet Sept 2022 online;
Thornhill Lancet 17/November 2022 (epub)

HIV and MPXV

- CDC dataset (n=755)
- Disparities:
  - 63% Black
  - 41% Hispanic/Latino
  - 22% Asian
- 82% virally suppressed
- Clinical differences observed
  - 8% PWH hospitalized vs 3% without HIV
  - Only 3% with CD4 < 200
  - PWH more likely to have rectal pain and other rectal manifestations

High prevalence in people living with HIV

- 38-50% of people with mpox also living with HIV
- Why???
- (Ideas: behavioural, ascertainment bias, biological/microbiome)

Thornhill J N Engl J Med 2022; 387:679-69; https://worldhealthorg.shinyapps.io/mpx_global;

Source: ECDC/WHO Europe. Monkeypox, Joint Epidemiological overview, 25 October, 2022. https://monkeypoxreport.ecdc.europa.eu/

Weekly / August 12, 2022 / 71(32);1018-1022

MPXV and HIV before 2022

- Retrospective review of 40 **hospitalized** patients (2017-18 Nigerian outbreaks)
  - 9 PLWH
  - 4 with CD4 <200c/ML
  - Most unsuppressed, or not known
  - PLWH : prolonged illness, larger more disseminated lesions, more superinfection

Ogoina, Clin Infect Dis. 2020;71:e210-e214.

HIV outcomes 2022 outbreak

- No differences in natural history, clinical presentation, admissions- multiple case series

Ogoina. Clin Infect Dis. 2020;71:e210-e214.
Thornhill J N Engl J Med 2022; 387:679-69

MPXV and HIV

- CDC: Retrospective review of 57 **hospitalized** patients poorer outcomes
- CDC large dataset 3% with CD4 <200
- Worse rectal disease, prolonged hospitalisations

CDC cohort Curran et al Ogoina. Clin Infect Dis. 2020;71:e210-e214.

MPXV Infection in People With Advanced HIV

382 people with advanced HIV
19 countries: Europe 25.9%, Americas 72.5%, Africa 1.6%

Characteristic, n (%)	Total (N = 382)
Cisgender men	367 (96.1)
Newly diagnosed with HIV Previously diagnosed with HIV and receiving ART	33 (8.6) 228 (59.7)
CD4 count <200 cells/mm^3	179(46.9%)
CD4 count <100 cells/mm^3 CD4 count 100-200 cells/mm^3	85 (22.3) 94 (24.6)
HIV-1 RNA <50 c/mL	193 (50.5)
Vaccination for smallpox prior to 2022 Vaccination in 2022	16 (4.2) 26 (7.2)

Orkin, CROI 2023. Abstr 173.

MPXV Infection in People With Advanced HIV

- Patients developed a severe necrotizing and disseminated form of MPXV with complications affecting a range of organs, including sepsis
- No deaths with CD4 counts > 200 cells/mm^3
  - Mortality **15% with CD4 counts <200 cells/mm^3**, **27.1% with CD4 counts <100 cells/mm^3**
  - No smallpox-vaccinated patients died
- Tecovirimat (oral and/or IV) use **limited to 62 patients (16.2%)** due to lack of availability outside of Europe and the United States
- Only 21 people received pre-exposure vaccination (43% of cohort came from countries where it was available)
- Initiation of or restarting ART in 85 patients led to suspected **IRIS in 21 (25%),** with **12** of these patients **dying (57.1%)**
- Patients should be monitored for sepsis, and timing of ART initiation or restart should be carefully considered

Orkin, CROI 2023. Abstr 173.

Facing the outbreak

Diagnosis
Self-isolation
Contact tracing

Exposure mitigation

Vaccination

Men who have sex with men took steps to protect themselves and their partners from mpox

48%

reduced number of sex partners

50%

reduced one-time sexual encounters

49%

reported reducing sex with partners met on dating apps or at sex venues

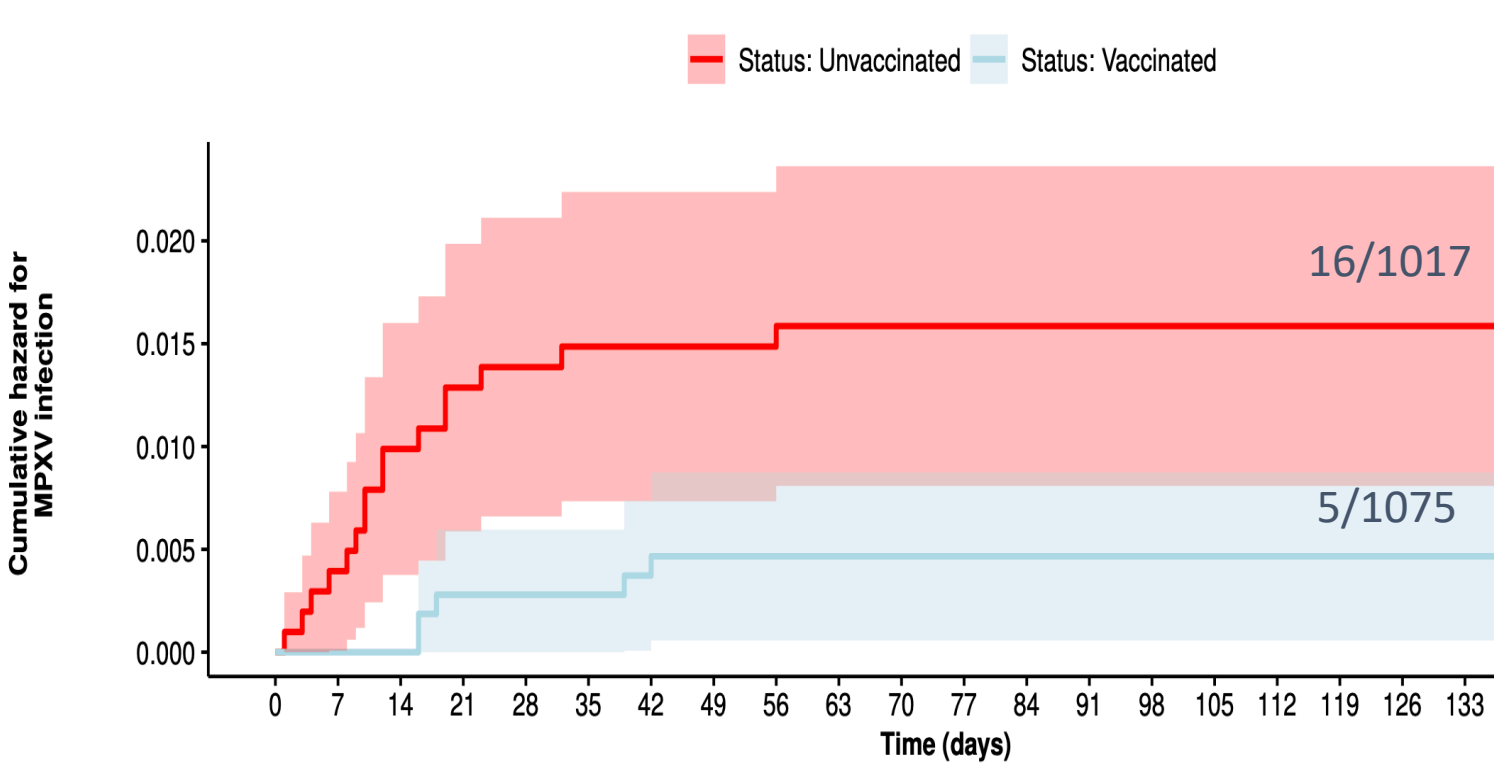
Source: Impact of Monkeypox Outbreak on Select Behaviors | Monkeypox | Poxvirus | CDC

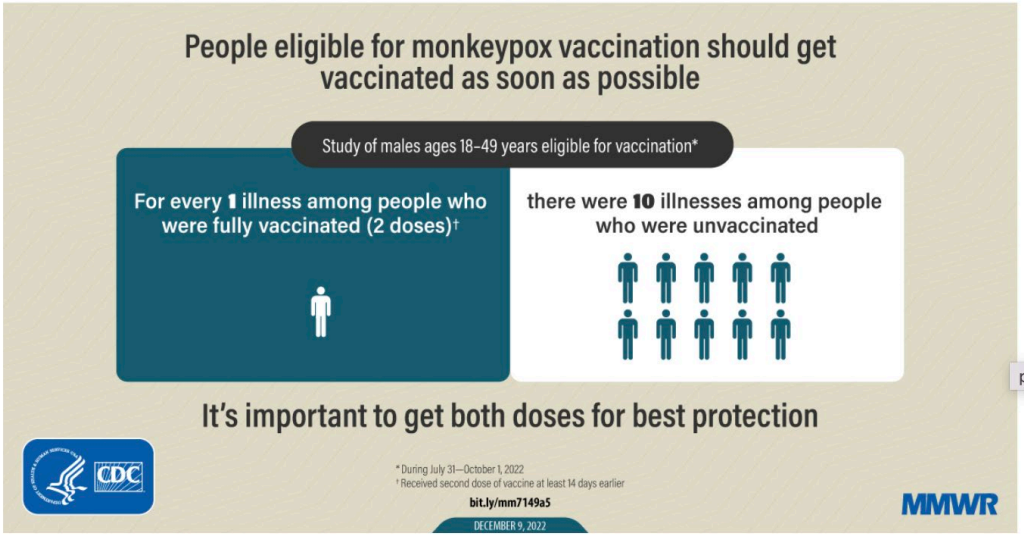
Vaccination MVA-BVN as prevention

- Jynneos/Imvanex:
  - – 3rd gen live replication deficient modified vaccinia ankara
- One dose if vaxxed against smallpox in childhood
- Two doses 28 days apart if not
- Low level of mpox virus neutralization after one dose
- Better response in those vaccinated during childhood
- Second dose is key

Zaeck L, Nature Medicine 2022

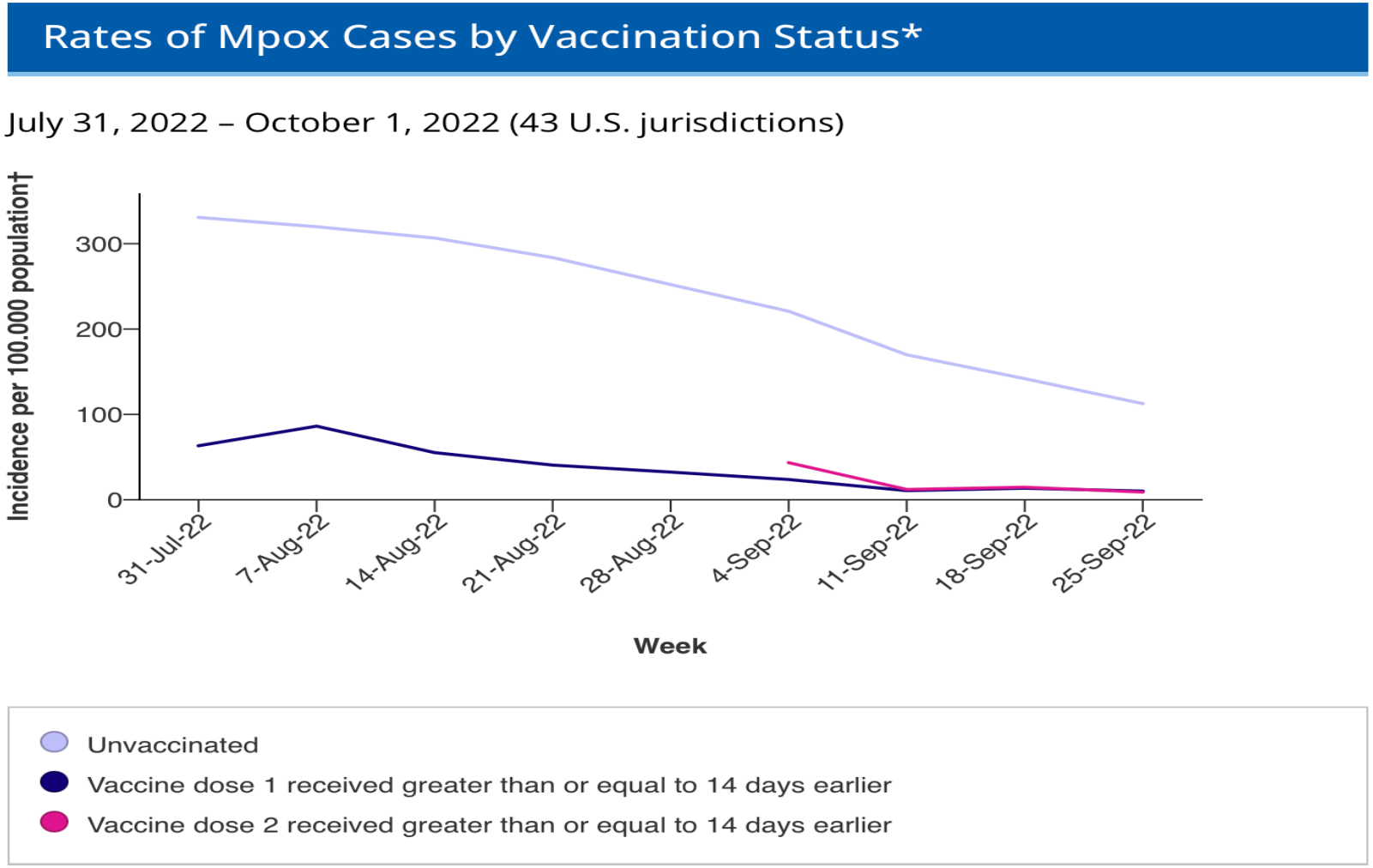
Vaccination Efficacy- 86% after 1 dose





Wolff Sagy Y, Nature Medicine 2023 / Azra A, JAMA 2022 / Payne A, MMWR 2022

Vaccination effect or behavioral change?



