MPOX: Epidemiology, Clinical Presentation, Treatment, and Prevention

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01. EPIDEMIOLOGY

#39, STAGE THE SETTING: THE EPIDEMIOLOGY OF THE MPOX VIRUS John Brooks

#209, HOUSEHOLD TRANSMISSION OF MPOX TO CHILDREN AND ADOLESCENTS – Bazzy A

02. CLINICAL PRESENTATION AND TREATMENT

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#40, MOLECULAR PATHOGENESIS AND THERAPEUTIC TARGETS FOR MPOX VIRUS Stuart N. Isaacs

03. VACCINE EFFECTIVENESS

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Mpox case count: 86,173 as of 3-mar-2023

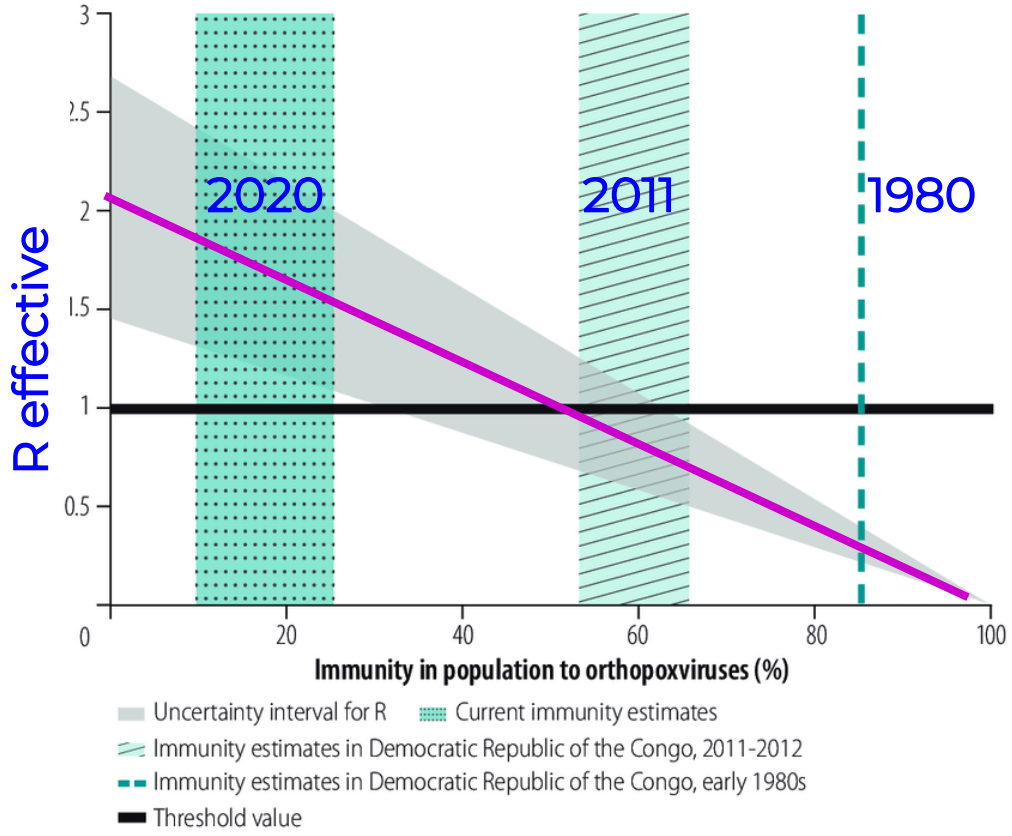
Country	Case count
United States	30,193
Brazil	10,808
Spain	7,538
Colombia	4,080
Mexico	3,828
Peru	3,752
United kingdom	3,735

Number of deaths	Countries
1	Cuba, Belgium, Czechia, India, CAR, Sudan, Mozambique
2	Chile, Argentina
3	Ecuador, Spain, Cameroon
4	Ghana, Mexico
8	Nigeria
15	Brazil, Peru
34	United States

Source: 2022 Mpox Outbreak Global Map / CDC and WHO

In absence of immunity there is a risk for an outbreak if the number of contacts is higher than 14

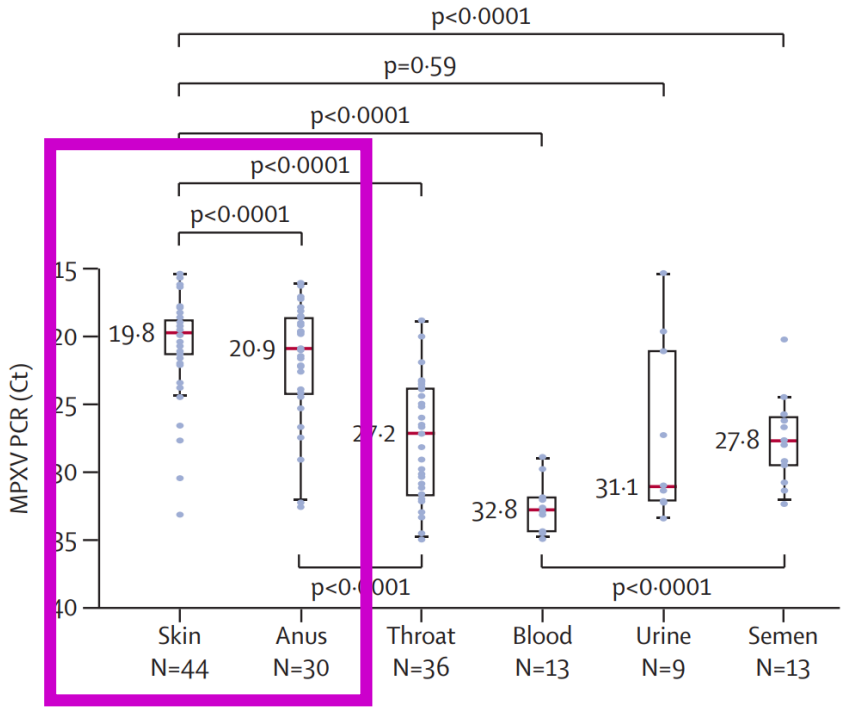
Rt effective
- Ro
- Population immunity
- Population interaction



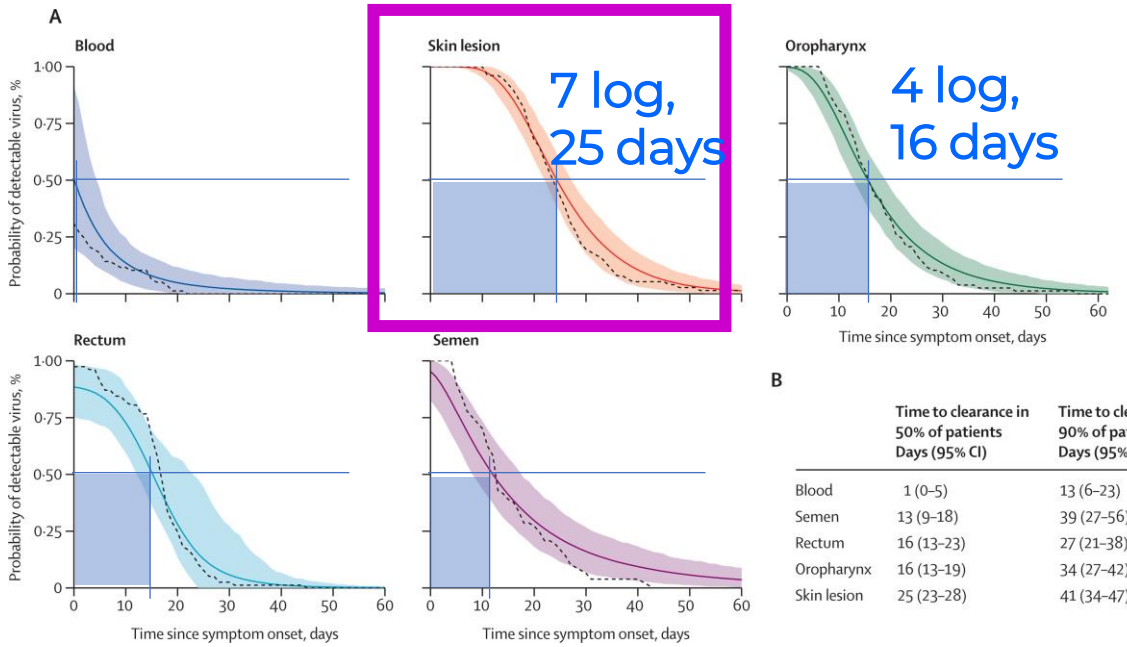
Source: Reynolds Op Virol 2012. Grant et al BWHO 2022.

