UNIVERSITÀ DEGLI STUDI DI MILANO
DIPARTIMENTO DI SCIENZE BIOMEDICHE E CLINICHE

Inquadramento diagnostico-terapeutico dell'infezione da Mpox (in precedenza Monkeypox)

Spinello Antinori

Firenze 10 gennaio 2023

XV Workshop Nazionale-Innovazione e Ricerca per la Pratica Clinica

Ongoing Monkeypox outbreak outside Africa

Event background

On 7 May 2022, the United Kingdom (UK) reported an imported case of monkeypox (MPX) in a person travelling from Nigeria. The case reported developing a rash-like illness on 29 April 2022 and travelled from Lagos to London on 3-4 May. The diagnosis was confirmed by monkeypox virus (MPXV) PCR on a vesicular swab on 6 May by the UK Health Security Agency (UKHSA) Rare and Imported Pathogens Laboratory.

On 13 May 2022, the UK reported two further cases of MPX who are part of the same family and not linked to the single imported case from Nigeria which was notified on 7 May. The cases were confirmed by PCR testing on vesicle swabs. A third family member had previously developed a rash but recovered fully. None of the individuals in this cluster had travelled or had contact with anyone with a relevant travel history [1].

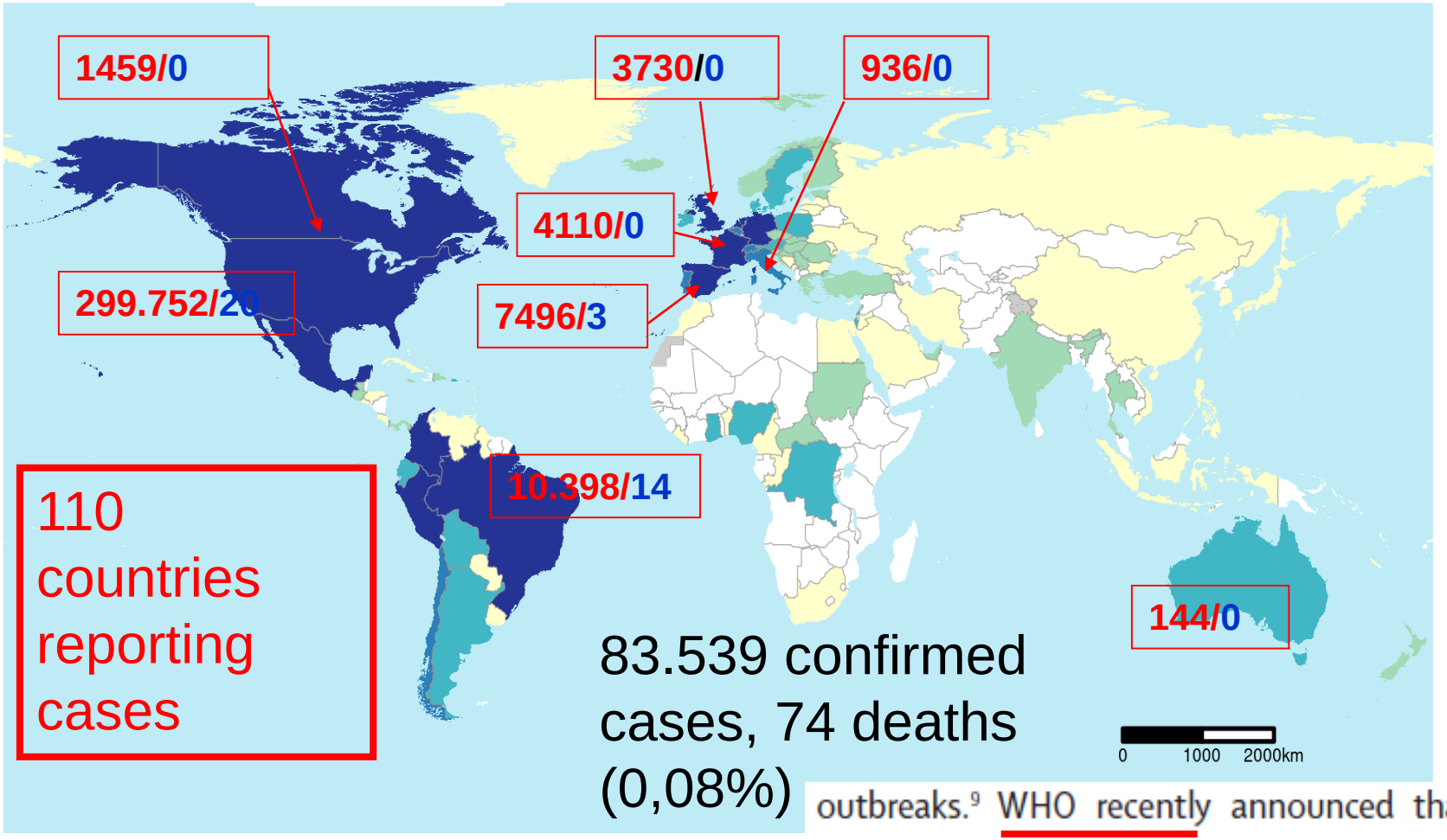
On 15 May 2022, the UK reported four additional cases of MPX, confirmed by PCR. None of these cases have known epidemiological links to the imported case from Nigeria (notified on 7 May) or to the family cluster (notified on 13 May). The four cases were men who have sex with men (MSM) and presented with a vesicular rash-like illness. They were identified through attendance at genitourinary medicine (GUM) clinics. The cases are being managed in high consequence infectious diseases units in the UK [1].