Payne A, MMWR 2022

Treatment

- IV Immunoglobulins
- Post-exposure vaccination
- Tecovirimat
- Brincidofovir/Cidofovir
- Trifluorodine (eye disease)
- Supportive

Adler et al., Lancet ID 2022; O'Laughlin et al., MMWR, 2022

Tecovirimat (TPOXX)

- Approved for smallpox (not monkeypox)
- Emergency access programme
- Inhibits viral envelope protein to stop virus leaving cell
- Shown to be safe so far in CDC case series
- Possibly shortens duration
- Need intact immunity to clear virus from cells, less effective in immunosuppression
- Low barrier to resistance
  - F13L amino acid substitutions detected in our case series

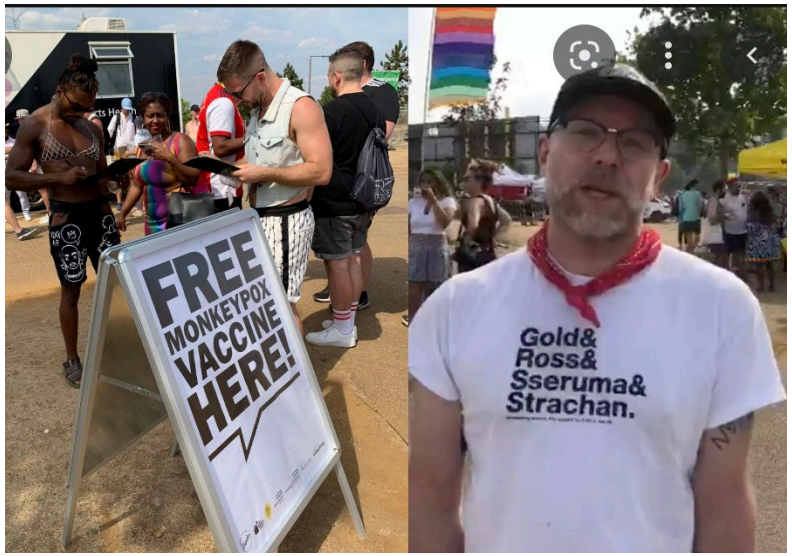
Adler et al., Lancet ID 2022; O'Laughlin et al., MMWR, 2022

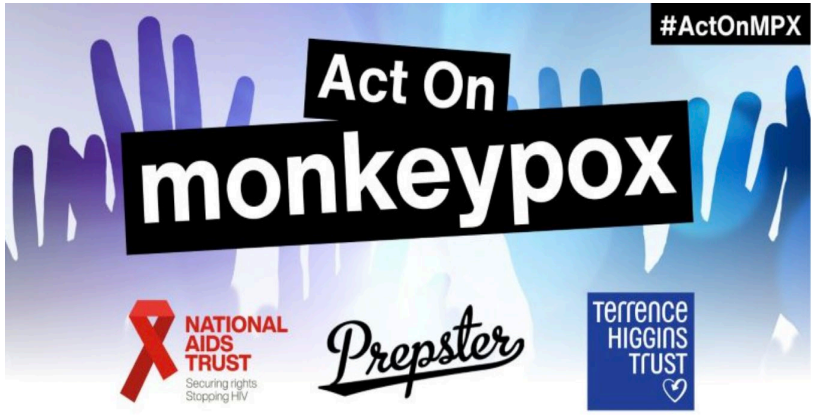
Tecovirimat (TPOXX) indications

Compassionate Use

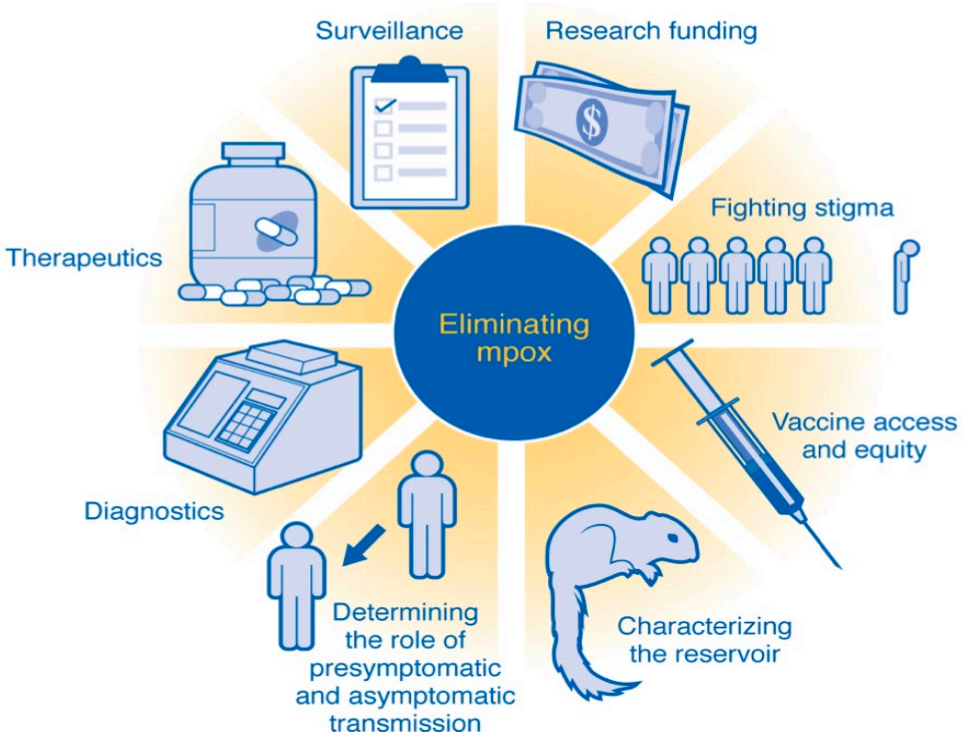
- Lesions in sensitive or high-risk sites (near eye, urethral meatus, or causing pain)
- Severe pharyngeal or rectal pain
- High number of lesions (>50-100)
- Rapidly progressing lesions
- Immunocompromising condition including HIV with unsuppressed viremia and/or low CD4+ T-cell count

UK – magnificent activists and activism





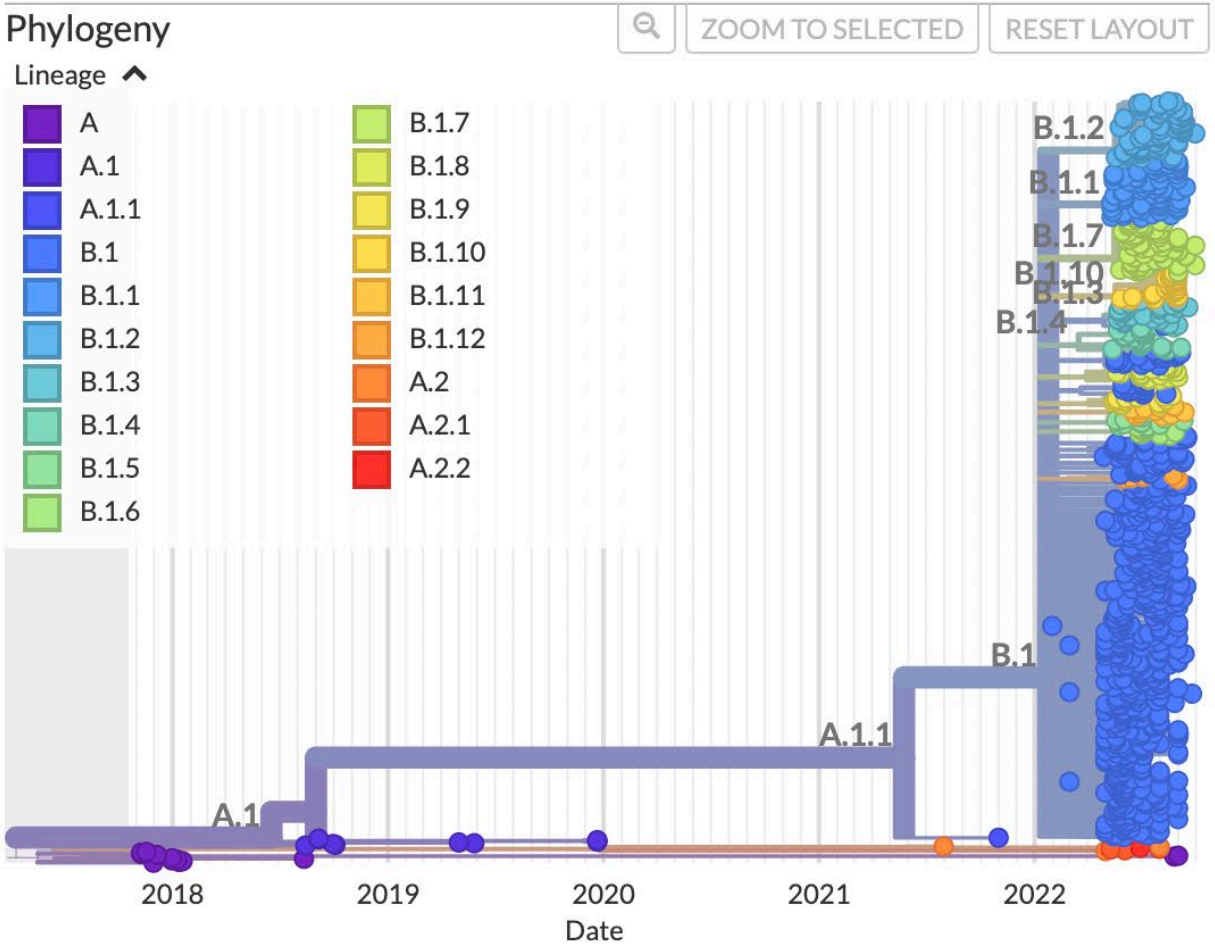
Future

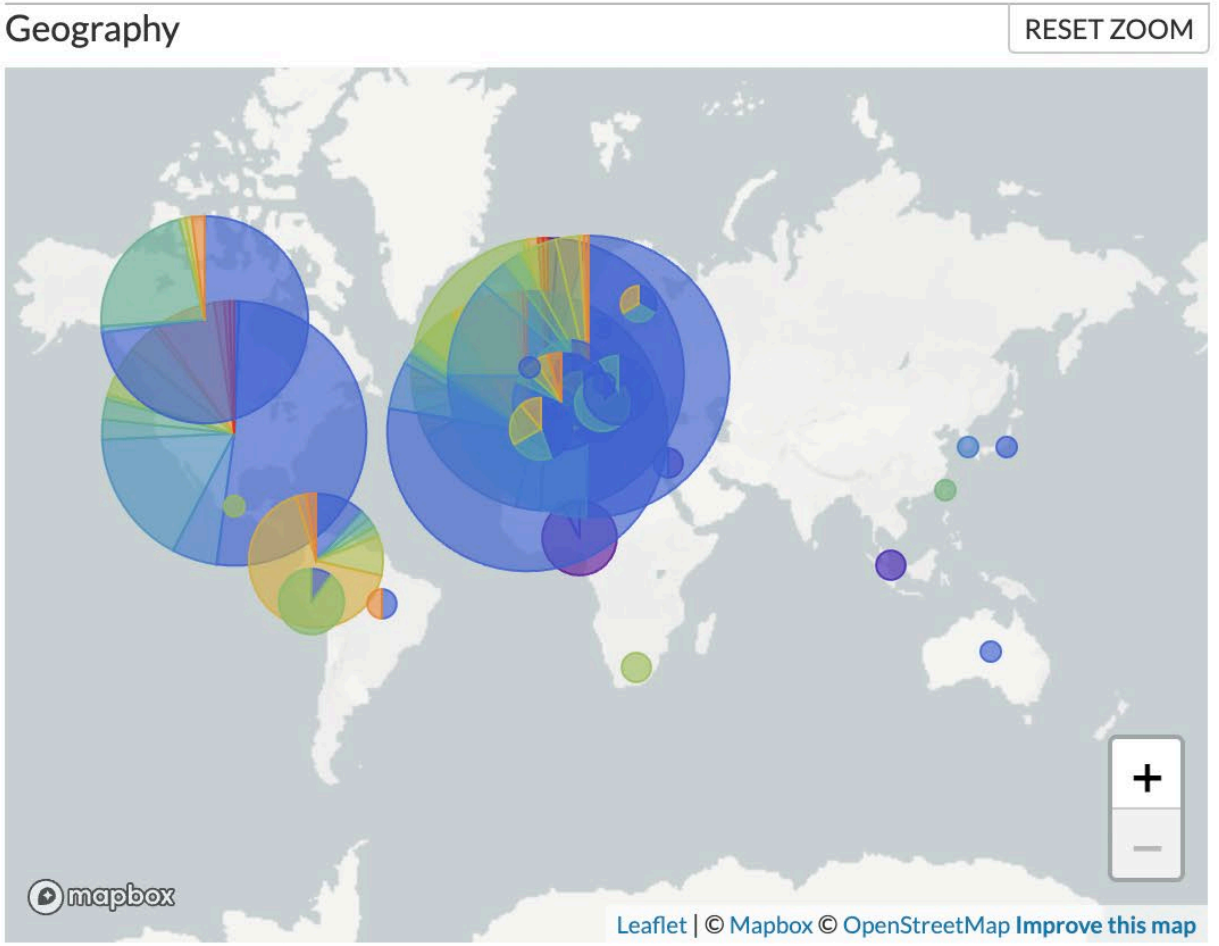


- Viral characteristics - genetic sequence and biological properties
  - Have any mutations resulted in enhanced human transmission or pathogenesis
- Treatment
  - Effectiveness of tecovirimat: PLATINUM and STOMP trial
  - Treatment strategies for those with severe immunodeficiencies
  - Need for additional therapeutics
- Diagnostics
  - Utility of non-lesion specimen types
  - Mpox-specific serology
- Characterize the epidemiology
  - Transmission parameters including asymptomatic infection
  - Reverse zoonosis risk