Exposure of skin and anorectum carries greatest risk of transmitting infection

Skin and anorectal samples have highest viral burden



Time to clearance in 50% of patients is longer in skin samples



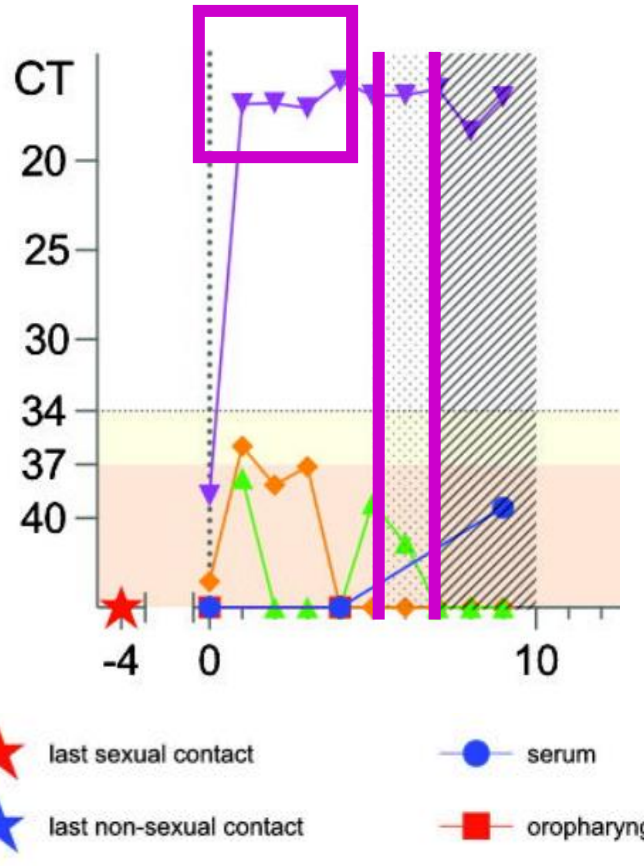
B

	Time to clearance in 50% of patients Days (95% CI)	Time to clearance in 90% of patients Days (95% CI)	Time to clearance in 95% of patients Days (95% CI)
Blood	1 (0–5)	13 (6–23)	20 (10–39)
Semen	13 (9–18)	39 (27–56)	53 (34–84)
Rectum	16 (13–23)	27 (21–38)	31 (23–42)
Oropharynx	16 (13–19)	34 (27–42)	42 (32–53)
Skin lesion	25 (23–28)	41 (34–47)	47 (38–56)

1663 samples were collected from 77 study participants

Source: Palich et al. Lancet Infet Dis 2022. Suñer et al Lancet Inf Dis 2022.

Some people can transmit mpox before they develop symptomatic illness



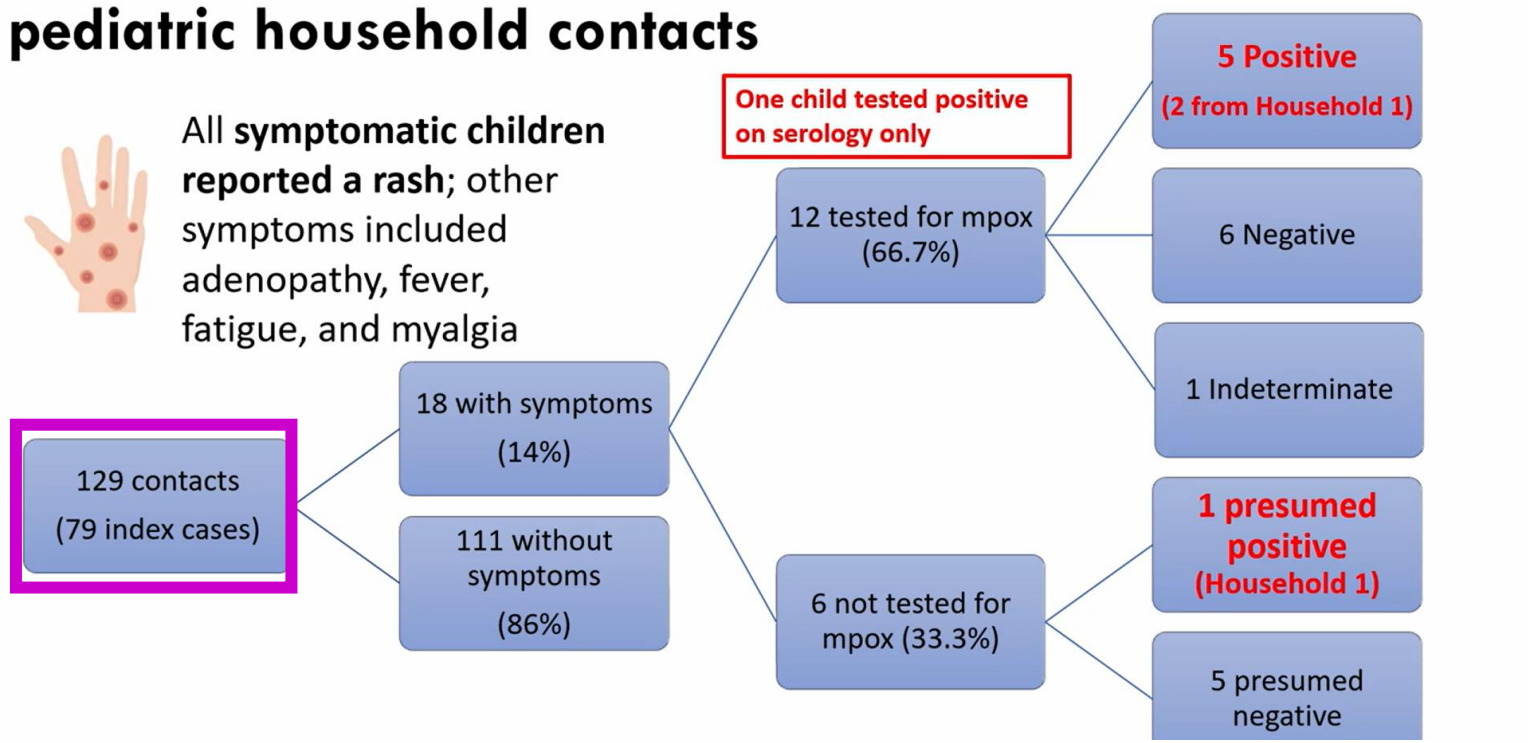
Prospective follow up of 25 individuals after high-risk exposure, daily swabs, 13 had MPXV PCR+ results

High concentrations of DNA were detectable in some 5/6 patients with symptoms up to 4 days earlier

Another study on asymptomatic carriage, 13/200 (6,5%) MPXV PCR+

Source: Brosius et al. medRxiv. Ferré et al. Annal Int Med 2022.

Contact tracing outcomes of 129 children



RESULTS

6 infected pediatric contacts were identified

Attack rate 4.7%

Range of 2 -9 years old

Children had direct contact with parenting adults

Mpox epidemiology

- MPXV DNA is detected more frequently, at higher viral loads and during more time in the skin compared to other body parts.
- Subclinical or asymptomatic infection could contribute to outbreak spread.
- Risk of transmission can vary in diferent settings and household transmission has been rare in 2022.

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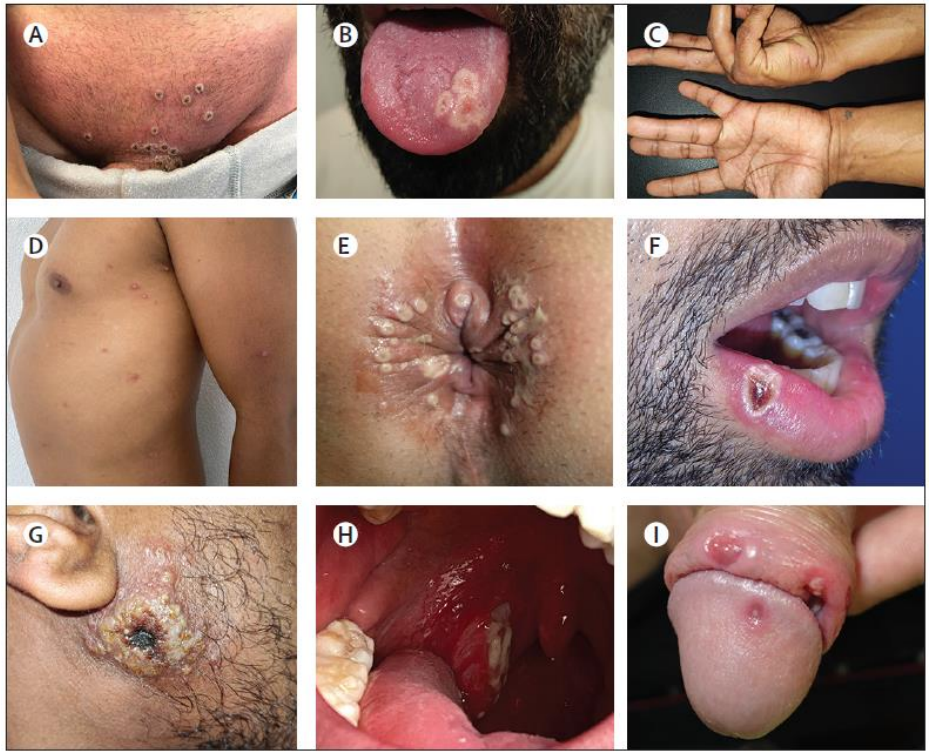
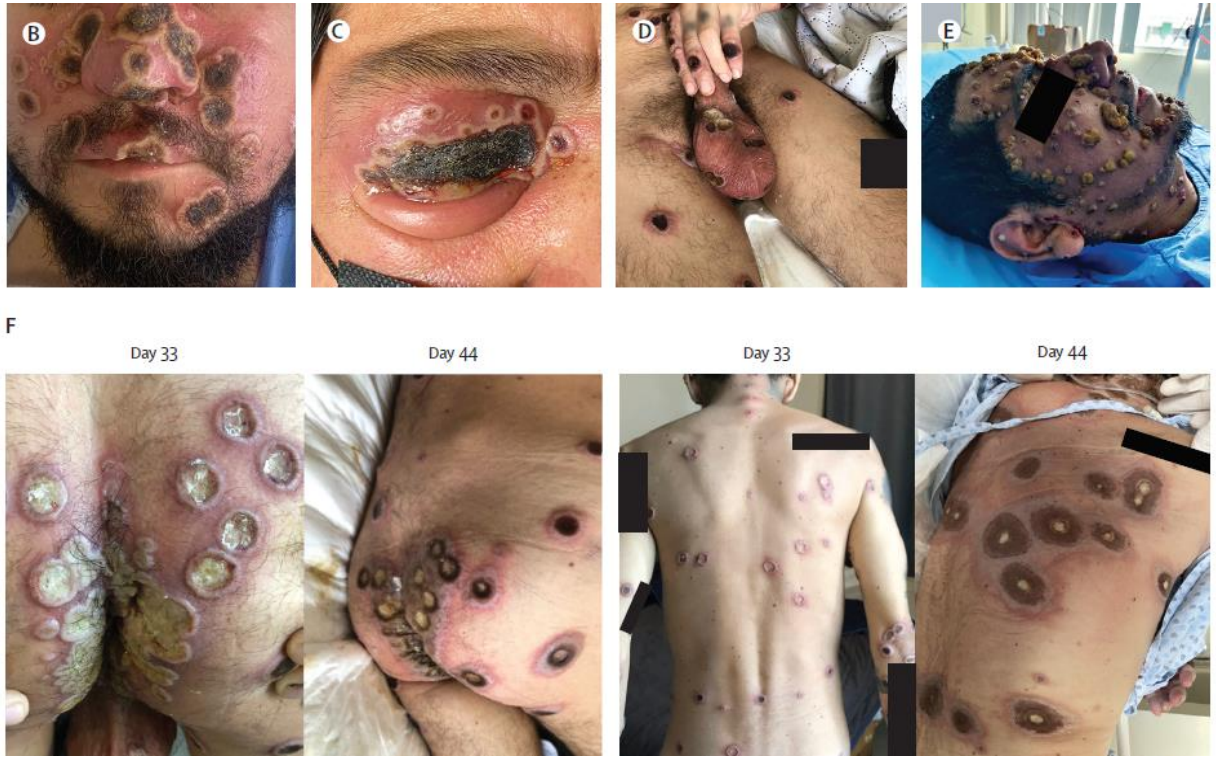
Clinical presentation of human mpox cases in Spain