On 18 May 2022, two additional cases (also MSM) were reported, one in London and one in the South-East of England[1].

Confirmed cases of Monkeypox

from 1 Jan 2022, as of 28 Dec 2022

World Health Organization



Mpox: a new name for a new disease?

*Anne-Lise Beaumont, Nathan Peiffer-Smadja

Lancet Infect Dis 2022

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outbreaks.[9] WHO recently announced that the term mpox should be used rather than monkeypox, notably to avoid stigmatisation. Notably, this new name also reflects a new natural history and clinical presentation of this disease, with much still to discover including effective treatment strategies.

Reemergence of Human Monkeypox and Declining Population Immunity in the Context of Urbanization, Nigeria, 2017–2020

Phi-Yen Nguyen, Whenayon Simeon Ajisegiri, Valentina Costantino, Abrar A. Chughtai, C. Raina MacIntyre

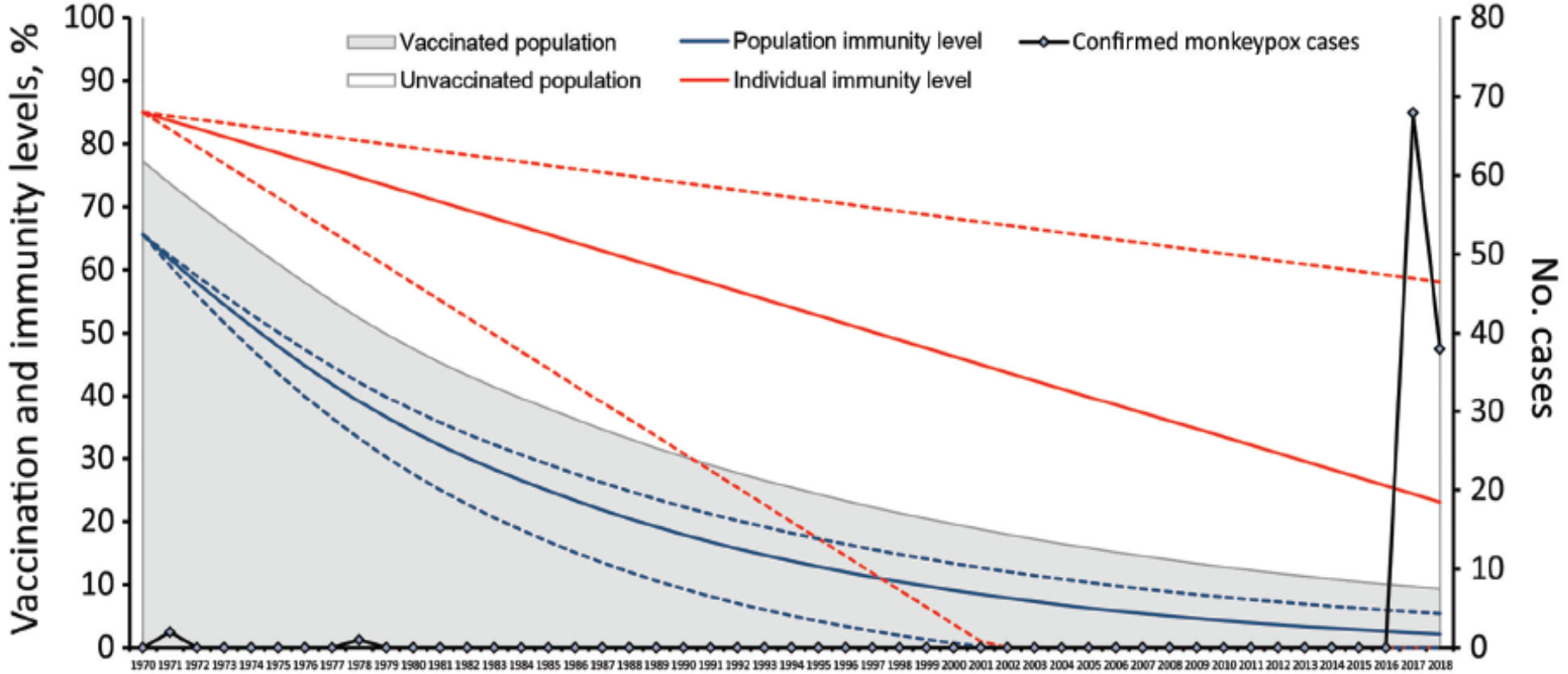
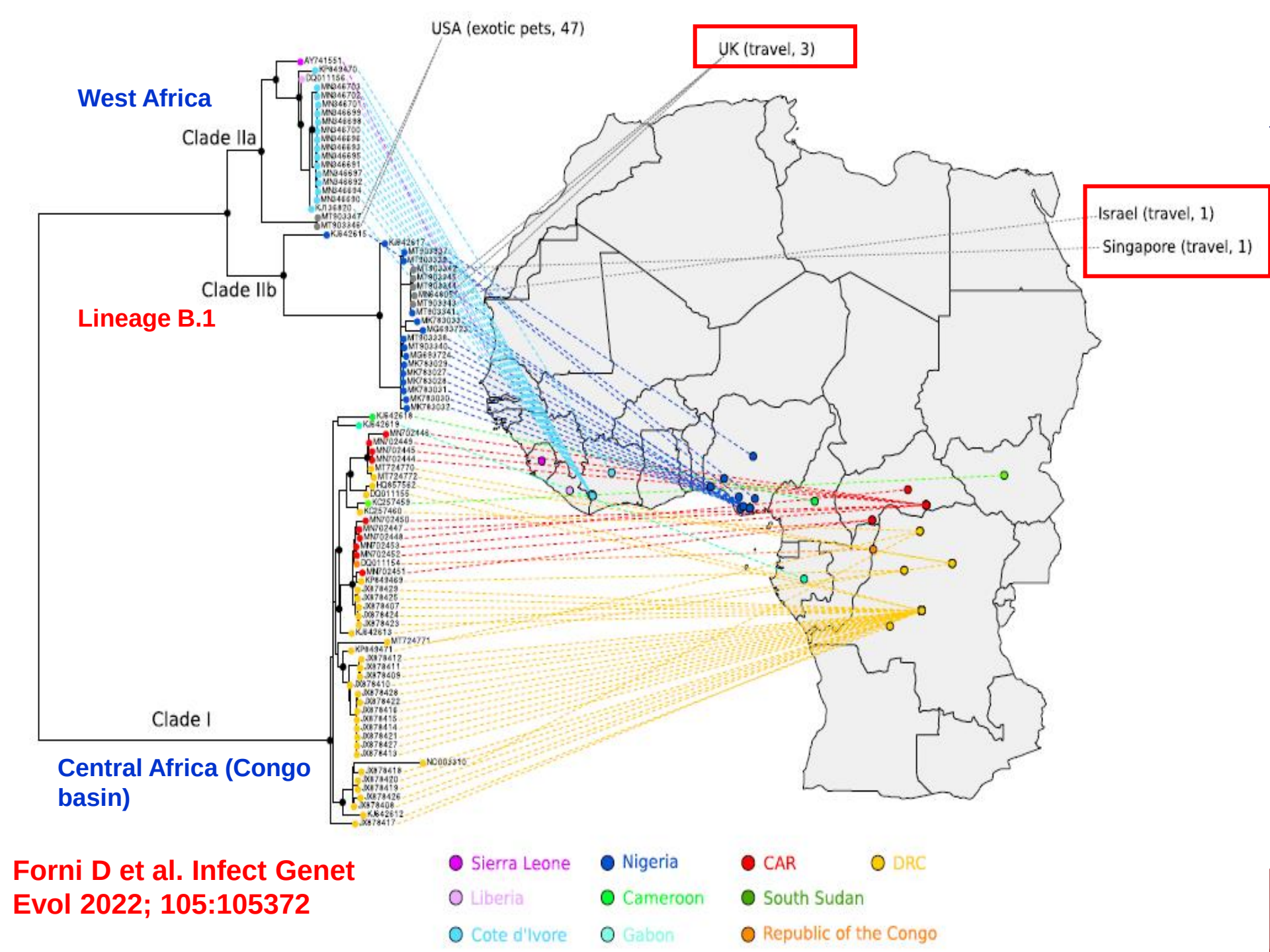
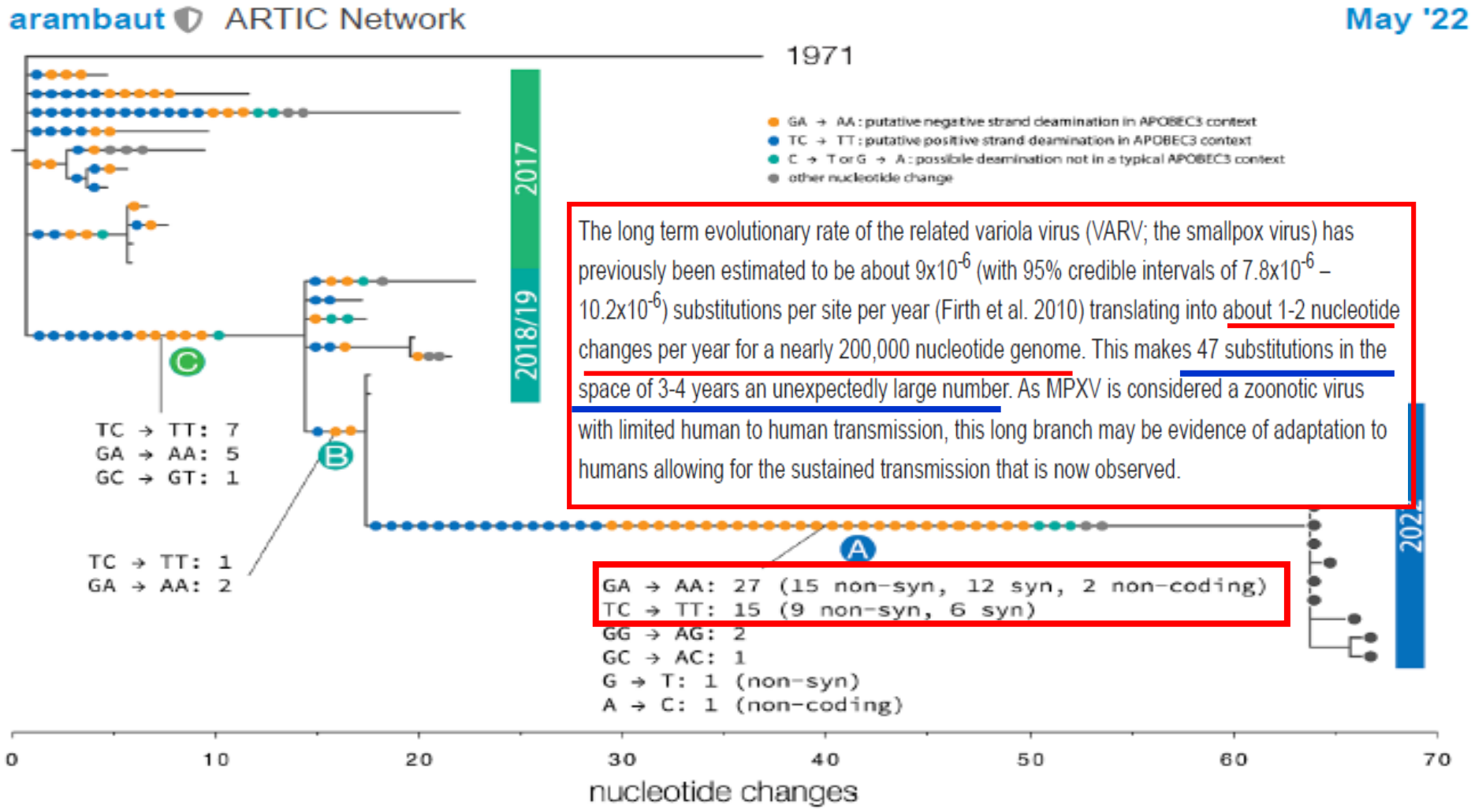