QUESTIONS

Evolutionary rate higher than expected for a DNA virus (50 vs 4 mutations)



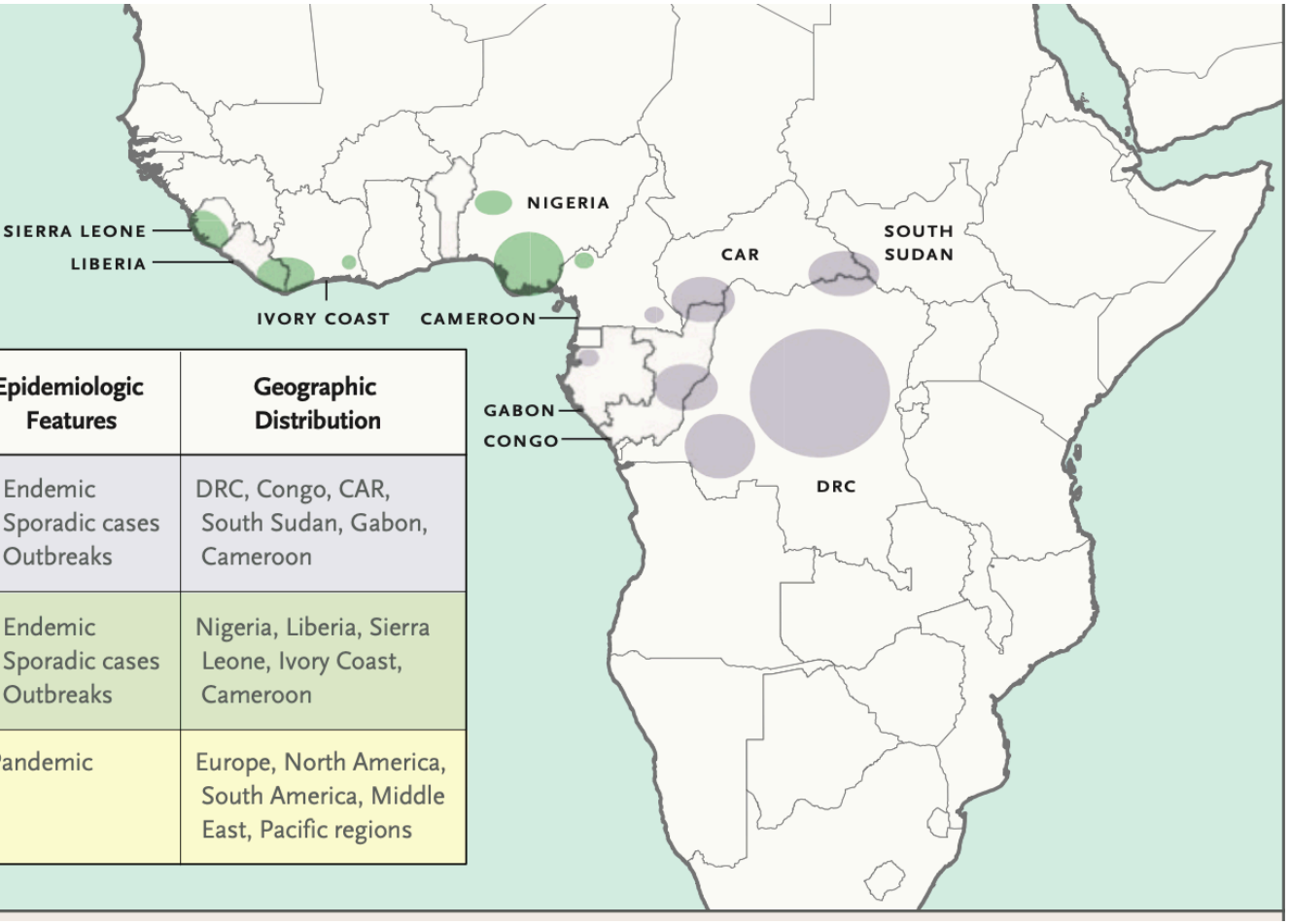


APOBEC3-associated adaptive evolution may account for the global outbreak

https://nextstrain.org/monkeypox/hmpxv1?d=tree,map&p=grid

New proposed nomenclature to avoid stigmatising countries where viruses originate

B Geographic Distribution and Nomenclature



Original Clade Nomenclature	Revised Clade Nomenclature	Epidemiologic Features	Geographic Distribution
Central Africa	1	• Endemic • Sporadic cases • Outbreaks	DRC, Congo, CAR, South Sudan, Gabon, Cameroon
West Africa	2	• Endemic • Sporadic cases • Outbreaks	Nigeria, Liberia, Sierra Leone, Ivory Coast, Cameroon
New from West Africa	3	Pandemic	Europe, North America, South America, Middle East, Pacific regions

*Currently Clade 2 includes Clade 2 and 3 as two lineages a and b

Gessain et al N Engl J Med 2022;387:1783-93.

Testing

- PCR from lesion swab
- Swabbing of two lesions recommended
- Test for STIs too and HIV
- Serology identifies exposure to general orthopoxviridae
- People who have been vaccinated against smallpox may test positive

Penile/scrotal lesions

Thornhill J N Engl J Med 2022; 387:679-69

Perianal, anal and rectal lesions.

A. Anal and perianal lesions, day 6. **B, C.** rectal and anal lesions in a single individual **D.** Perianal ulcers. **E.** Anal lesions, PCR positive
F. Umbilicated perianal lesion, day 3, PCR positive. **G.** Umbilicated perianal lesions, day 3, PCR positive. **H.** Perianal ulcer, day 2, PCR positive

Thornhill J N Engl J Med 2022; 387:679-69

Oral and perioral presentations

A. perioral umbilicated lesions. **B.** Perioral vesicular lesion, day 8, PCR positive. **C.** Ulcer left corner of the mouth, day 7, PCR positive. **D.** Tongue ulcer. **E.** Tongue lesion, day 5, PCR positive. **F, G, H.** Pharyngeal lesions, day 0, 3 and 21 respectively. PCR positive on day 0 and 3 and negative on day 21.

Thornhill J N Engl J Med 2022; 387:679-69

Asymptomatic Carriage

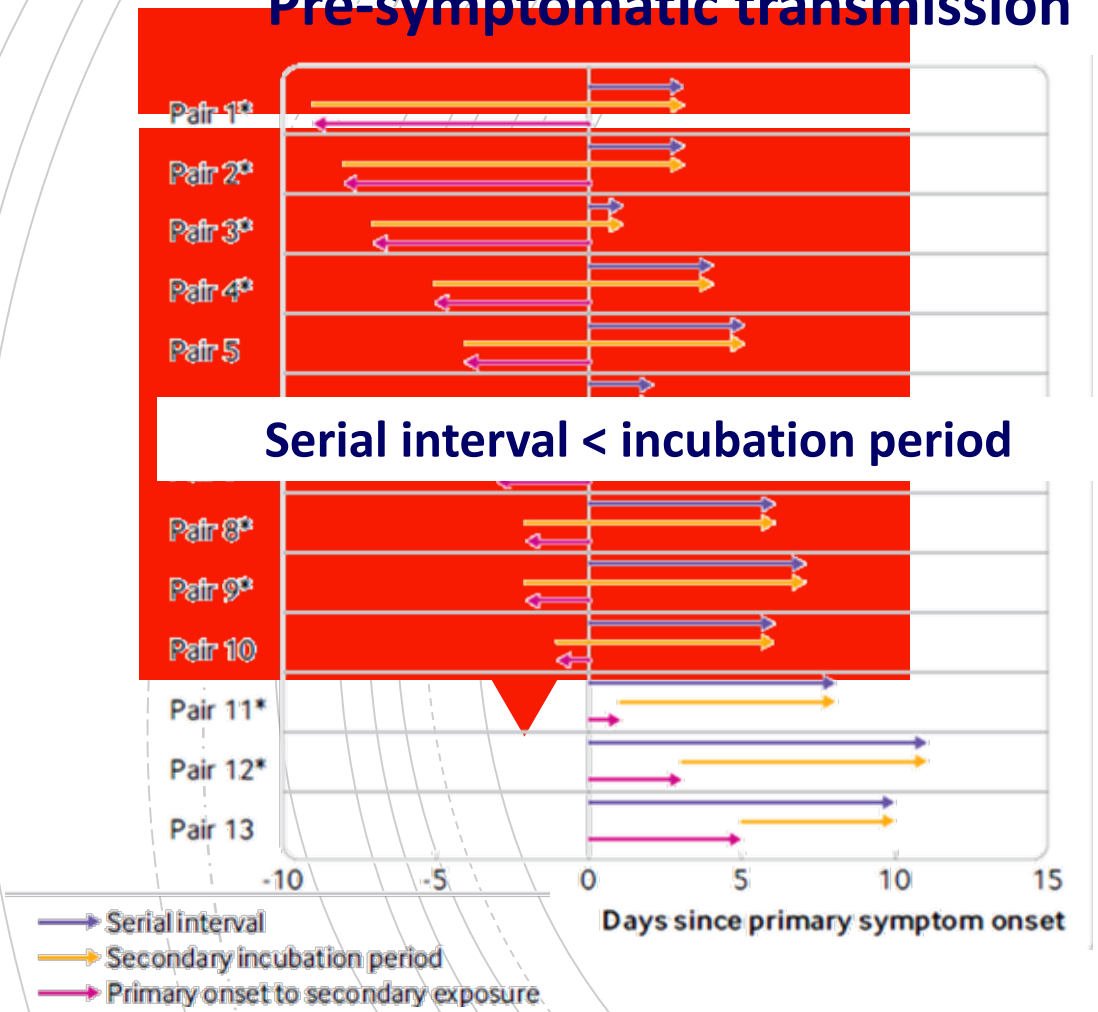
1. Ferré VM et al Detection of monkeypox virus in anorectal swabs from asymptomatic men who have sex with men in a sexually transmitted infection screening program in Paris, France. Annals Internal Medicine, Letter. DOI: 10.7326/M22-2183. (16 August 2022).
2. De Baetselier P et al Asymptomatic monkeypox virus infections among male sexual health clinic attendees in Belgium. MedRxiv preprint. doi: 10.1101/2022.07.04.22277226.

Vaccination

There is a high degree of sequence similarity between orthopoxviruses[1] especially among immunologically relevant proteins, leading to a large number of shared immune epitopes[2,3]

1. Shchelkunov SN et al. Analysis of the monkeypox virus genome.*Virology.* 2002; 297: 172-194
2. Manes NP et al. Comparative proteomics of human monkeypox and vaccinia intracellular mature and extracellular enveloped virions.*J Proteome Res.* 2008; 7: 960-968
3. Molero-Abraham M et al. EPIPOX: Immunoinformatic characterization of the shared T-cell epitome between variola virus and related pathogenic orthopoxviruses.*J Immunol Res.* 2015; 2015738020

Pre-symptomatic transmission



Ward T, BMJ 2022

Asymptomatic carriage

213 MSM attended the Clinic for routine follow-up (PrEP or HIV) between June 5 and July 11, 2022

had anal swabs collected in our center

no clinical symptoms

CT/NG NEG

MPXV PCR successful in 200/213

13/200 MPXV+ (6,5%)

Férré V, Annals of Internal Medicine 2022De Baetselier, Nature Medicine 2022

Outcomes of mpox cases in the European region

	Yes	No	Total
Hospitalized*	757 (6.4%)	11,103 (93.6%)	11,860 (100%)
Admitted to ICU	6 (0.1%)	6,855 (99.9%)	6,861 (100%)
Died**	4 (0.0%)	17,627 (100%)	17,631 (100%)

** Includes cases hospitalized for isolation or treatment (187 cases were hospitalized for isolation purposes,* ***255 required clinical care*** *and 315 were hospitalized for unknown reasons)*

*** 2 Spain, 1 Belgium, 1 Czech Republic*

Source: ECDC/WHO Europe. Monkeypox, Joint Epidemiological overview, 25 October, 2022. https://monkeypoxreport.ecdc.europa.eu/

Vaccination Recommendations

- Vaccination for PEP, ideally within 4 days of exposure, but up to 14 and expanded PrEP for those at risk

Vaccine	JYNNEOS/Imvanex (MVA-BN)	ACAM2000
Vaccine virus	Replication-deficient modified vaccinia Ankara	Replication-competent vaccinia virus
Indication	Smallpox and monkeypox	Smallpox
Recommendations in adults not previously vaccinated against smallpox with:	**0.5 mL SC/IM** or **0.1 mL intradermal** (with supply constraints) + Second dose after ≥28 days	Not in HIV
Recommendations in PWH not previously vaccinated against smallpox with: **CD4 cell count <200 cells/mm^3**	**0.5 mL SC/IM** + Second dose after ≥28 days	Not in HIV

cdc.gov/poxvirus/monkeypox/interim-considerations/special-populations.html.
assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1100600/recommendations-for-pre-and-post-exposure-vaccination-during-a-monkeypox-incident-26-august-2022.pdf.