Mpox in people with advanced HIV infection, Global Series



Source: Tarin Vicente et al. Lancet 2022. Mitja O et al. Lancet 2023.

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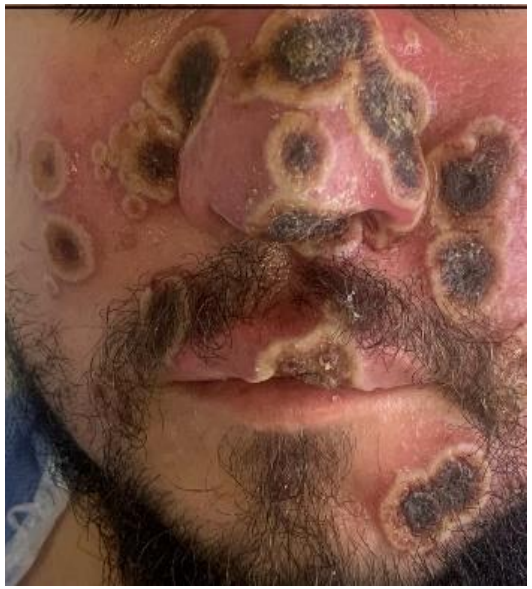
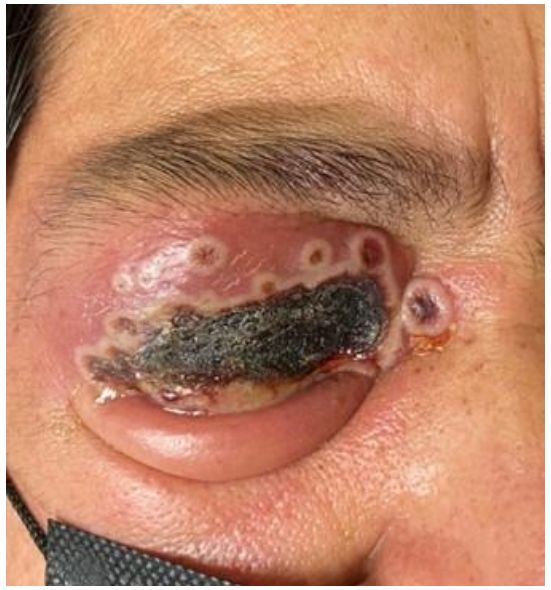
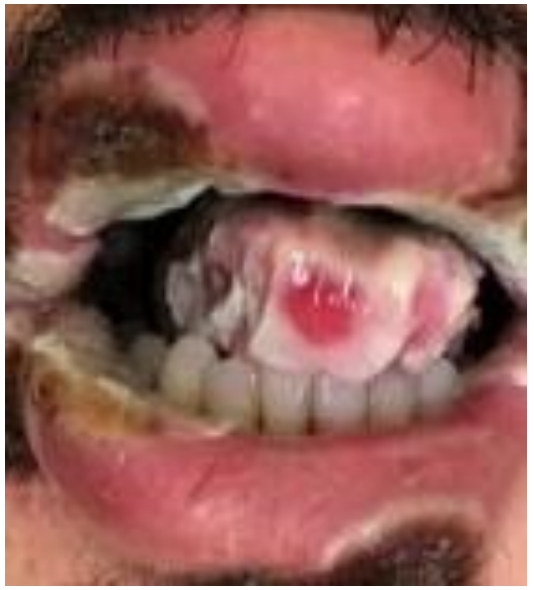

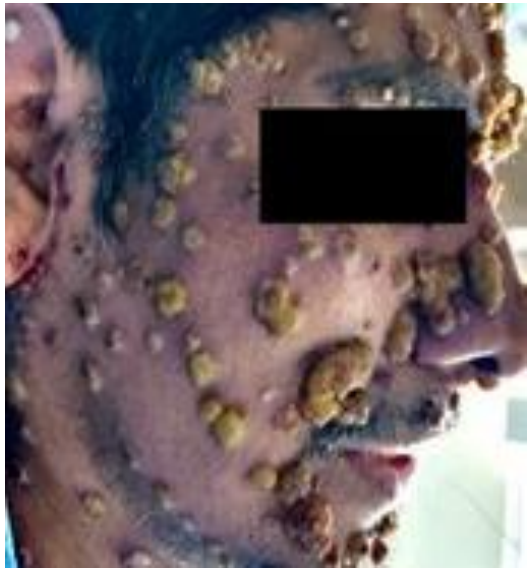
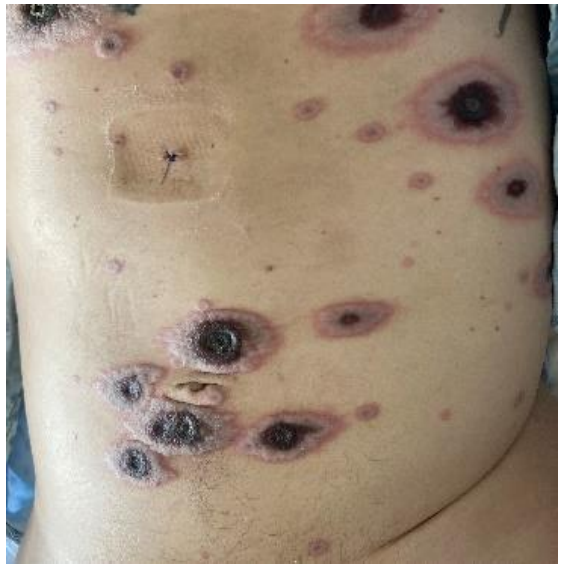
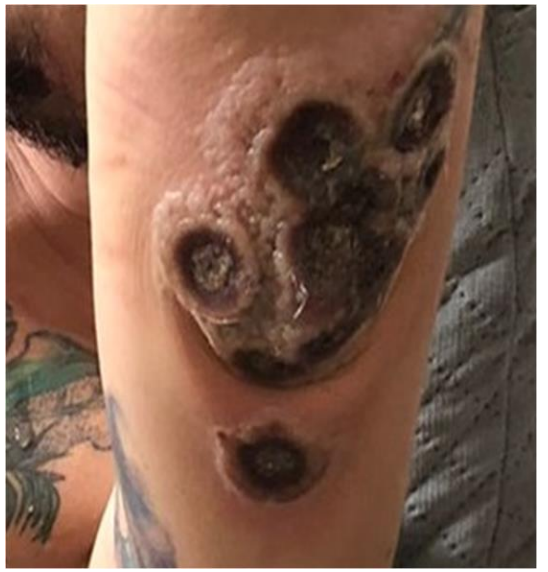
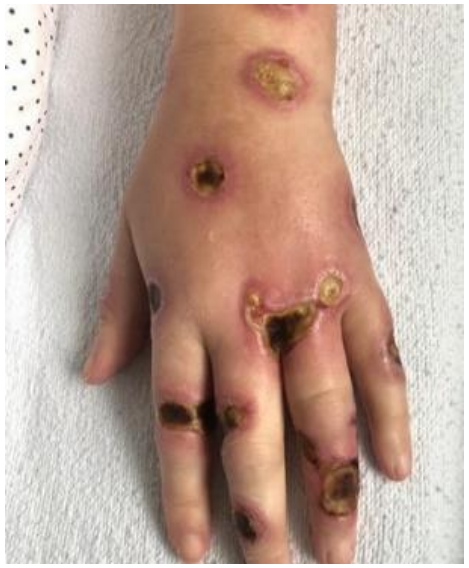

Source: Mitja O et al. Lancet 2023.