Figure 1. Relationship between population- and individual-level smallpox vaccination and immunity rates and resurgence of monkeypox cases in Nigeria, 1970–2018.



Forni D et al. Infect Genet Evol 2022; 105:105372

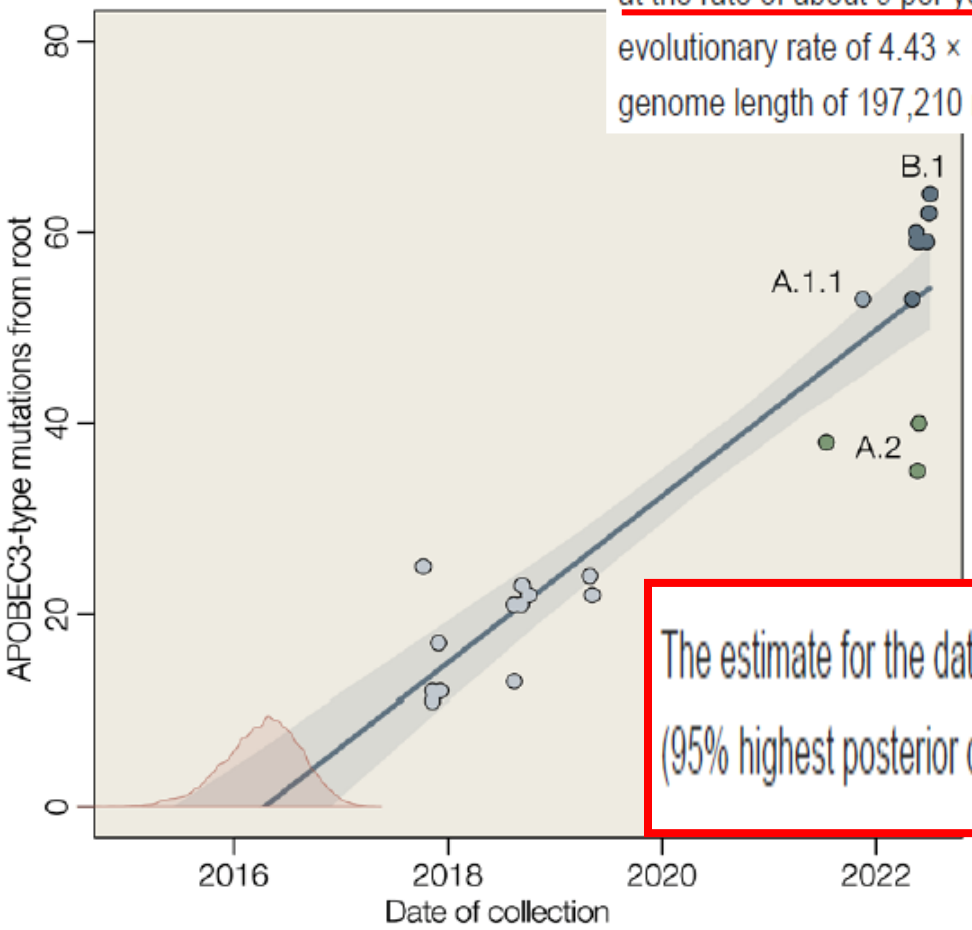
Initial observations about putative APOBEC3 deaminase editing driving short-term evolution of MPXV since 2017