Effectiveness of one dose of MVA-BN smallpox vaccine against monkeypox in England using the case-coverage method

UKHSA preprint

Vaccine effectiveness was calculated using the case coverage method i.e. vaccine coverage in cases is compared to the coverage in the eligible population

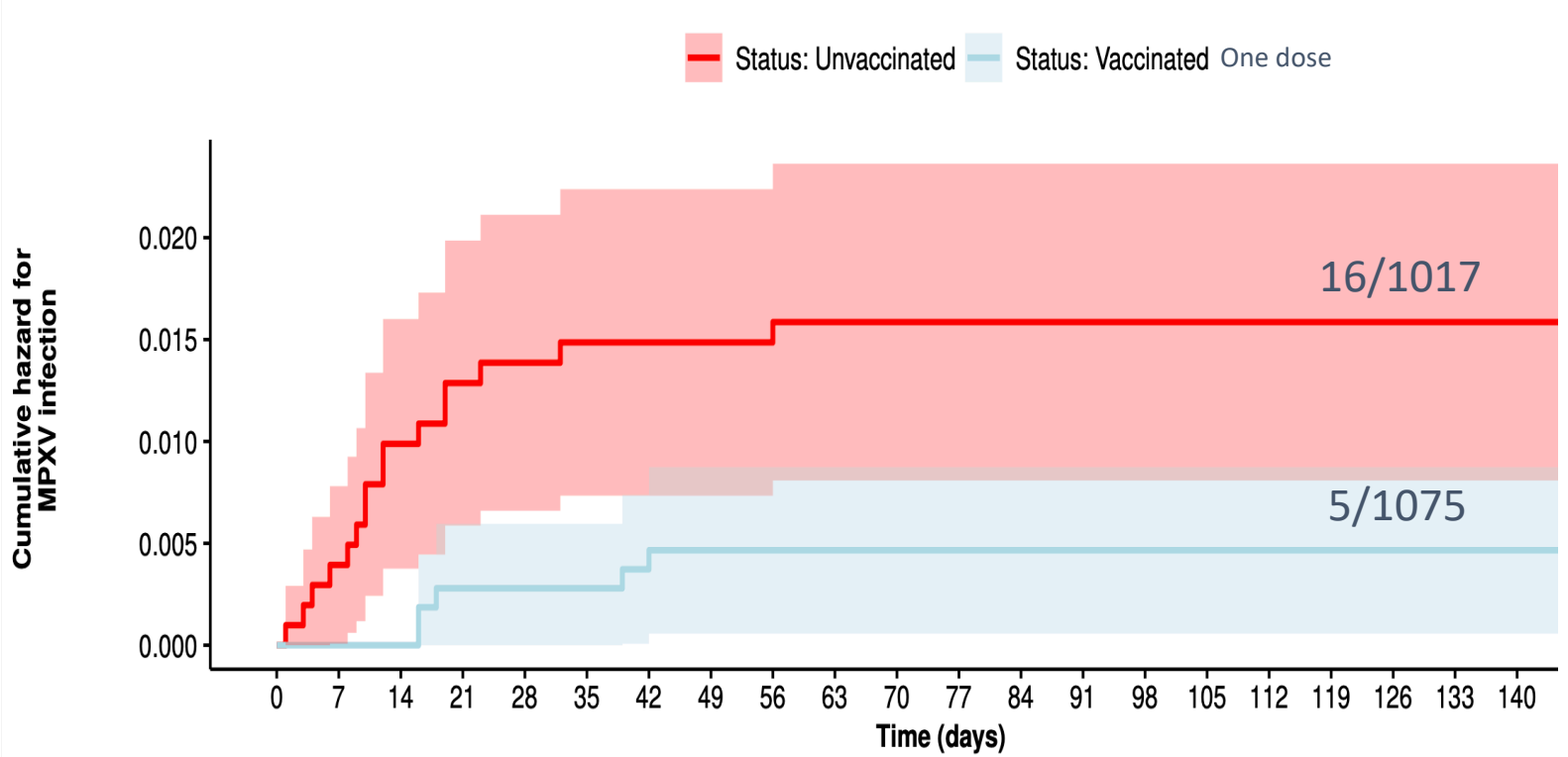
Of 363 confirmed cases, 8 occurred >14 days after vaccination, 32 within 0 to 14 days after vaccination, the rest were unvaccinated

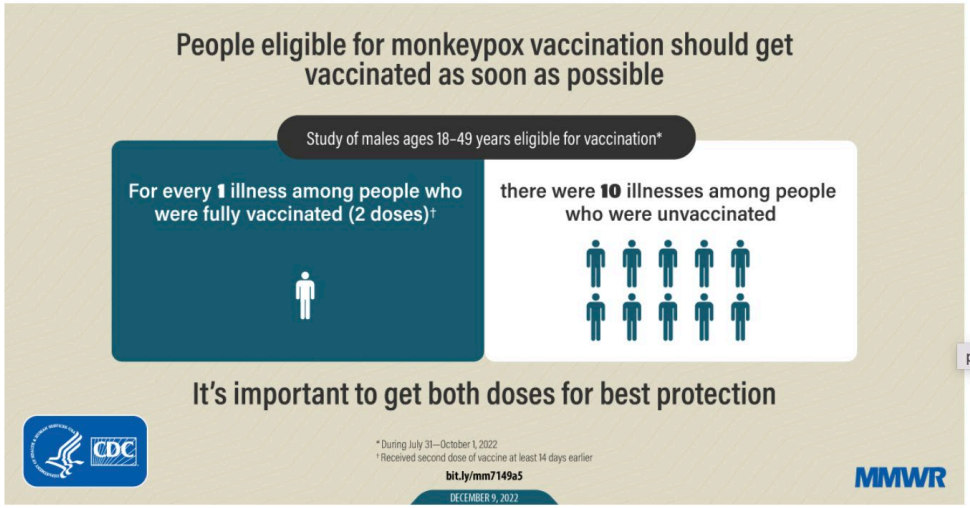
The estimated vaccine effectiveness >14 days after a single dose was 78% (95% CI 54% - 89%)

Vaccine effectiveness within 0-13 days after vaccination was -4% (95% CI: -50% to 29%)

Bertran et al, 2022 Preprint

Vaccine effectiveness : prophylactic vaccination



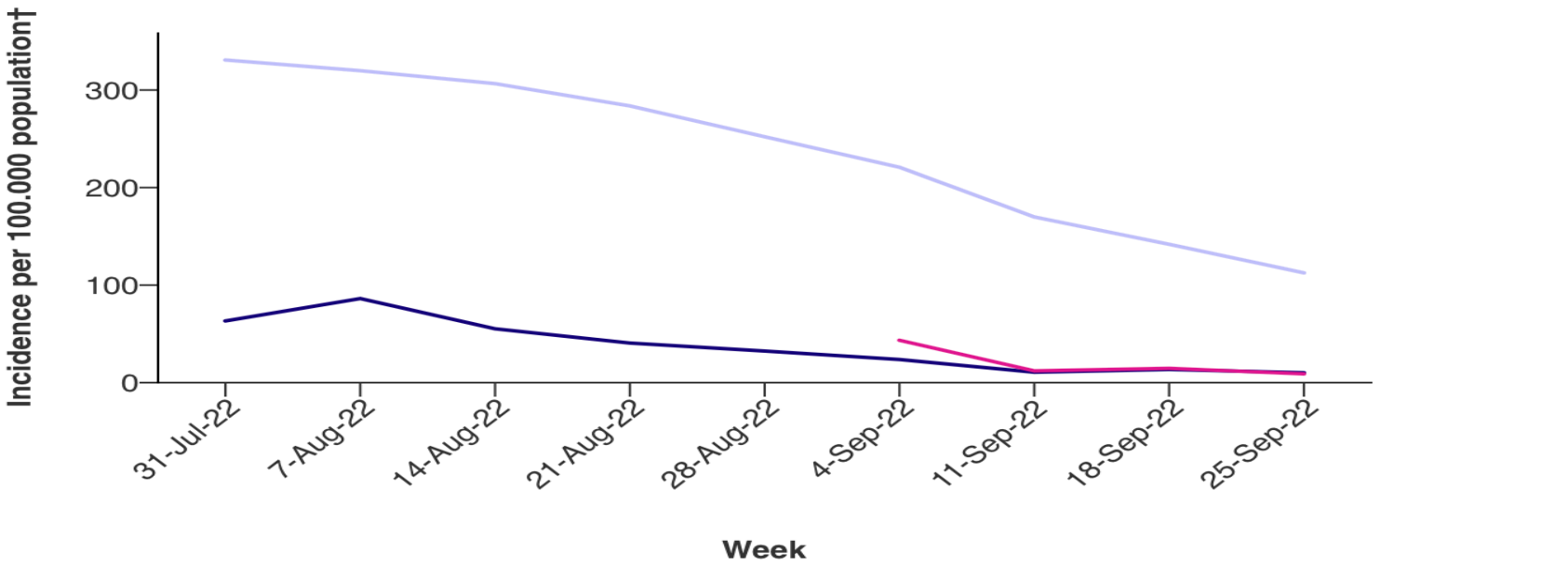


86% effectiveness after one dose

Wolff Sagy Y, Nature Medicine 2023 / Azra A, JAMA 2022 / Payne A, MMWR 2022

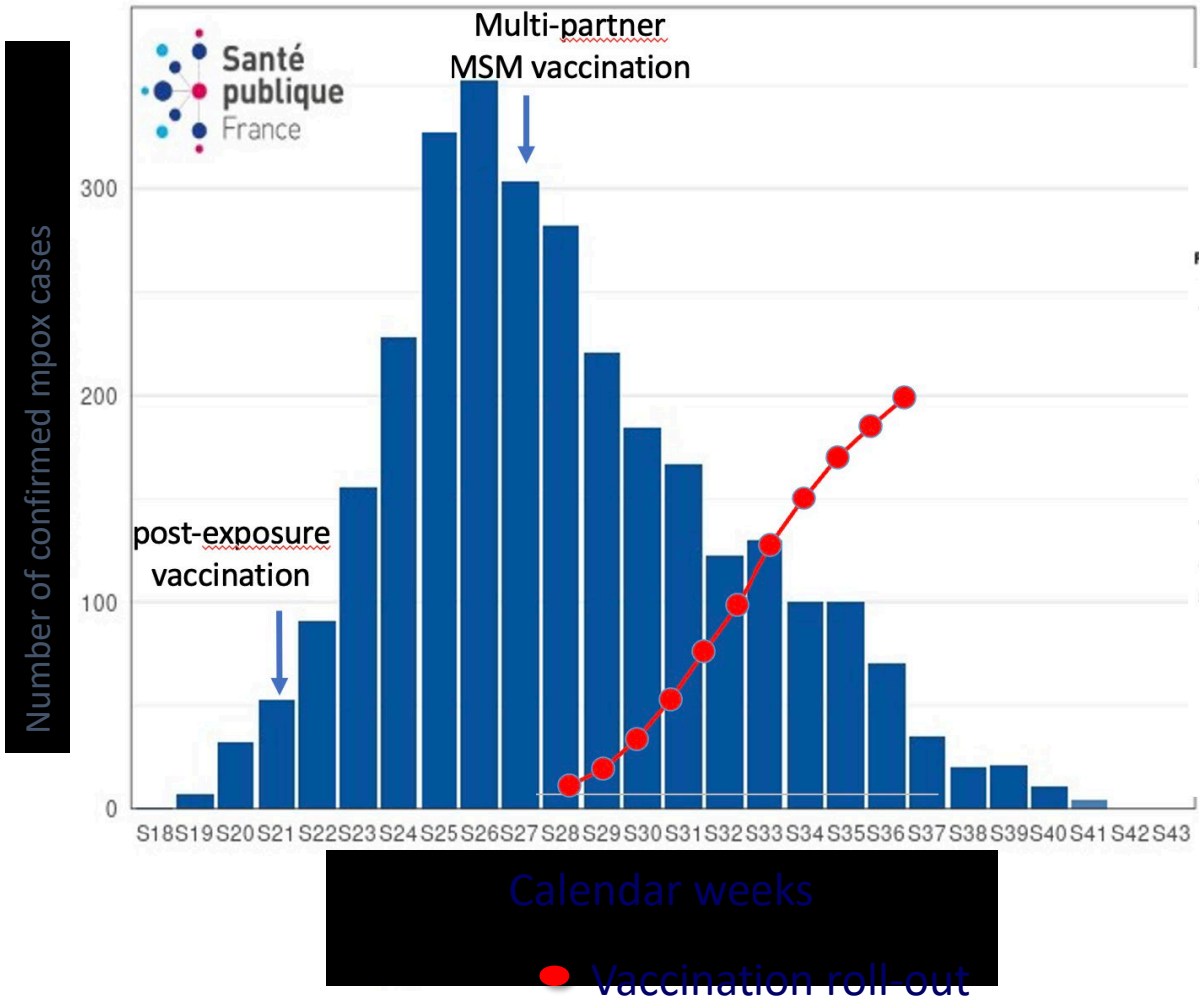
Rates of Mpox Cases by Vaccination Status*