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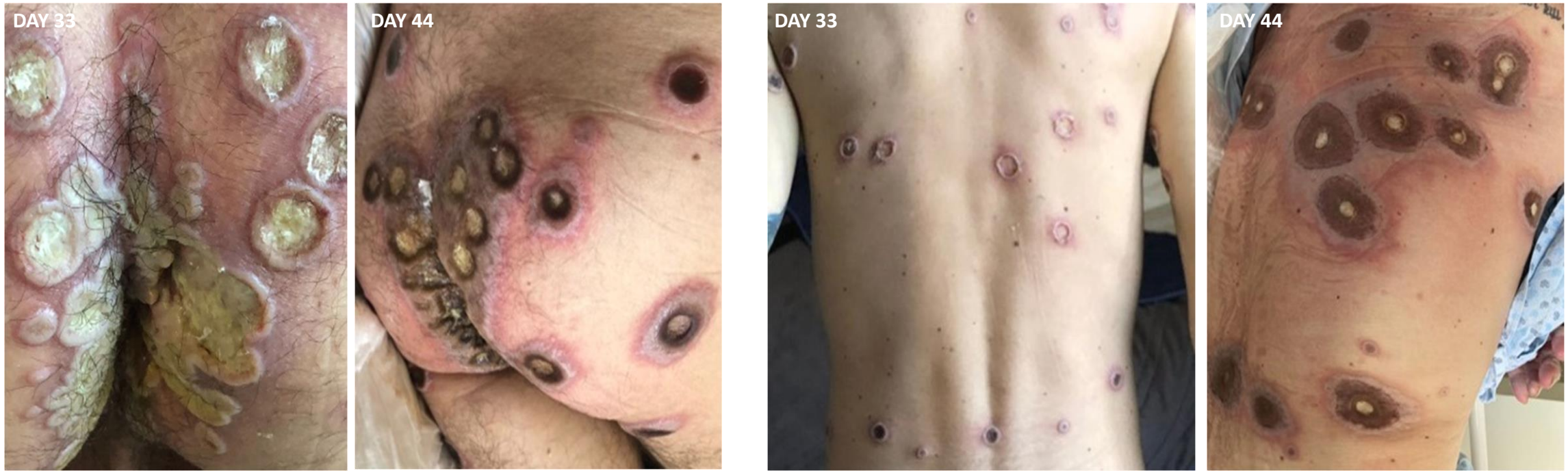

Lancet 2023;

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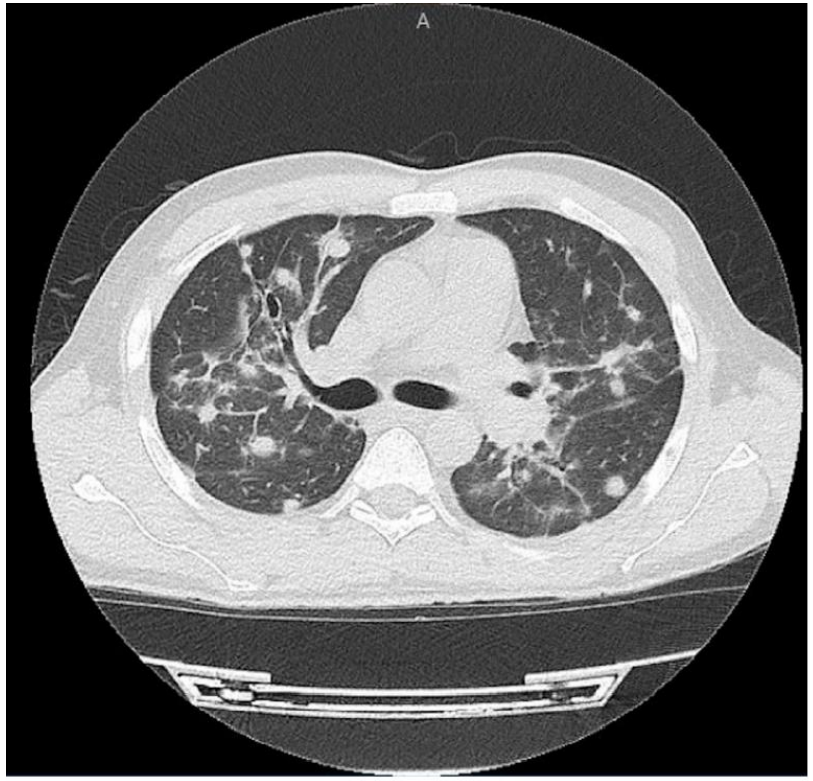
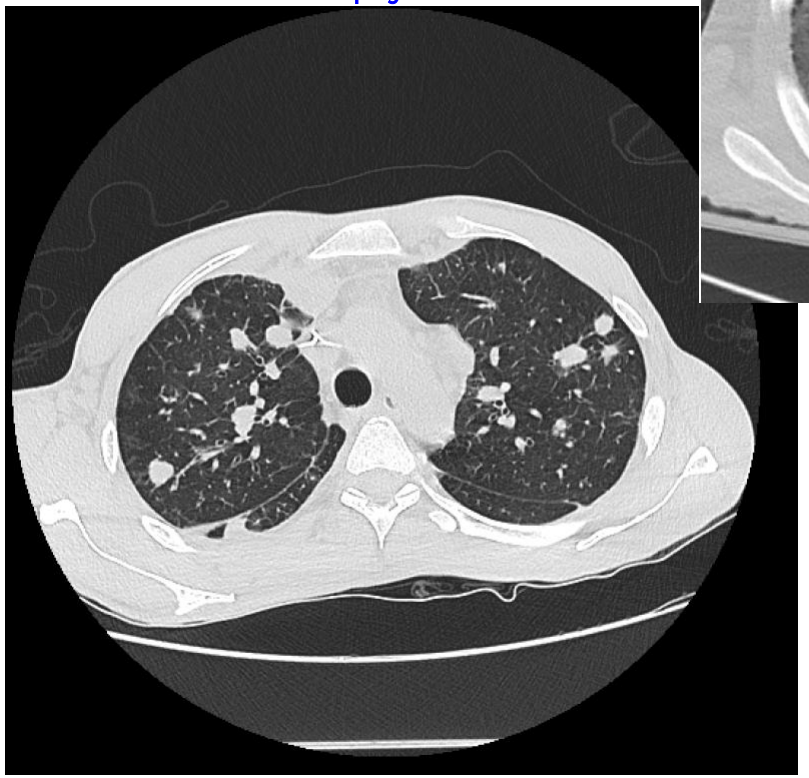
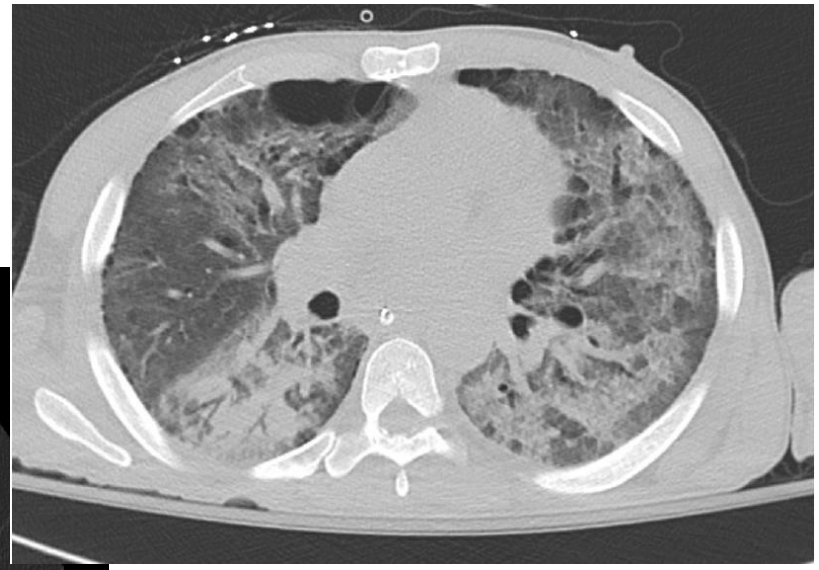
Perivascular nodules with MPXV PCR + in BAL



Perivascular nodules with MPXV PCR + in transthoracic biopsy



Ground-glass opacification and emphysematous changes with MPXV PCR + in BAL



Source: Mitja O et al. Lancet 2023.

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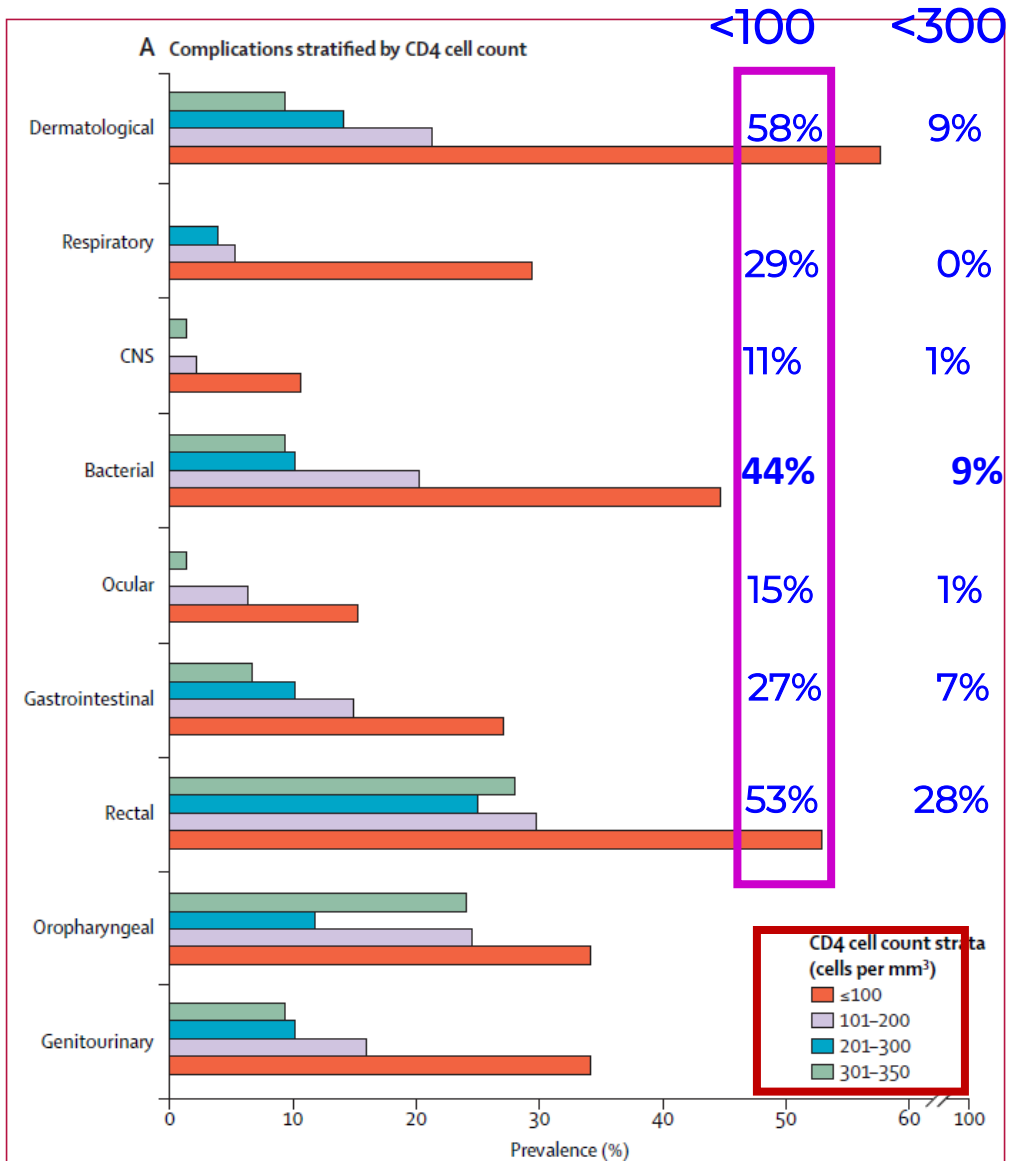
Necrotizing mpox as a new form of disease