The long term evolutionary rate of the related variola virus (VARV; the smallpox virus) has previously been estimated to be about $9x10^{-6}$ (with 95% credible intervals of $7.8x10^{-6}$ – $10.2x10^{-6}$) substitutions per site per year (Firth et al. 2010) translating into about 1-2 nucleotide changes per year for a nearly 200,000 nucleotide genome. This makes 47 substitutions in the space of 3-4 years an unexpectedly large number. As MPXV is considered a zoonotic virus with limited human to human transmission, this long branch may be evidence of adaptation to humans allowing for the sustained transmission that is now observed.

An APOBEC3 molecular clock to estimate the date of emergence of hMPXV

We estimate that APOBEC3-type mutations accumulate during human to human transmission at the rate of about 9 per year (8.74 with a 95% interval 7.34 – 10.15) which corresponds to an evolutionary rate of 4.43×10^{-5} substitutions per site per year ($3.72 – 5.15 \times 10^{-5}$) for a genome length of 197,210 nucleotides. This rate is approximately 20-fold greater than the long



The estimate for the date of emergence of hMPXV1 in the human population is 5-Apr-2016 (95% highest posterior density intervals of 14-Jul-2015 – 18-Dec-2016).

nature medicine

https://doi.org/10.1038/s41591-022-02004-w

Accelerated Article Preview

Retrospective detection of asymptomatic monkeypox virus infections among male sexual health clinic attendees in Belgium

Table 1: Patient and sample characteristics

3/224 (1.4%)

Case	Time point	Sample type	Symptoms	MPXV-PCR on left-over DNA extract (Ct value)	MPXV-PCR on original sample (Ct value)	Orthopox virus-PCR on left-over DNA extract (Ct value)	Whole genome sequencing	Viral viability study	Orthopox virus IgG antibodies (titer)
1	Day 0	Pooled sample*	None reported	Positive (27.63)	Anorectal swab: positive (26.69); oropharyngeal swab: negative	Positive (30.35)	ND	Negative	Negative (<1:20)
	Day 37	Anorectal swab	None reported	NA	Negative	NA	NA	NA	Positive (1:320)
2	Day 0	Anorectal swab	None reported	Positive (22.25)	Positive (20.05)	Positive (23.50)	Yes	Positive	Negative (<1:20)
	Day 21	Anorectal swab	None reported	NA	Negative	NA	NA	NA	Positive (1:40)
3	Day 0	Anorectal swab	None reported	Positive (19.19)	Positive (17.16)	Positive (21.43)	ND	Positive	Negative (<1:20)
	Day 24	Anorectal swab	None reported	NA	Negative	NA	NA	NA	Positive (1:80)
4	Day 0	Anorectal swab	Painful vesicular perianal rash	Positive (29.06)	Positive (27.38)	Positive (28.3)	ND	Negative	NA

Ct = cycle threshold; MPXV = monkeypox virus; NA = not applicable/not available

* combination of a patient's first-void urine, oropharyngeal swab, and anorectal swab

Annals of Internal Medicine

OBSERVATION: BRIEF RESEARCH REPORT

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

Methods and Findings: We retrospectively performed testing for MPXV on all anorectal swabs that were collected in our center as part of a screening program for *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. Per French guidelines, this screening is performed every 3 months among MSM with multiple sexual partners who are either taking HIV preexposure prophylaxis (PrEP) or living with HIV and receiving antiretroviral treatment (2)

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

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

C trachomatis = *Chlamydia trachomatis*; MPXV = monkeypox virus; MSM = men who have sex with men; *N gonorrhoeae* = *Neisseria gonorrhoeae*.
* All 200 of the asymptomatic participants who were tested for MPXV were negative for both *C trachomatis* and *N gonorrhoeae* on anal swab.