July 31, 2022 – October 1, 2022 (43 U.S. jurisdictions)

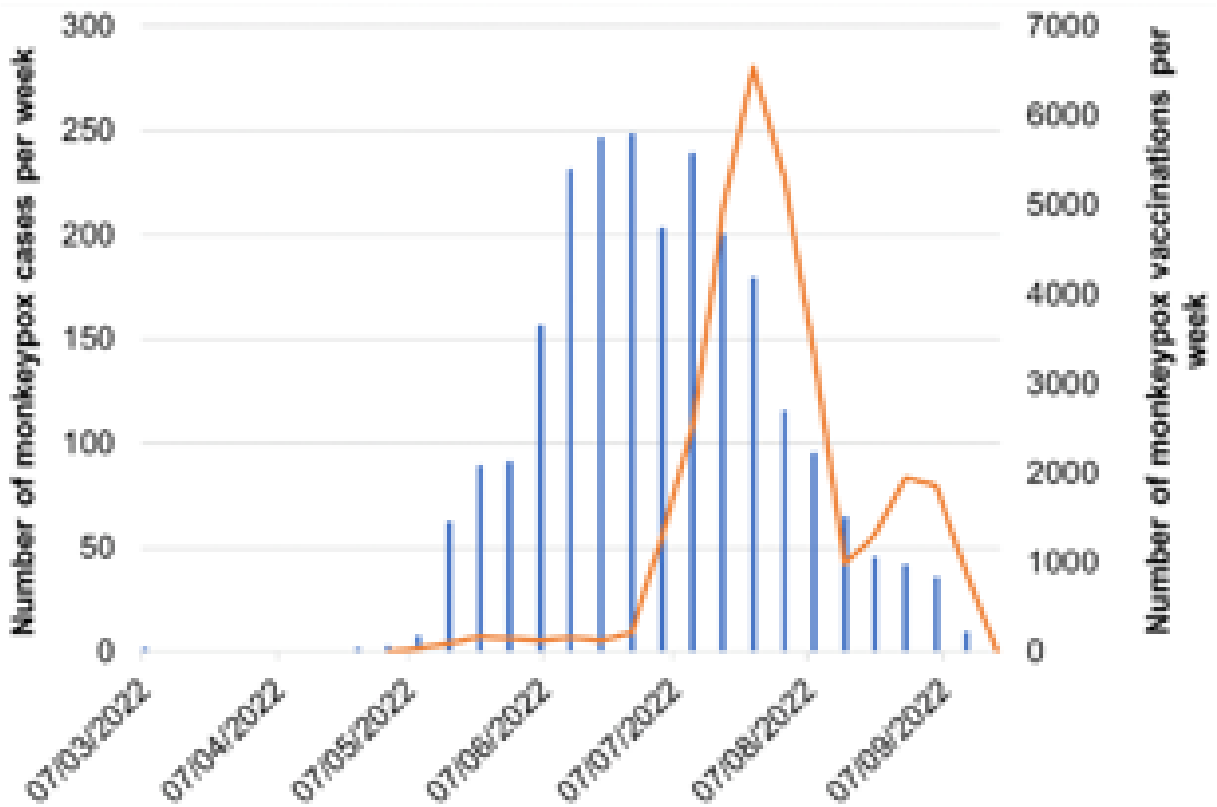


Vaccine effect versus behavior change ?

France



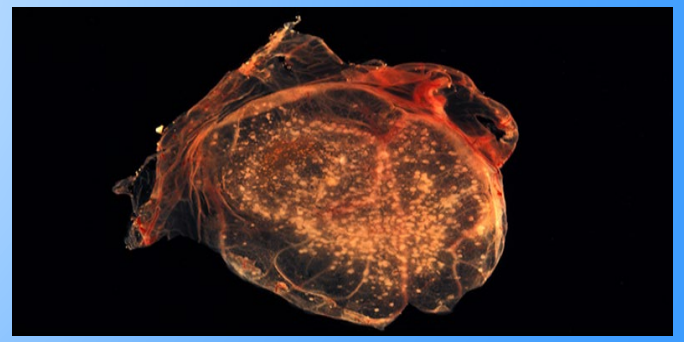
UK Health Security Agency London



Steps Leading to MVA Vaccine Development

- **1950's: Vaccinia virus strain Ankara (VVA)** was propagated on the **skin of calves & donkeys** at the Turkish Vaccine Institute in Ankara for smallpox vaccine production and provided to Germany.

- **1950's to 1974**: **Developed by multiple serial passage on chorioallantois membranes and later in chicken fibroblast** tissue culture to serve as a safer vaccine during the last years of the WHO smallpox eradication campaign.



- **Passage 516**: renamed **MVA modified vaccinia Anakara**

(Meseda, 2016), Volz, Advances in Virus Research, 2017)

MVA Is Severely Attenuated

- **Lost its ability to fully replicate in most mammalian cell types, including human cell lines**

- **Effectively infects mammalian cells**
  - Results in transcription of the viral genes,
  - Virus is NOT released from the cells due to a genetic block in the viral assembly and egress.
  - Infected cells undergo apoptosis (programmed cell death)

- **Severely attenuated from loss of ~15% of the viral genome**
  - mainly host-range and immunomodulatory genes
  - immune evasion genes, host interactive protein genes and some structural proteins.

Volz, Advances in Virus Research, 2017

Testing and Early Use of MVA Vaccine Against Smallpox

- **1971 - 1977:** Tested in humans to be used as a **primary vaccination followed by replicating vaccinia vaccine** *(Stickl and HochsteinMintzel, 1971)*, (Stickl et al., 1974)
- **1977:** Bavarian State Vaccine Institute in Munich obtained the **first marketing authorization for MVA** as primary prevaccine against smallpox in Germany *(Paul-Ehrlich-Institut, 31.01.1977)*
- **By1980: Administered to more >120,000 humans** without documentation of severe adverse events otherwise associated with the use of conventional VACV vaccines *(Mahnel and Mayr, 1994)*.
- **Immunizations with this first licensed MVA vaccine stopped** with the end of the smallpox vaccination program in Germany

Modified Vaccinia Virus Ankara: History, Value in Basic Research, and Current Perspectives for Vaccine Development A. Volz, G. Sutter German Center for Infection Research (DZIF), Institute for Infectious Diseases and Zoonoses, LMU University of Munich, Munich, Germany, 2017

MVA Products

- Licensed as a smallpox vaccine in Europe, Canada, and the US (also MPOX vaccine in the US)

- **Viral vector for vaccine candidates** as it **accommodates heterologous DNA and express encoded proteins**, eg, HIV, MTB, HPV, HCV, P. falciparum, Influenza, MERS, etc.

- **Europe -** approved vector for:
  - 2-part Ebola vaccination (Zabdeno (Ad26.ZEBOV) and **Mvabea Ebola (MVA-BN-Filo)**
  - **animal rabies vaccines in the wild**
  - **European (Western) tick-borne encephalitis (TBE) virus**

- **US - Raboral V-RG, wildlife vaccine bait** for raccoons and coyotes

- **Clinical trials: NIH-sponsored** DOSES study in adults and children 12-17 y.o.; RSV (phase 3 trials); ABNCoV2 (phase 3)

Reduced Risk for Mpox After Receipt of 1 or 2 Doses of JYNNEOS Vaccine Compared with Risk Among Unvaccinated Persons — 43 U.S. Jurisdictions, July 31-October 1, 2022 *(Payne AB et al, MMWR Vol 72, No.49.)*

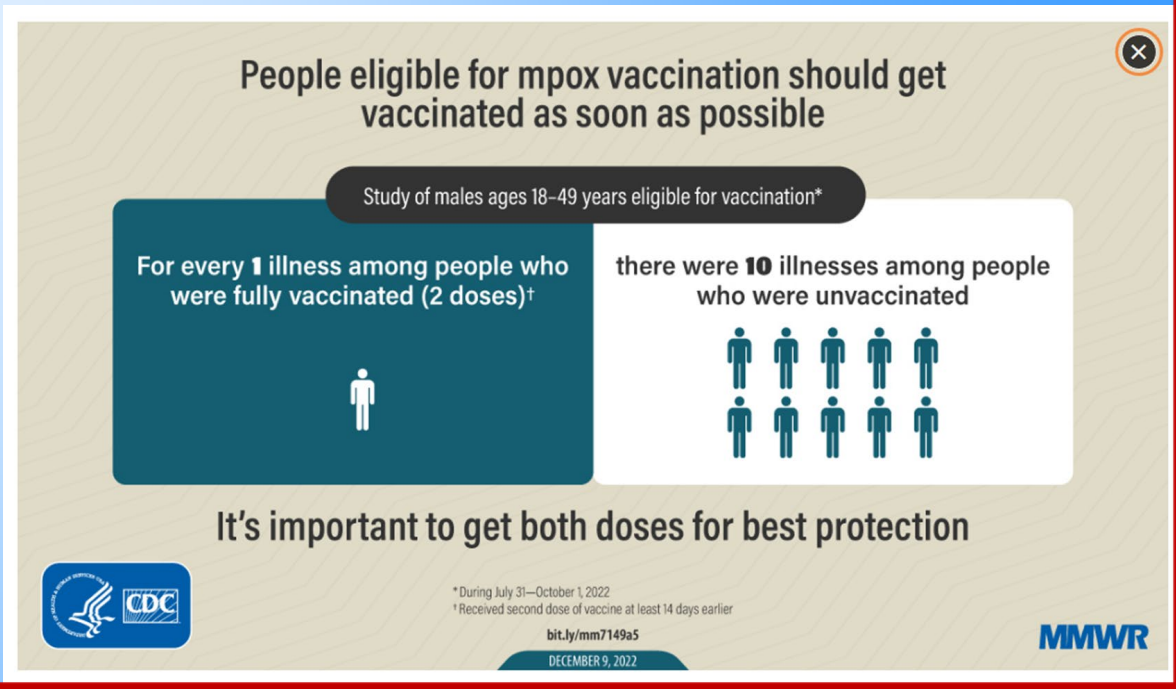
Total mpox cases reported in 18-49 y.o.: 9,544 (82.4% of total cases reported)

- Of these, only **1,224 (12.8%) were vaccinated**
  - Of these, only **1,006 (82.2%) knew their vaccination date**
    - Of these, **392 (39%) developed illness onset ≥ 14 days after dose one**
    - And **48 (12.2%) developed illness onset ≥ 14 days after two**

- Of these, **263 (87.1%) and 39 (12.9%)** rec'd **SC and ID** administration, respectively.

- **Mpox incidence estimates were higher among the unvaccinated** than among those who **received only 1 dose of JYNNEOS (IRR = 7.4; 95% CI = 6.0–9.1)** and among those who **received dose 2 (IRR = 9.6; 95% CI = 6.9–13.2)**

- **No difference in vaccine performance between SC and ID administration.**



Summary

- MVA is less reactogenic than live attenuated replicating vaccinia *(Frey et al, Vaccine 2007, Pittman et al, NEJM 2019)*
- Neutralizing antibody titers after two doses of MVA are non-inferior to those after live attenuated replicating vaccinia *(Frey et al, 2015)*
- One dose of MVA appears to limit mpox disease *(Payne et al, 2022)*
- The lower ID dose of MVA was immunologically non-inferior to the standard SC dose. (*Frey et al, 2015)*

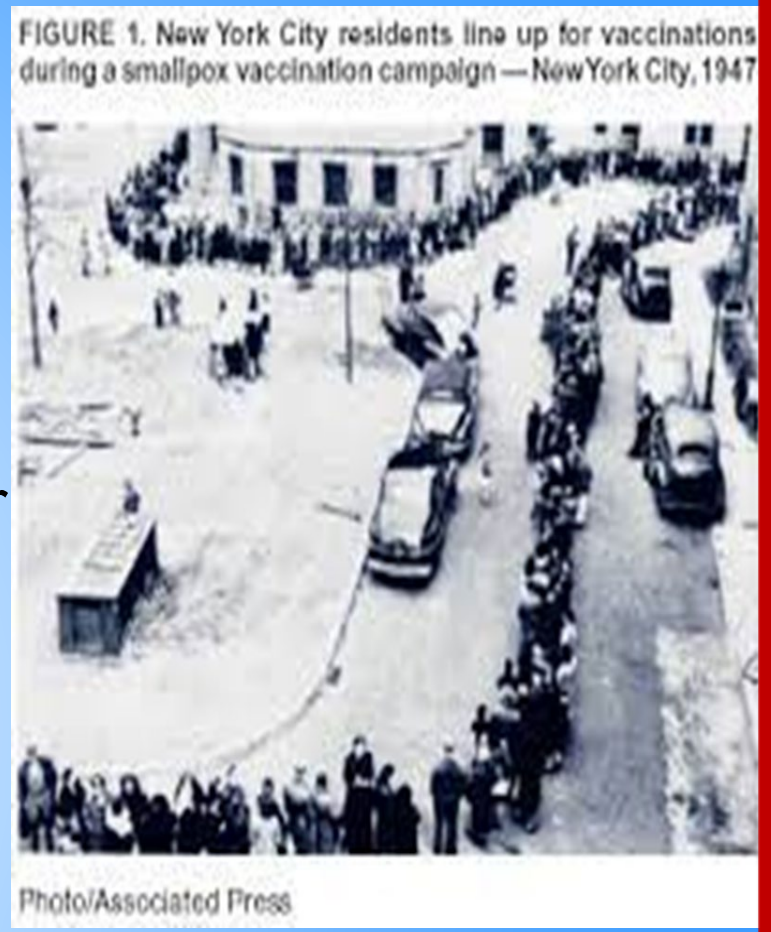


FIGURE 1. New York City residents line up for vaccinations during a smallpox vaccination campaign — NewYork City, 1947

Photo/Associated Press

- The ID route resulted in more erythema and/or induration than the SC route. (*Frey et al, 2015)*
- The ID route can increase the number of available doses in an emergency situation. (*Frey et al, 2015)*

MPX NYC

Community-Led Response to MPOX in New York City.