	Total (n=382)	CD4 <100 cells per mm³* (n=85)	CD4 100–200 cells per mm³ (n=94)	CD4 201–300 cells per mm³ (n=128)	CD4 >300 cells per mm³ (n=75)
Median age, years	35 (30–43)	35 (32–43)	35 (29–42)	34 (31–42)	36 (30–44)
Newly diagnosed with HIV infection	33 (9%)	15 (18%)	8 (9%)	3 (2%)	7 (9%)
CD4 cell count (cells per mm³)	211 (117–291)	47 (27–77)	156 (125–184)	259 (221–280)	326 (316–338)
CD4 count among 27 people who died, (cells per mm³)	35 (IQR 24–100)	32 (20–64)	118 (112–134)	..	..
HIV viral load strata RNA copies per mL					
Not available	28 (7%)	11 (13%)	4 (4%)	10 (8%)	3 (4%)
<50	193 (51%)	14 (16%)	50 (53%)	80 (63%)	49 (65%)
50–200	26 (7%)	3 (4%)	6 (6%)	8 (6%)	9 (12%)
201–log4	30 (8%)	10 (12%)	6 (6%)	10 (8%)	4 (5%)
≥log4	105 (27%)	47 (55%)	28 (30%)	20 (16%)	10 (13%)
Mpox rash presentation					
Peak number of skin lesions	15 (8–35)	30 (15–100)	20 (12–35)	12 (6–20)	10 (4–15)
Rash duration in days	23 (18–33)	31 (21–45)	26 (19–40)	21 (16–28)	21 (15–30)



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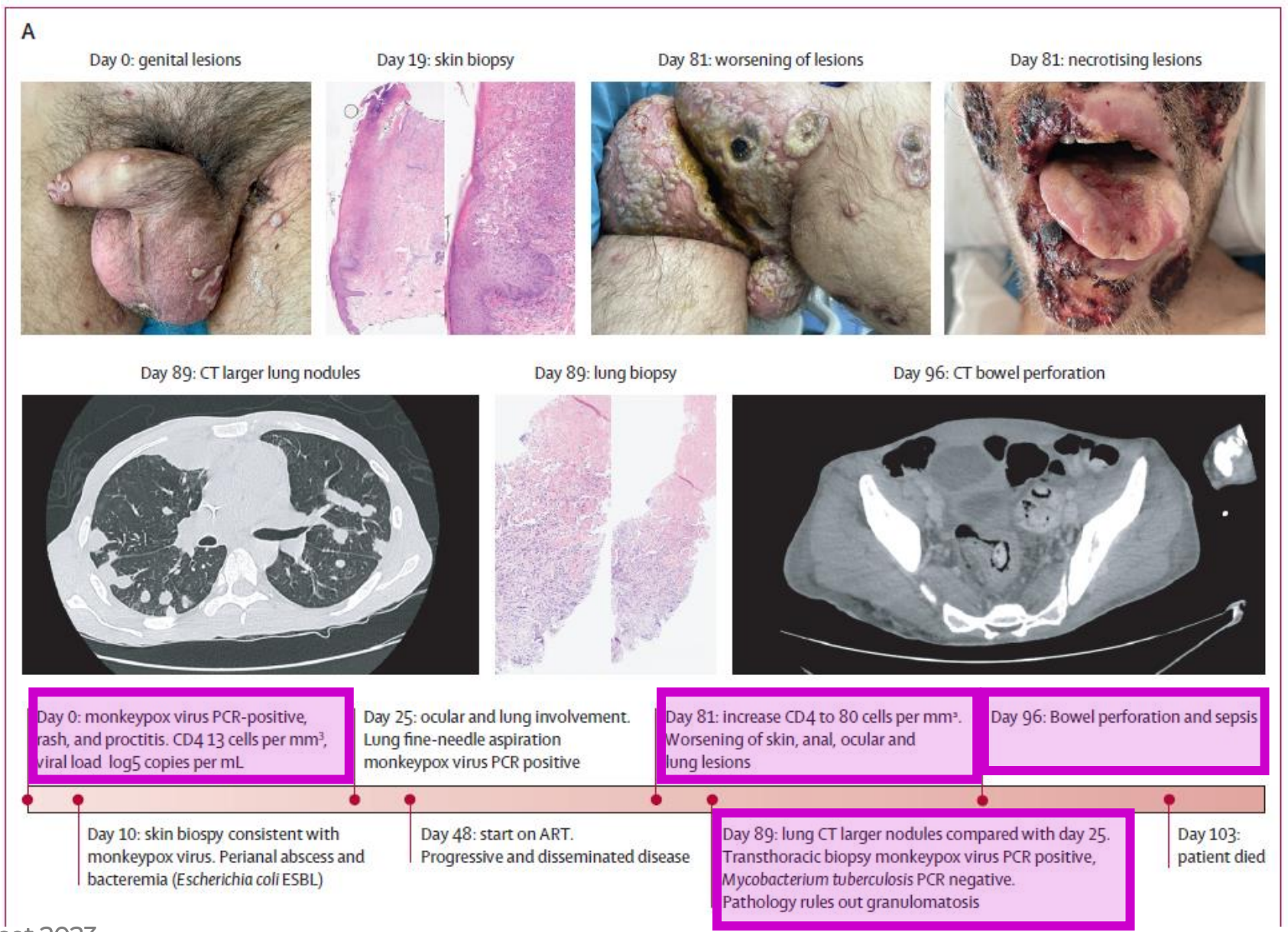

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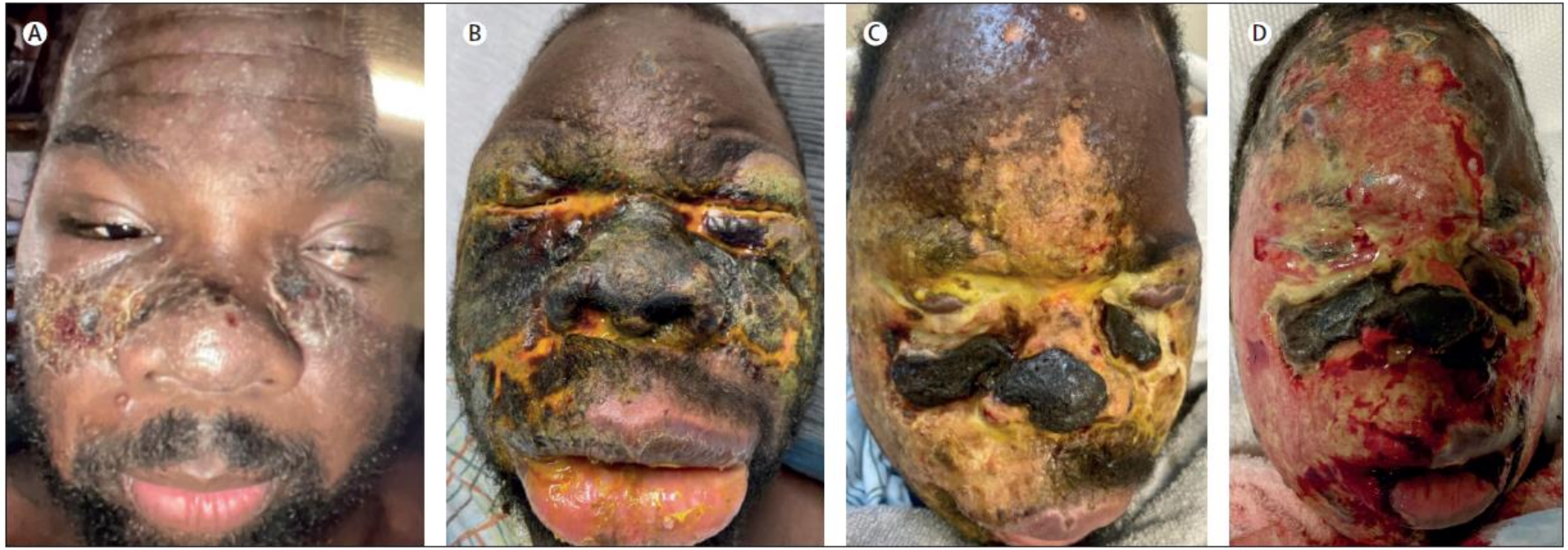

Figure 1: **Chronological progression of mpox facial rash (patient one)**
(A) 1 week after symptom onset: ulcerated vesiculopapular rash involving the malar areas and nasal bridge. Surrounding umbilicated papules. Left-sided periorbital oedema. Image courtesy of patient submission. (B) 3 weeks after symptom onset: confluent necrotic facial rash sparing the forehead with overlying honey-colored exudate. Upper and lower eyelids are oedematous, fibrotic, and immobile. There is substantial angio-oedema of the lips. (C) 7 weeks after symptom onset: prominent eschars of the nasal and malar aspects. Increased purulent exudation overlying necrotic skin. Progressive ulceration of the eyelids and distortion of periorbital contour. (D) 11 weeks after symptom onset: panfacial skin sloughing with obfuscation of baseline features. Patient passed away 1 week later.