Isolation of viable monkeypox virus from anal and urethral swabs, Italy, May to July 2022

Euro Surveill 2022

Davide Moschese[1], Giacomo Pozza[2], Davide Mileto[3], Andrea Giacomelli[2], Miriam Cutrera[3], Maria Vittoria Cossu[1], Maddalena Matone[1], Martina Beltrami[2], Federica Salari[3], Spinello Antinori[4], Alessandra Lombardi[3], Giuliano Rizzardini[1]

Case number	Anal swab ≤7 days		Urethral swab ≤7 days		Anal swab 8–14 days		Urethral swab 8–14 days		Anal swab 15–21 days		Urethral swab 15–21 days	
	Days since symptom onset (Cq)	Viral culture (days to viral culture positivity)	Days since symptom onset (Cq)	Viral culture (days to viral culture positivity)	Days since symptom onset (Cq)	Viral culture (days to viral culture positivity)	Days since symptom onset (Cq)	Viral culture (days to viral culture positivity)	Days since symptom onset (Cq)	Viral culture (days to viral culture positivity)	Days since symptom onset (Cq)	Viral culture (days to viral culture positivity)
1	5 (17)	POS (3)	NA (NA)	NA (NA)	12 (24)	POS (4)	12 (34)	NEG (NA)	19 (38)	NEG (NA)	19 (NEG)	NA(NA)
2	4 (18)	POS (4)	4 (NEG)	NA (NA)	11 (28)	POS (5)	11 (NEG)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	NA (NA)
3	NA (NA)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	8 (34)	NEG (NA)	16 (33)	POS (6)	16 (26)	POS (5)
4	NA (NA)	NA (NA)	NA (NA)	NA (NA)	14 (35)	Contaminated[c]	14 (NEG)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	NA (NA)
5	4 (24)	Contaminated[c]	4 (34)	NEG (NA)	14 (NEG)	NA (NA)	14 (NEG)	NA (NA)	21 (NEG)	NA (NA)	21 (NEG)	NA (NA)
6	7 (20)	POS (4)	7 (19)	POS (4)	14 (36)	NEG (NA)	14 (NEG)	NA (NA)	21 (35)	NEG (NA)	21 (36)	NEG (NA)
7	3 (35)	NEG (NA)	3 (28)	POS (6)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	21 (NEG)	NA (NA)	21 (NEG)	NA (NA)
8	NA (NA)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	10 (29)	POS (6)	NA (NA)	NA (NA)	NA (NA)	NA (NA)
9	NA (NA)	NA (NA)	NA (NA)	NA (NA)	13 (37)	Contaminated[c]	13 (NEG)	NA (NA)	19 (NEG)	NA (NA)	19 (37)	NEG (NA)
10	NA (NA)	NA (NA)	NA (NA)	NA (NA)	14 (NEG)	NA (NA)	14 (NEG)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	NA (NA)
11	7 (31)	Contaminated[c]	7 (25)	POS (5)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	NA (NA)
12	2 (NEG)	NA (NA)	NA (NA)	NA (NA)	11 (NEG)	NA (NA)	11 (NEG)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	NA (NA)
13	6 (16)	POS (3)	NA (NA)	NA (NA)	11 (21)	POS (4)	11 (34)	NEG (NA)	18 (NEG)	NA (NA)	18 (NEG)	NA (NA)
14	1 (23)	POS (5)	NA (NA)	NA (NA)	13 (NEG)	NA (NA)	13 (NEG)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	NA (NA)
15[a]	3 (NEG)	NA (NA)	3 (35)	NEG (NA)	9 (NEG)	NA (NA)	9 (NEG)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	NA (NA)
16	5 (34)	POS (7)	5 (35)	POS (7)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	NA (NA)	NA (NA)
17	2 (34)	POS (7)	2 (30)	POS (6)	8 (NEG)	NA (NA)	8 (33)	POS (6)	NA (NA)	NA (NA)	NA (NA)	NA (NA)
18	7 (19)	POS (4)	7 (32)	NEG (NA)	8 (NEG)	NA (NA)	NA (NA)	NA (NA)	21 (NEG)	NA (NA)	NA	NA (NA)
19[b]	7 (NEG)	NA (NA)	7 (36)	POS (7)	14 (NEG)	NA (NA)	14 (NEG)	NA (NA)	NA (NA)	NA (NA)	NA	NA (NA)