Keletso Makofane, MPH, PhD

RESPND-MI Study Group

Harvard FXB Center for Health and Human Rights

keletso.makofane@gmail.com

The New York Times

By James Krellenstein, Joseph Osmundson and Keletso Makofane

Mr. Krellenstein, Dr. Osmundson and Dr. Makofane are public health experts and advocates focused on infectious disease prevention.

Novel Infectious Disease

No (plans to collect) Prevalence/Incidence Data

Limited Vaccine Stock

Outdated Understanding of Sex

Creative Requirements + Guidelines

Name

- Convey scientific-rigor and expertise of the survey and its team.
- Build trust with queer NYC community.
- Adaptable to changing nature of the situation.

Design

- Appeal to and build trust with queer NYC community.
- Stand out among crowded online space, where we are recruiting survey takers.
- Push the boundaries where the name can’t.

burness

Newsletters

The Atlantic

to confuse with those of STIs, and their severity. Some of them, including Makofane, are also working to scale up diagnostics, and map the networks that have allowed the poxvirus to spread. That knowledge will hopefully bolster efforts to root out cases and close contacts, get them into isolation and quarantine, and vaccinate the (for now) limited number of vulnerable people.

Epidemiologist @klts0 speaks about how the Biden administration is responding to the monkeypox outbreak.

@MSNBC

JOURNALS

Science

LOG IN

"It's entirely possible for this epidemic to rage among a subset of people just because that subset is connected in a network differently than everyone else," says Keletso Makofane, a social network epidemiologist at the FXB Center for Health and Human Rights at Harvard University. Together with colleagues, Makofane hopes to launch a study in New York City in August to better understand the spread of the disease. "The idea is to get a sense of how many people report symptoms that are consistent with monkeypox and how they are connected," he says.

The New York Times

By James Krellenstein, Joseph Osmundson and Keletso Makofane

Mr. Krellenstein, Dr. Osmundson and Dr. Makofane are public health experts and advocates focused on infectious disease prevention.

RESPND-MI Study Team.

A collective of 19 queer and trans experts in clinical medicine, epidemiology, biostatistics, virology, activism, policy, marketing, and communications innovating community-based participatory research.

Jennifer Barnes-Balenciaga
CO-INVESTIGATOR

Pedro Botti Carneiro, MPH
CO-INVESTIGATOR

Tom Carpino, MPH
CO-INVESTIGATOR

Nicholas Diamond, MPH
CO-INVESTIGATOR

Seema Kara, MPH
CO-INVESTIGATOR

James Krellenstein
CO-INVESTIGATOR

Elle Lett, PhD, MA, MBiostat
CO-INVESTIGATOR

Ken Nadolski, MPH
CO-INVESTIGATOR

Cody Nolan, MD
CO-INVESTIGATOR

Joseph Osmundson, PhD
CO-INVESTIGATOR

Robert Pitts, MD
CO-INVESTIGATOR

Grant Roth, MPH
CO-INVESTIGATOR

Sudipta Saha, MS
CO-INVESTIGATOR

Martez Smith, MSW
CO-INVESTIGATOR

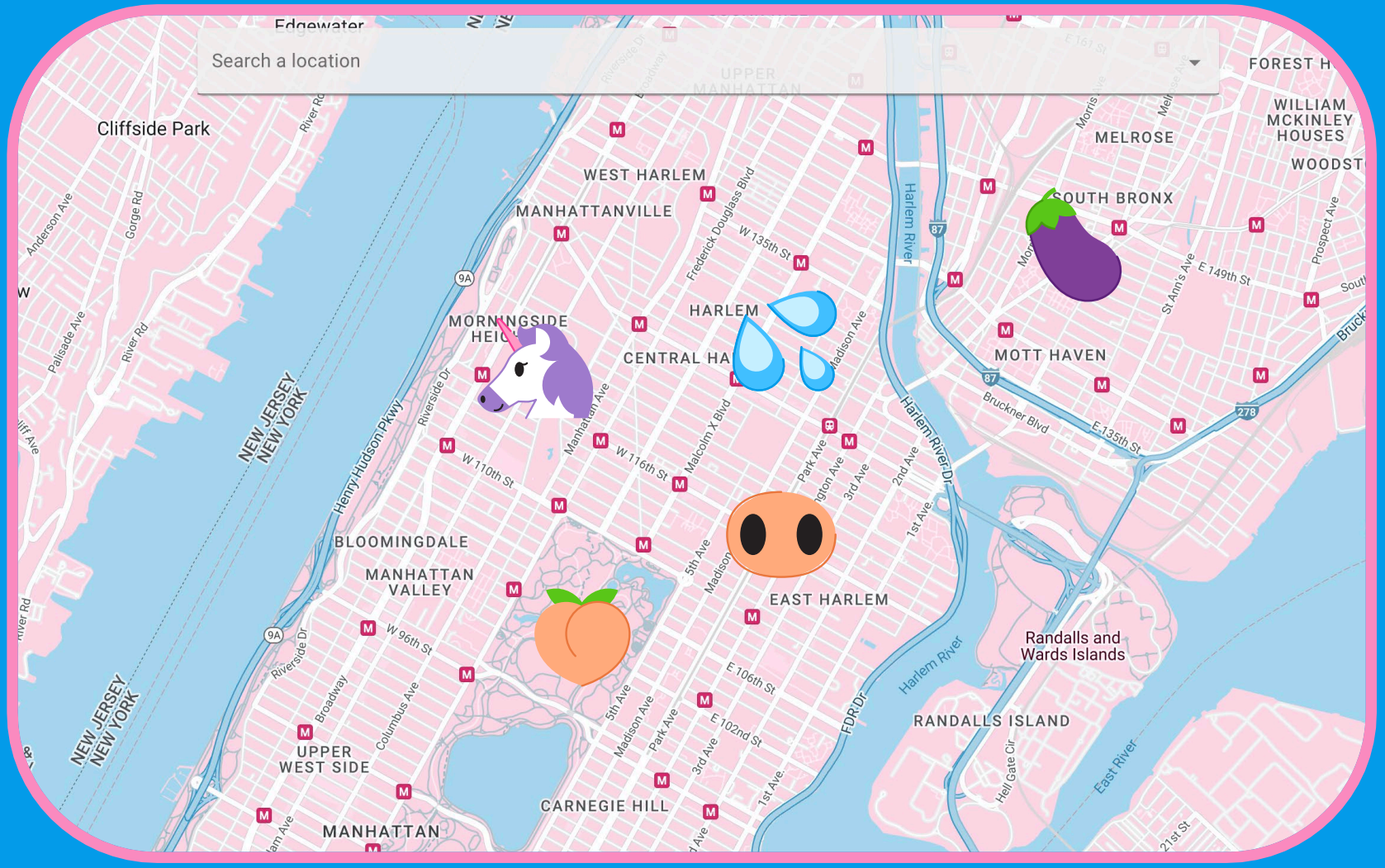
Nguyen Tran, MPH, PhD
CO-INVESTIGATOR

Antón Castellanos Usigli, MPH, PhD
CO-INVESTIGATOR

Chris Wyman
CO-INVESTIGATOR

Keletso Makofane, MPH, PhD
PRINCIPAL INVESTIGATOR, HARVARD UNIVERSITY

Christian Urrutia
PRINCIPAL INVESTIGATOR, PrEP4All



What kind of place is this?

Dance party

Sex party

Darkroom

Sport game

Concert

Theatre/Show

Private residence

Something else

English Survey

for

(Cisgender) Gay and Bisexual Men

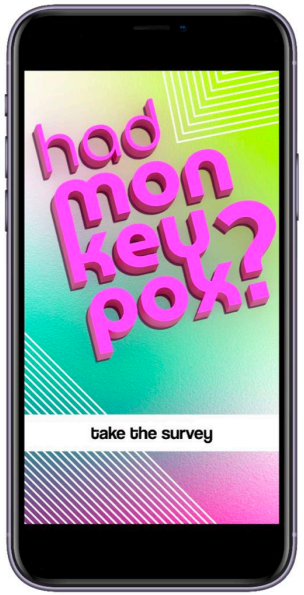
Consultation

English + Spanish Survey

for

Queer and Trans People


MEN
who have
sex
with men
take our survey


had
monkey
pox?
take the survey


Monkeypox
is spreading
in NYC.
take the survey


MPXNYC
take the survey

Grindr

PrEP4All

CFAR
HARVARD UNIVERSITY
CENTER FOR AIDS RESEARCH

amfAR
MAKING AIDS HISTORY

NEW YORK STATE

VE RI TAS

FXB Center
for Health & Human Rights
at Harvard University

Time stolen back from employers of RESPND-MI Investigators

MPOX RESOURCES FOR AND BY QUEER AND TRANS COMMUNITIES.

Click below to access community-led tools for prevention, vaccines, treatment, and policy.

MPOX Vaccine Locator

So You Got MPOX

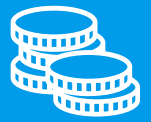
Six Ways We Can Have Safer Sex in the Time of MPOX

An Open Letter to Drs. Vasan and Bassett

An Open Letter to the Biden Administration on MPOX

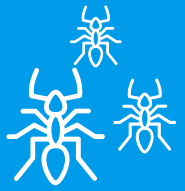
a community-led response to MPOX:

Consultation



Resourcing

Surveillance



Coordination

rooted in global health advocacy principles.

- Consultation
- Resourcing
- Surveillance
- Coordination

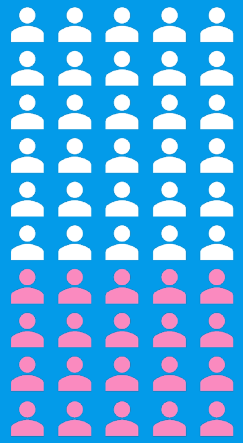
MPX NYC

1500

respondents

40%

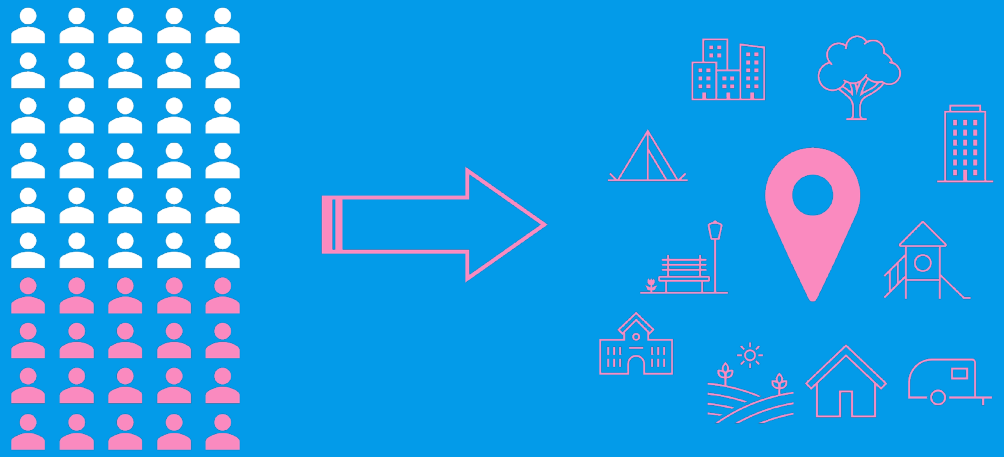
reported
group sex or physical contact



MPX NYC

group sex or physical contact
happened in

700
places



MPX NYC 101

5 actionable insights.