Source: Carubba at al. Lancet Inf Dis 2023.

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Highest care level					
Outpatient	275 (72%)	32 (38%)	69 (73%)	111 (87%)	63 (84%)
Hospitalisation in general ward	73 (19%)	26 (31%)	19 (20%)	16 (13%)	12 (16%)
Intensive care unit§	34 (9%)	27 (32%)	6 (6%)	1 (1%)	0
Ultimate Outcome					
Death§	27 (7%)	23 (27%)	4 (4%)	0	0

15% (27/179) death rate when CD4 count <200 cells/mm3; median time to death 47 days

	Total (n=382)	CD4 <100 cells per mm³* (n=85)	CD4 100–200 cells per mm³ (n=94)	CD4 201–300 cells per mm³ (n=128)	CD4 >300 cells per mm³ (n=75)
(Continued from previous page)					
Antimicrobial and antiviral treatment					
Antibiotics	144 (38%)	52 (61%)	34 (36%)	38 (30%)	20 (27%)
Tecovirimat (oral)	52 (14%)	21 (25%)	11 (12%)	15 (12%)	5 (7%)
Tecovirimat (intravenous)	15 (4%)	13 (15%)	1 (1%)	1 (1%)	0

11/30 (33%) people CD4 <100 died despite receiving Tecovirimat

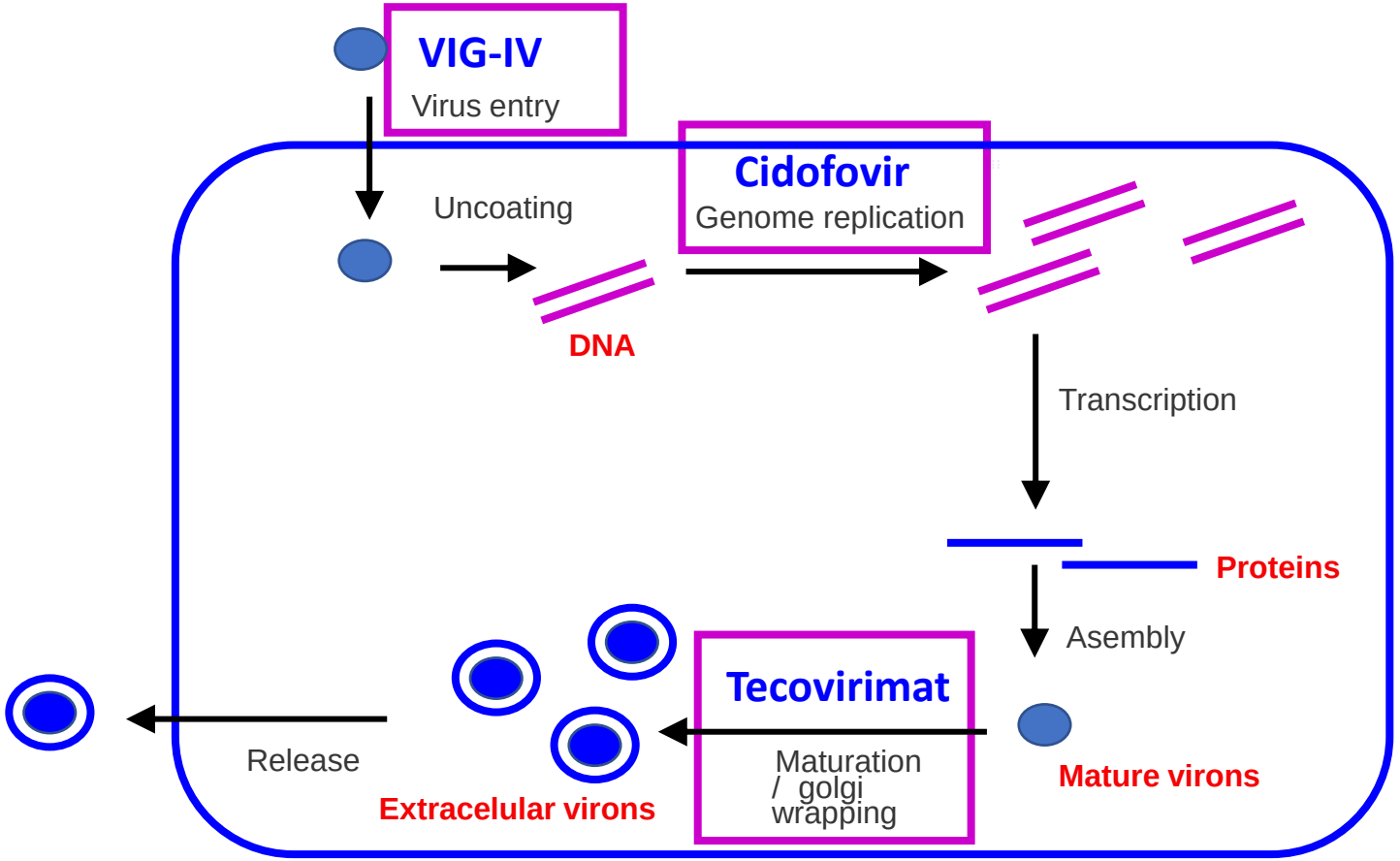
Genotypic resistance to tecovirimat, n					
Samples sequenced	5	4	1	0	0
Presence of F13L mutations conferring resistance	3	3	0	0	0

Immune restitution inflammatory syndrome					
Antiretroviral started or restarted	85 (22%)	40 (47%)	23 (24%)	15 (12%)	7 (9%)
Deterioration consistent with immune restitution inflammatory syndrome	21 (5%)	15 (18%)	6 (6%)	0	0

Mpox IRIS, median time 14 days from ART start, with 57% (12/21) mortality rate

Source: Mitja O et al. Lancet 2023.

Tecovirimat has low barrier to resistance and may be less efficacious in immunocompromised



Source: Brosius et al. medRxiv

Mpox clinical presentation and treatment

- Necrotizing mpox behaves as an AIDS-defining condition

- Recommendations for people with HIV and CD4 <200 and development of guidelines with best practices:
  - Every case of mpox **should be tested for HIV and CD4.**
  - Prioritize for tecovirimat (possibly to every case CD4<200), and consider adding a second antiviral agent.
  - Use antibiotic coverage early in the course of an infection.
  - Best chance of curing infection is a funcional immune system, but be aware of potential of deterioration related to IRIS

- Data on the efficacy of Tecovirimat for mpox is limited (STOMP-US, PLATINIUM-UK, PALM007-RDC) and **PROTECT-HUGTiP (Prioritize Tecovirimat for Advanced HIV).**

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High effectiveness of first and second generation vaccines, 66% and 72%

METHODS:

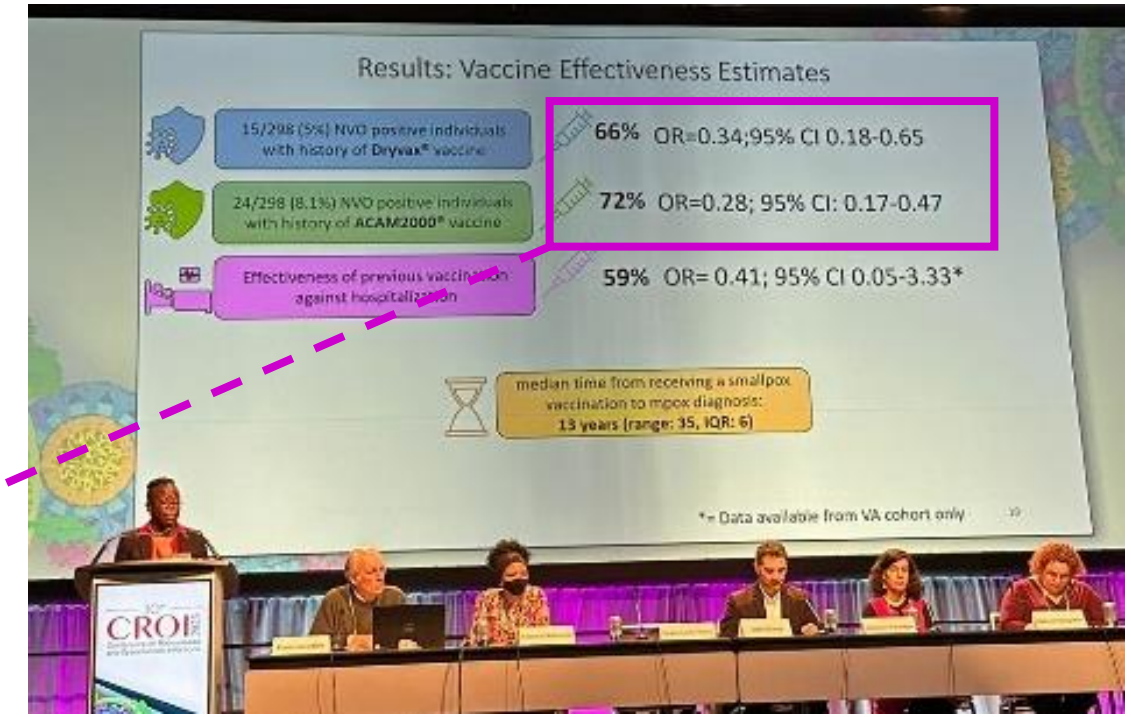
- Design: analysis using military health data
- Population: US military personnel (vaccinated in the period 2002-2017)