(from MPX NYC Data)

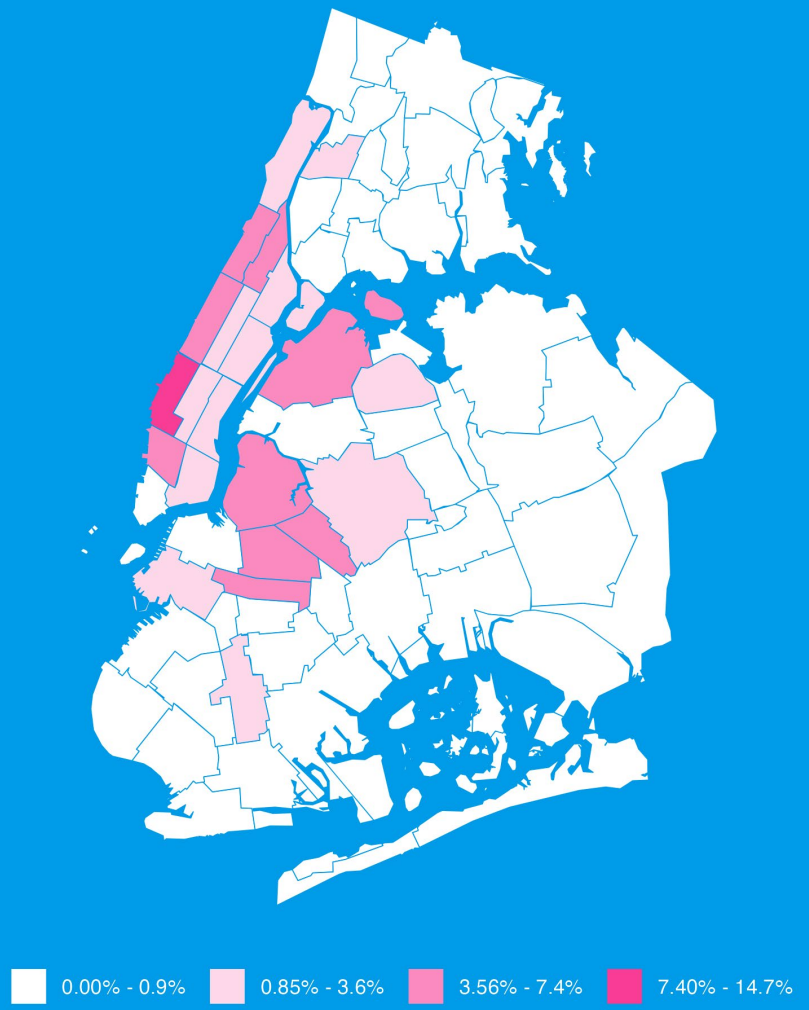
1. Most group sex happens in private residences, not public venues...

60%

of places* were private residences

*named by people who reported sexual contact

2. queer and trans people's residences cluster in certain parts of the city...



... but subgroups do not all cluster in the same places.

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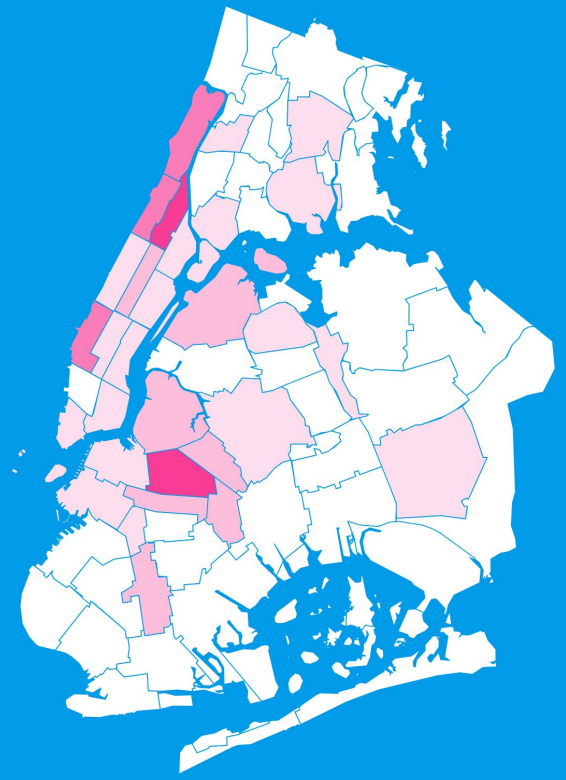
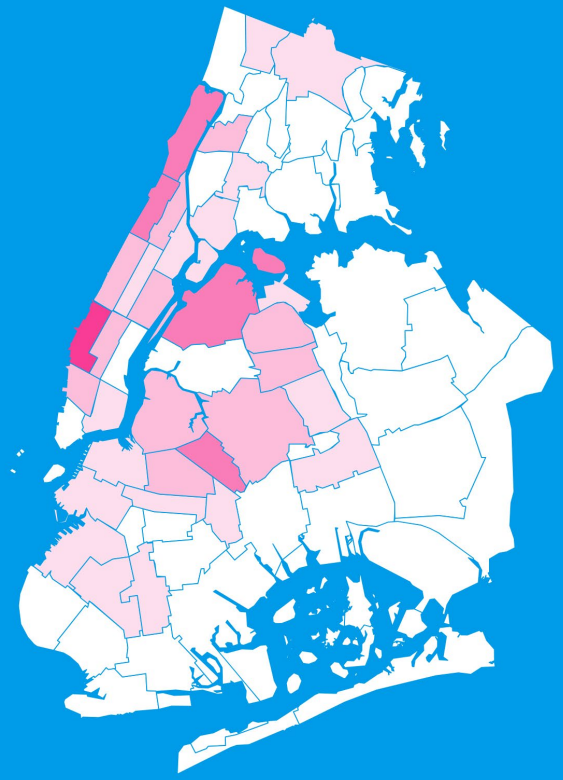


Latinx



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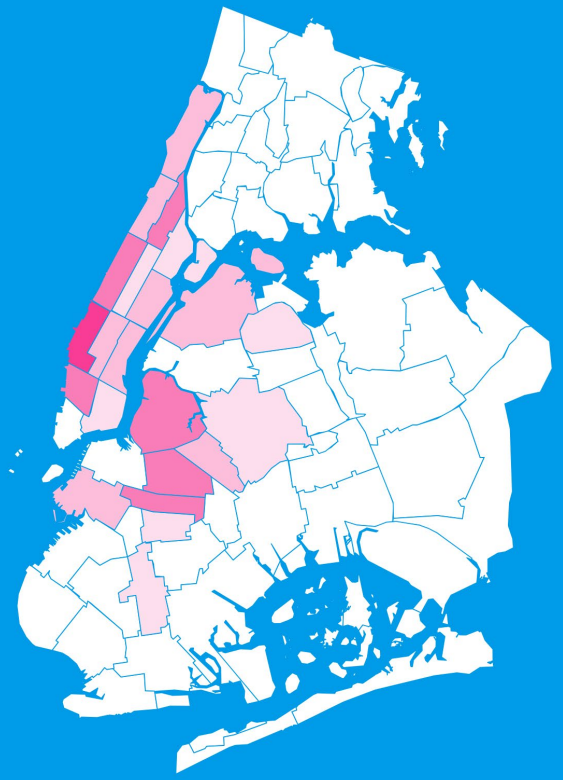
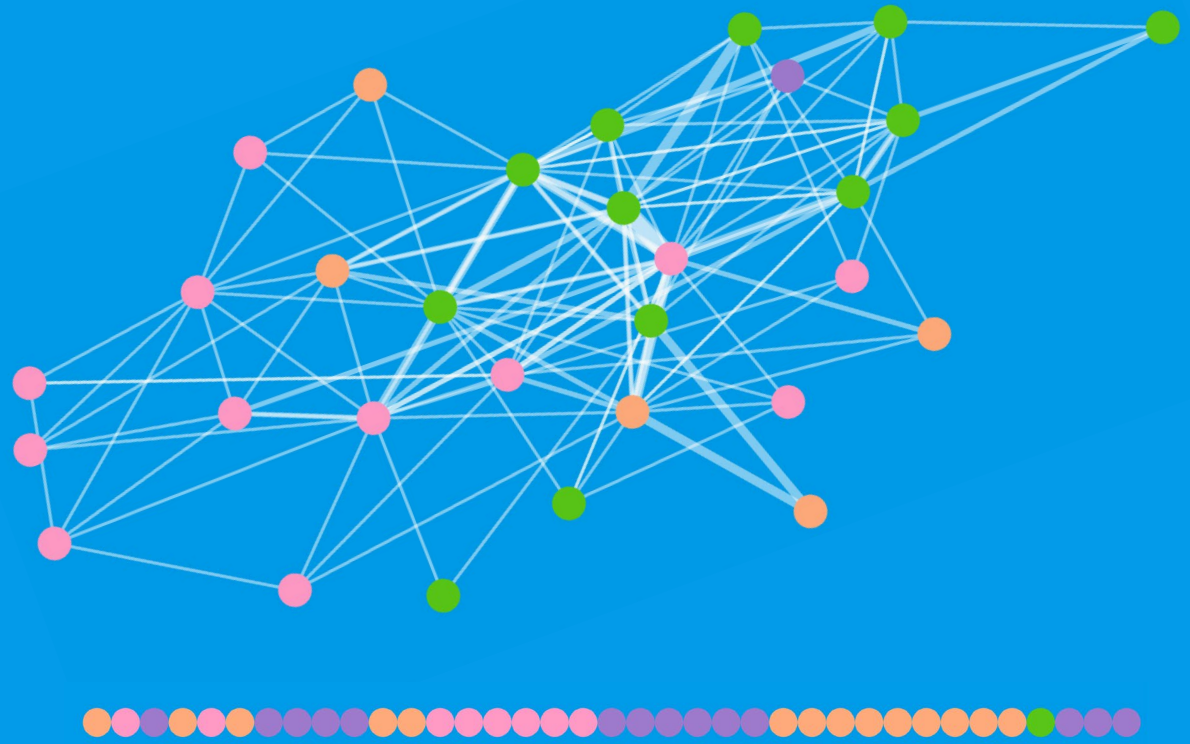
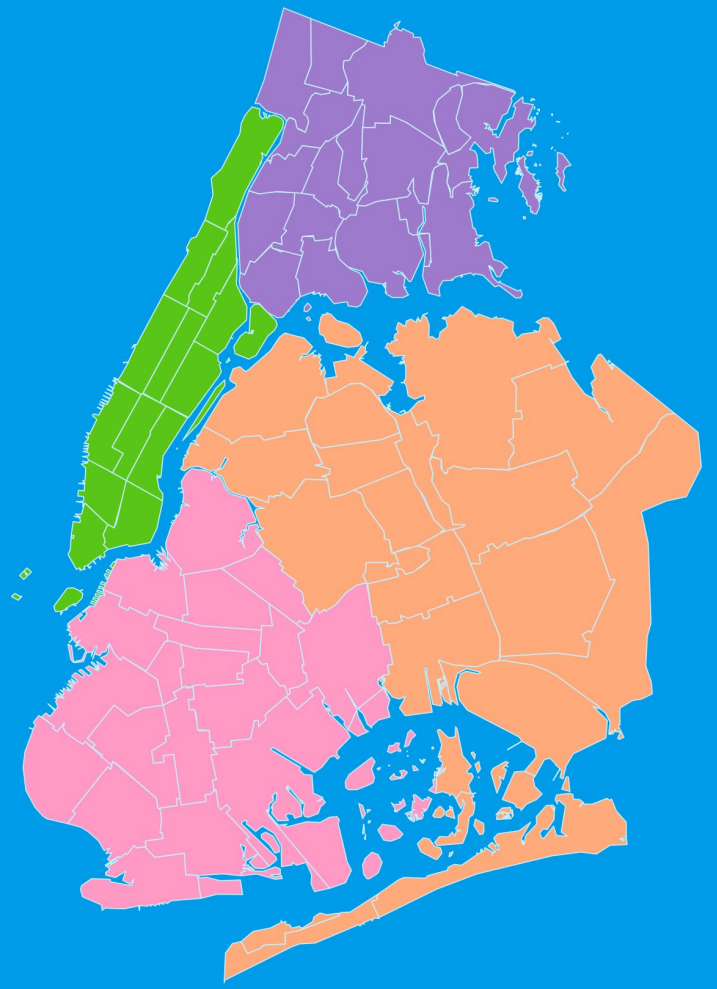
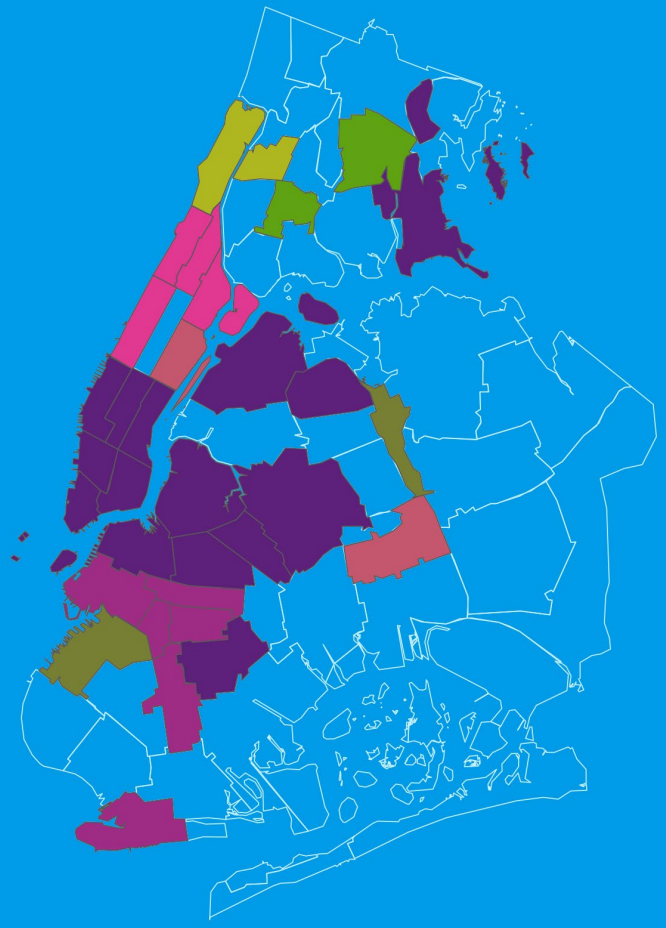


3. communities are connected by individuals who move through them...