RESULTS:

- **1007** people tested, including 298 previously vaccinated with Dryvax or ACAM 2000
- **300** positive for mpox

15 positive Dryvax (OR 0,34), VE 66%

24 positive ACAM2000 (OR 0,28), VE 72%



Source: Unpublished

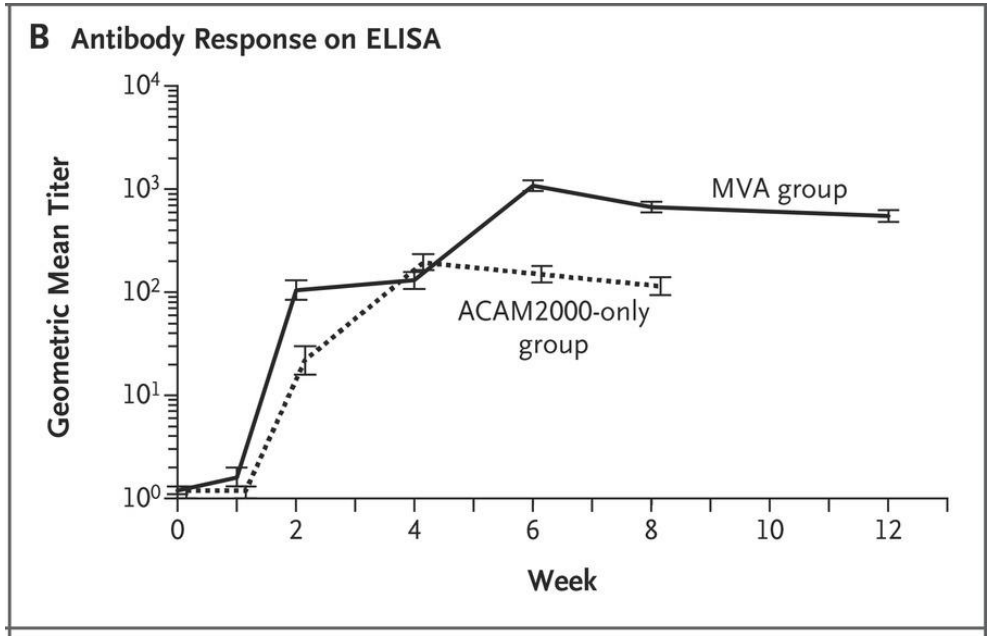
Third generation: high level of VAC neutralizing antibodies after two doses

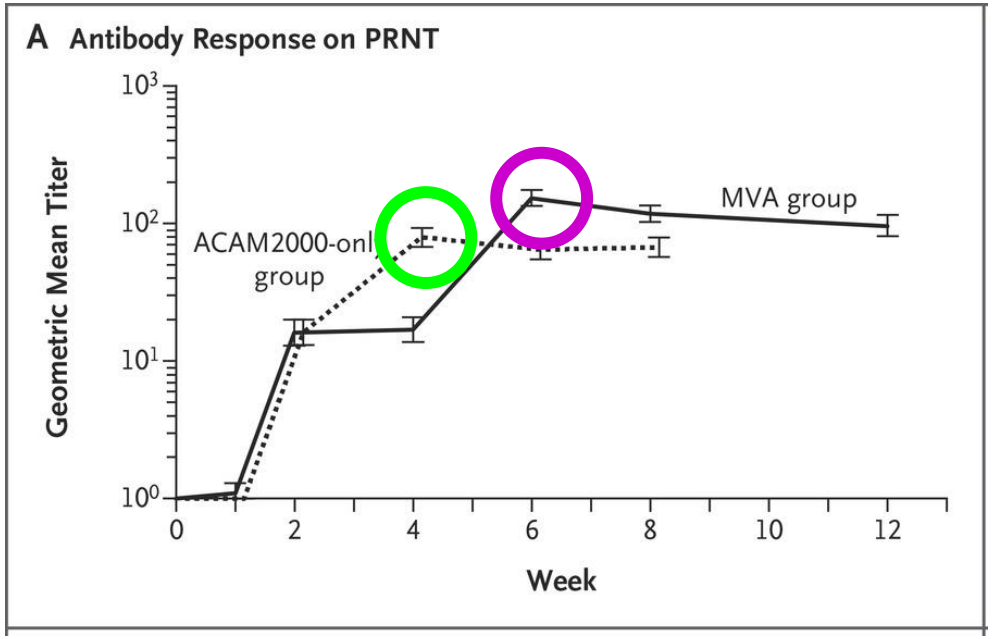
MVA antibodies

MVA-neutralizing antibodies

n = 185 Jynneos 0,5ml sc (2 doses)

N= 186 ACAM2000 (1 dose)



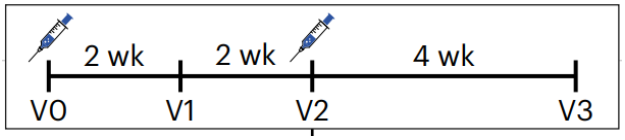


Association with a clinical surrogate marker of cutaneous reactions induced by poxvirus challenge

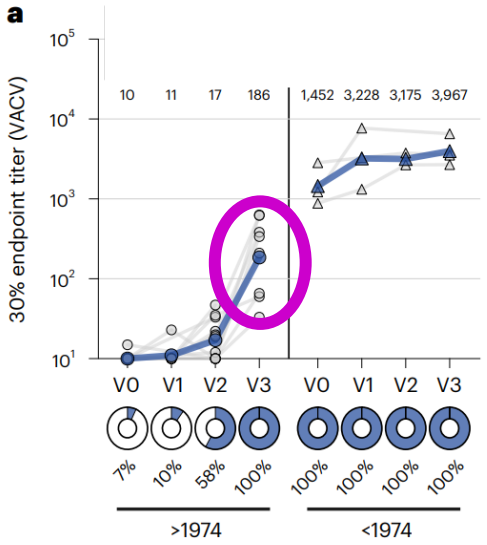
Source: Pittman et al. NEJM 2019.

Third generation: low level of MPXV neutralizing antibodies

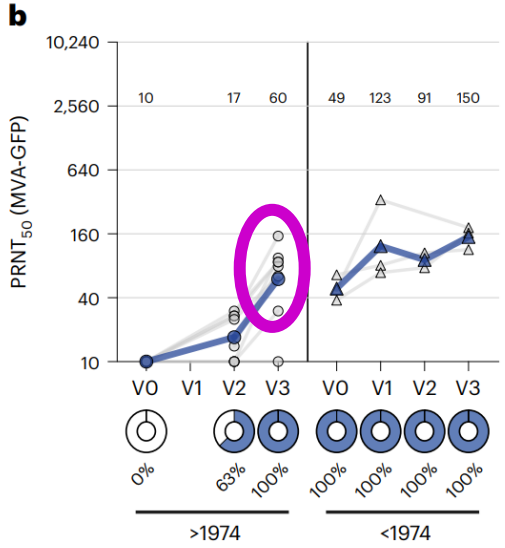
n = 18 Jynneos
(3 born before 1974)
2 sc doses 4 weeks apart