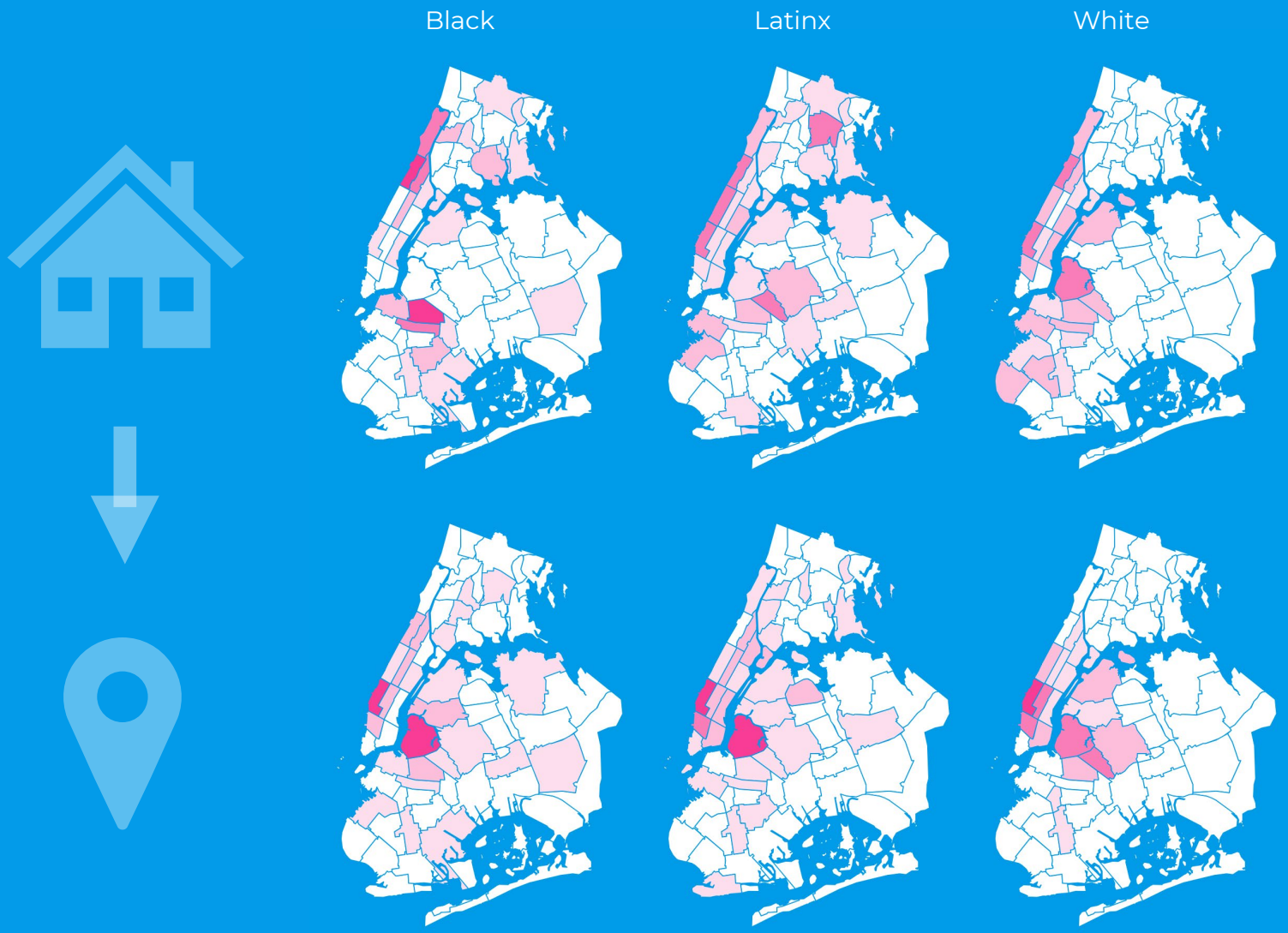




... so we can figure out which groups of communities are more densely connected to each other.



4. Some communities are popular across different subgroups



... but subgroups also have distinct preferences.

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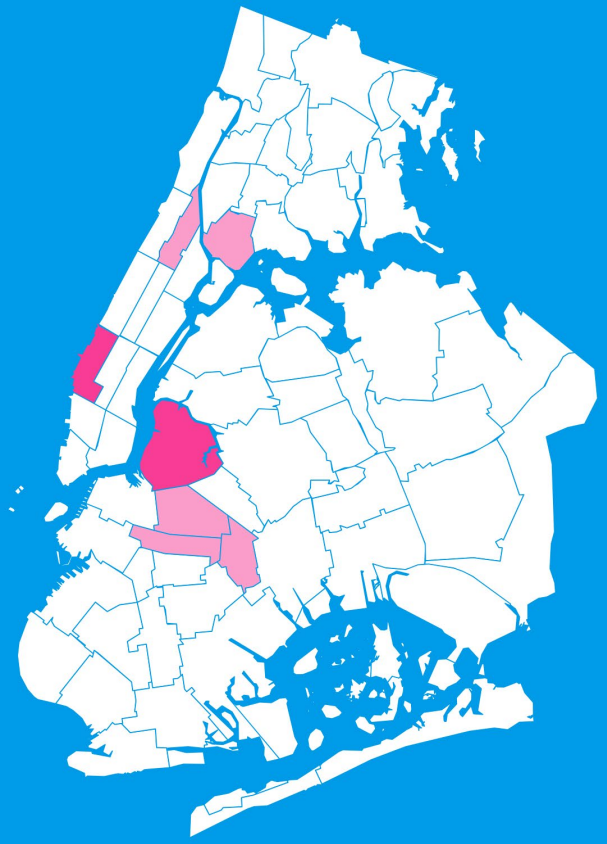
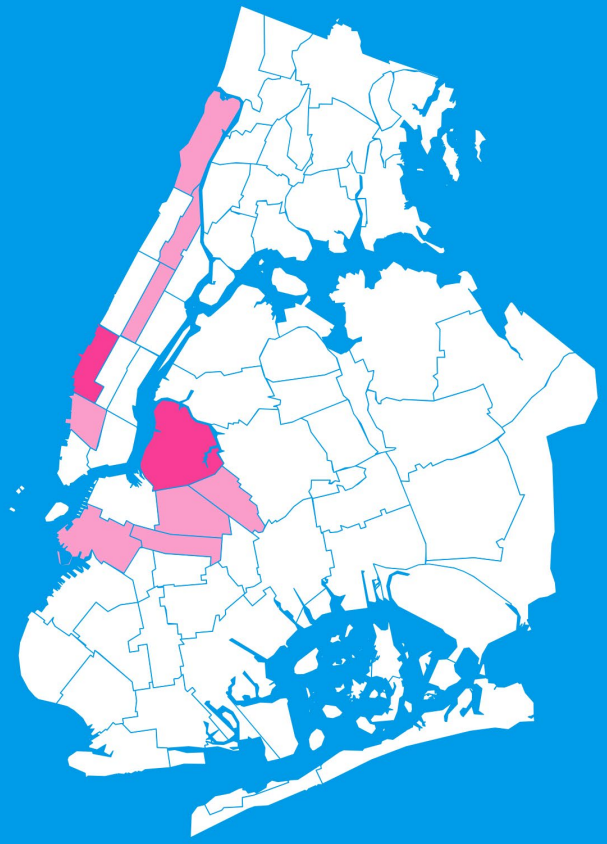


Latinx



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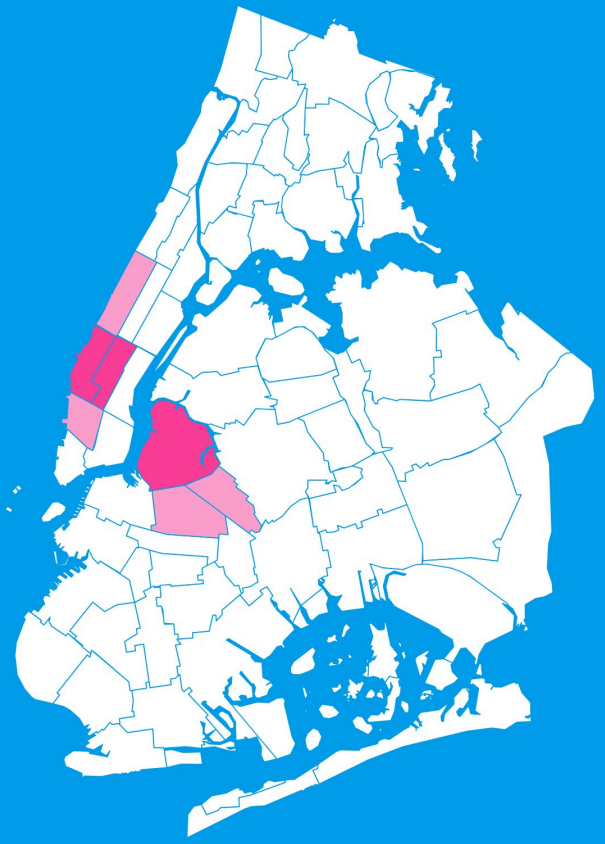

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5. we can use the subway to make intervention plans by subgroup.

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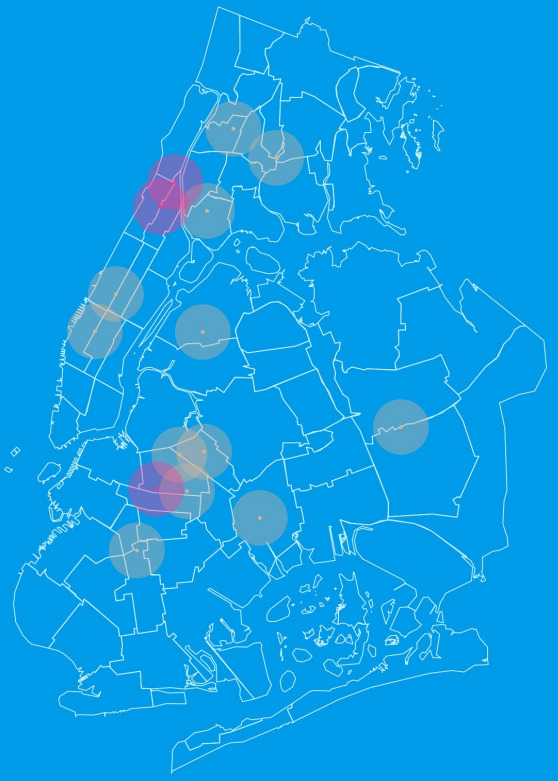

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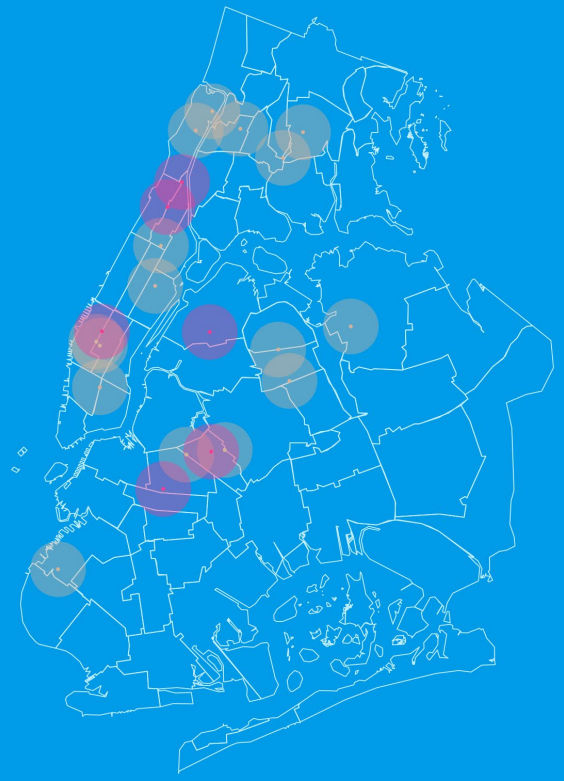

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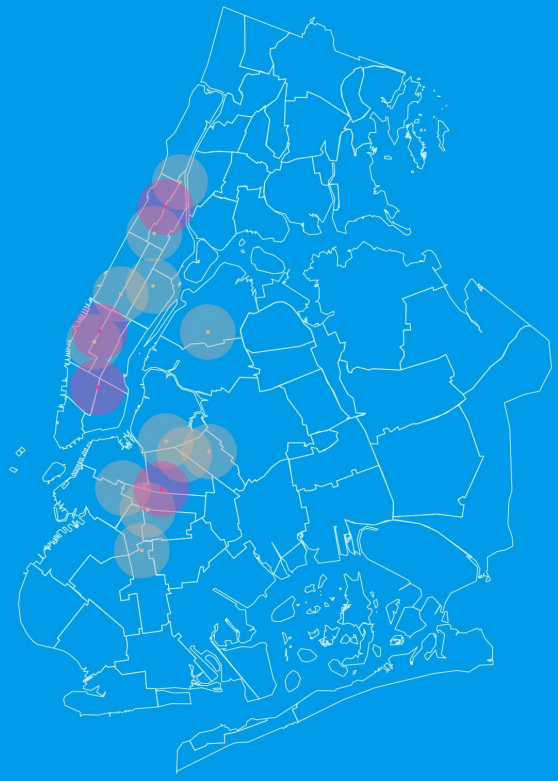

First Third Second Third

Thank you !

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https://www.mpxresponse.org