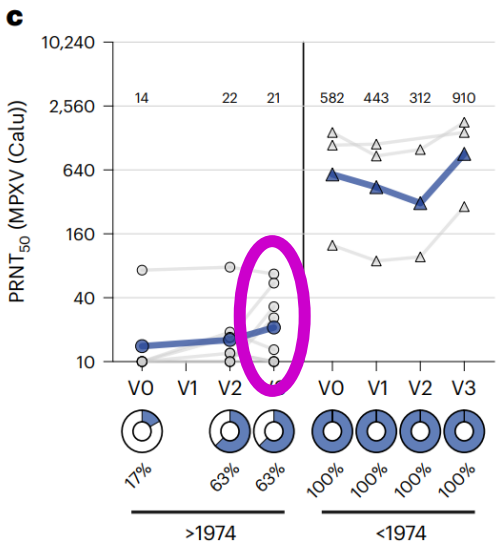
MVA antibodies



MVA-neutralizing antibodies

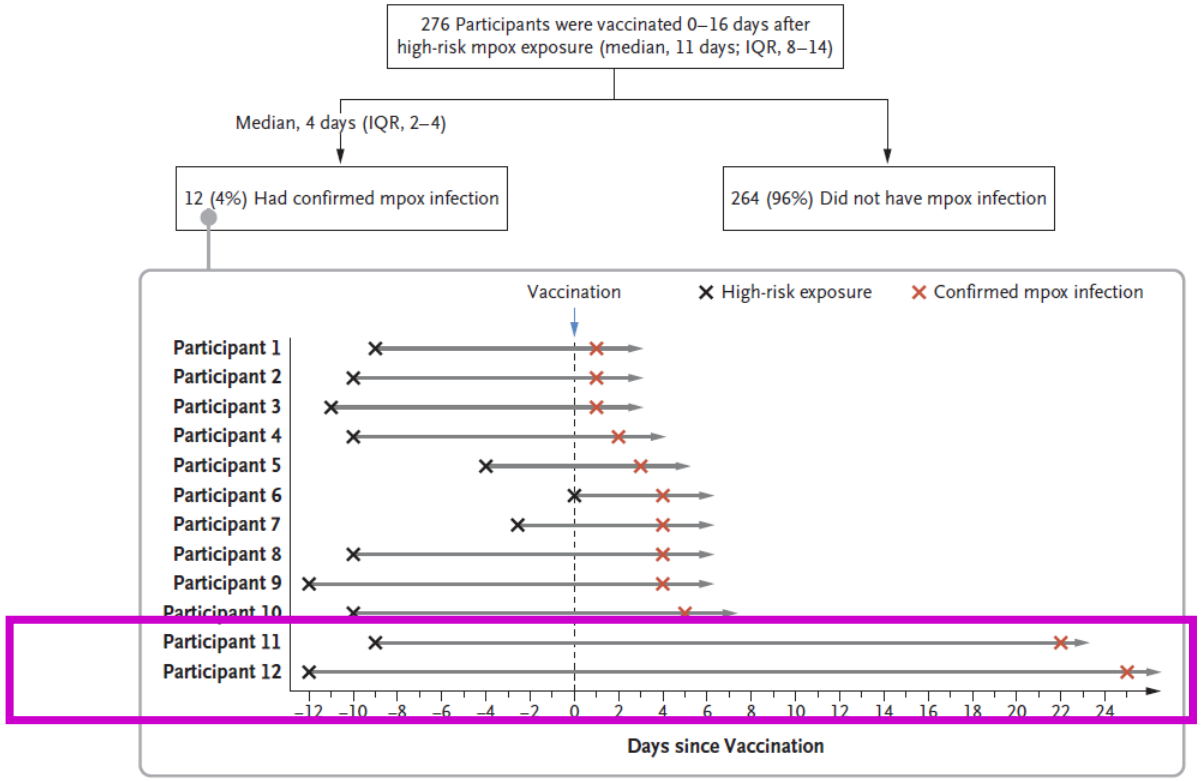


MPXV-neutralizing antibodies



Source: Zaeck et al. Nature Medicine 2022.

Breakthrough infections after PEP JYNNEOS sc. 0,5ml dose among 276 participants



Source: Thy M (...) Goshn J. NEJM 2022.

Vaccine performance using case-coverage method in 43 US jurisdictions

METHODS

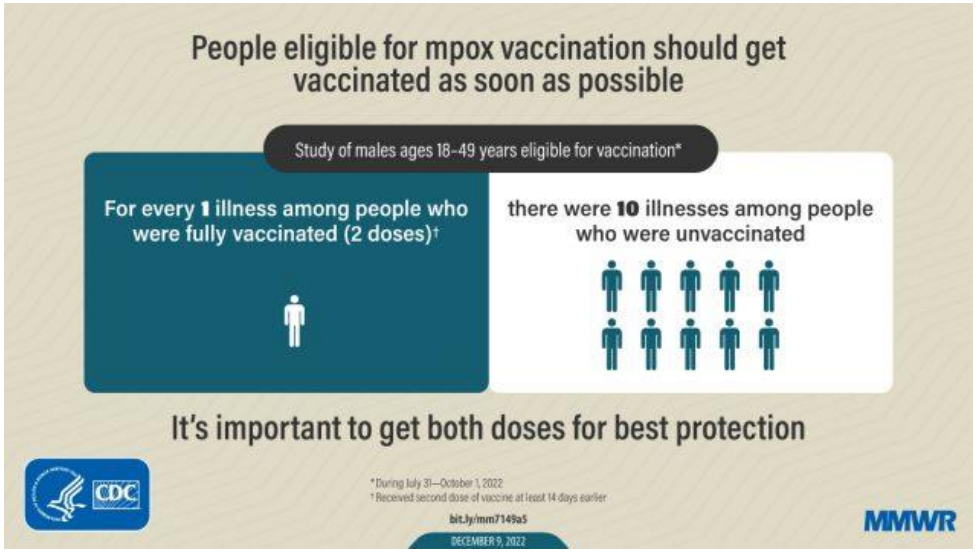
- **Design:** Case –coverage method
- **Population:** Mpox cases by vaccination status
- **Outcome:** Incidence risk ratio

$$1-\frac{\frac{\text{Number of cases that are vaccinated}}{\text{Number of total population that is vaccinated}}}{\frac{\text{Number of cases that are unvaccinated}}{\text{Number of total population that is unvaccinated}}} \times 100$$

RESULTS

- 9,544 reported mpox cases, 1,224 in vaccinated and 8,320 in unvaccinated
- Mpox incidence was higher among unvaccinated compared to vaccinated

With 1 dose IRR 7,4 (95CI 6,0-9,1)
With 2 doses IRR 9.6 (95% CI 6,9-13,2)

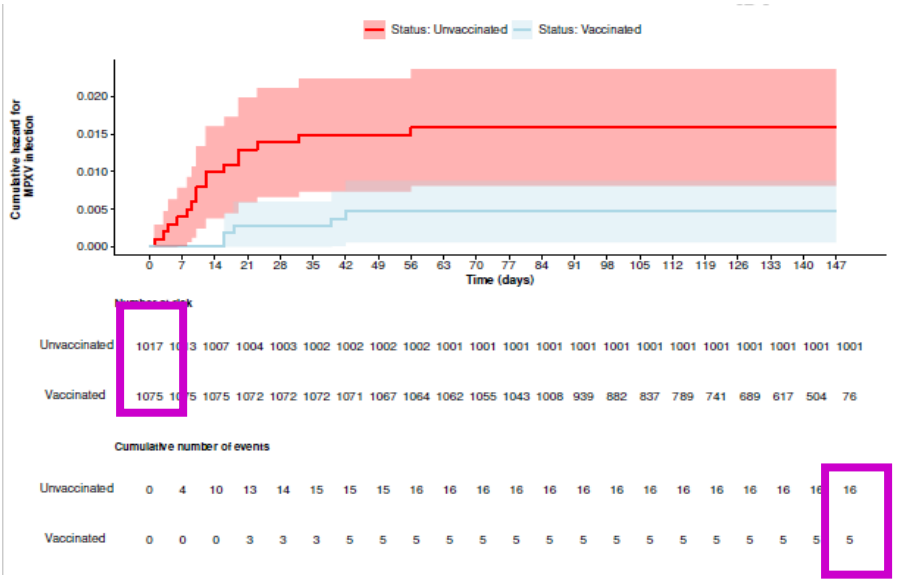


Source: Payne et al. MMWR 2022.

Vaccine effectiveness was 86% in a cohort study (n 2054) in Israel

METHODS:

- **Vaccination**: Single, sc MVA-BN
- **Design:** Retrospective observational cohort of data from electronic records.
- **Population:** Dispensed HIV-PreP or diagnosed with HIV and one STI
- **Primary endpoint:** Mpox diagnosis



	Unvaccinated N (%)	Vaccinated N (%)	HR (95% CI)
	1017 (50%)	1037 (50%)	
Tel Aviv District	406 (40%)	783 (76%)	2,2 (1,9-2,6)
Low socio demographic status	501 (49%)	326 (31%)	0,8 (0,7-0,9)
History of HIV	511 (50%)	136 (13%)	0,46 (0,3-0,6)

Hazard Rate 0.14 (0.05-0.41); VE 86%

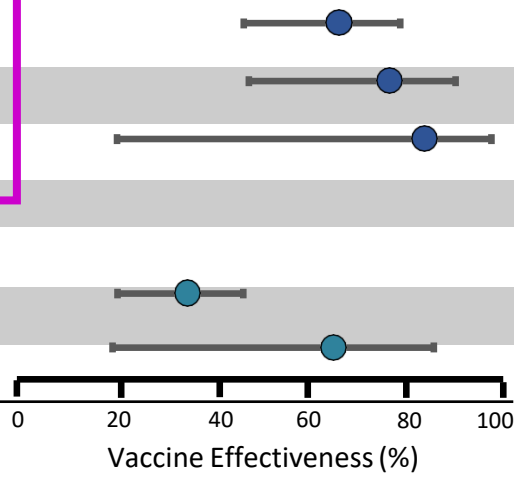
Source: Sagy et al. Nature Medicine 2022.

Vaccine effectiveness ranges from 66% - 83% for full vaccination in case-control studies

METHODS:

- **Design:** Case -control
- **Population:**
  - Case patients are people with an mpox diagnosis;
  - Control patients are people dispensed HIV-PreP or with an incident HIV.

	Cases with mpox	Controls	Adjusted* VE (95% CI)
Full vaccination (2 doses)			
Epic Cosmos case-control study n 11,232	25 /2913	335/8319	**66%** (47%- 78%)
Multi-jurisdictional case-control n423	14 /167	122 /256	**76%** (48%-89%)
New York State case-control study n507	2 /252	21 /255	**83%** (22%-96%)
Partial vaccination (1 dose)			
Epic Cosmos case-control study n 11,232	146 /2913	1000 /8319	36% (22%-47%)
New York State case-control study n507	10 /252	24 /255	65% (21%-85%)



Source: Unpublished

Mpox vaccine effectiveness

- There are two available orthopoxvirus vaccines: one is a replication-deficient modified vaccinia Ankara (MVA) vaccine, and the other is a replication-competent smallpox vaccine (ACAM2000).
- Estimations from cohort and case control studies show vaccine effectiveness ranges between 66-86%.
- Studies are being conducted to better control for bias, eg., TraX study-Australia, REMAIN study-HGTiP (Trial Emulation)

STEPS FORWARD

- We are designing the PROTECT study (Prioritize Tecovirimat for Advanced HIV) – RCT to assess efficacy of Tecoviritmat in Latin-America.
- We are implementing the REMAIN study (Breaktrhough infection following Mpox vaccination) – Trial emulation study to assess efficacy of MVA-BN.
- We are also implementing the TREP-AB trial (Neuropenetrative antibiòtics for syphilis) – RCT to asses efficacy of linezolid.

We'd love to work with you:

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Gràcies

Thanks