Potentially Asymptomatic Infection of Monkeypox Virus: A Systematic Review and Meta-Analysis

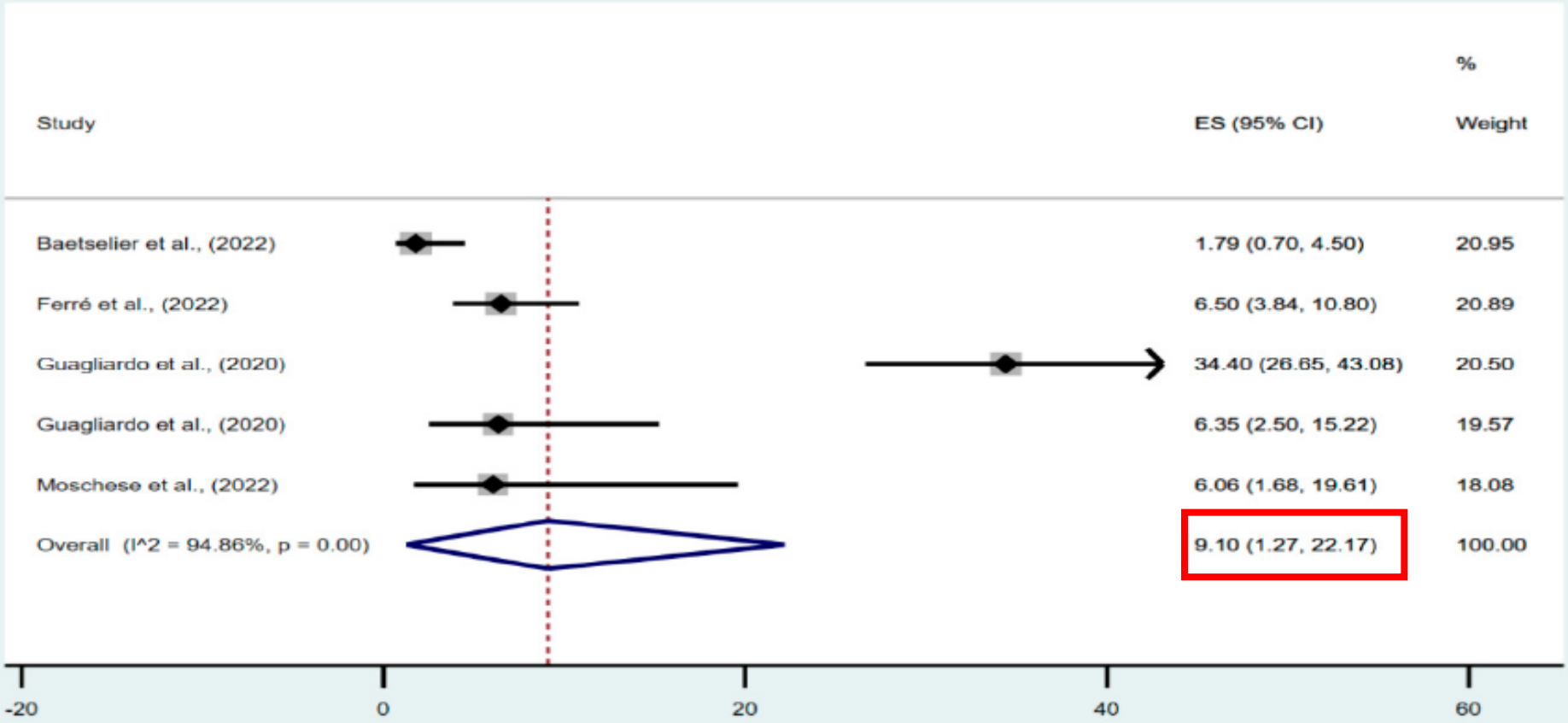


Figure 2. Pooled prevalence forest plot of asymptomatic monkeypox [11–14].

Satapathy P et al. Vaccines 2022;10:2083

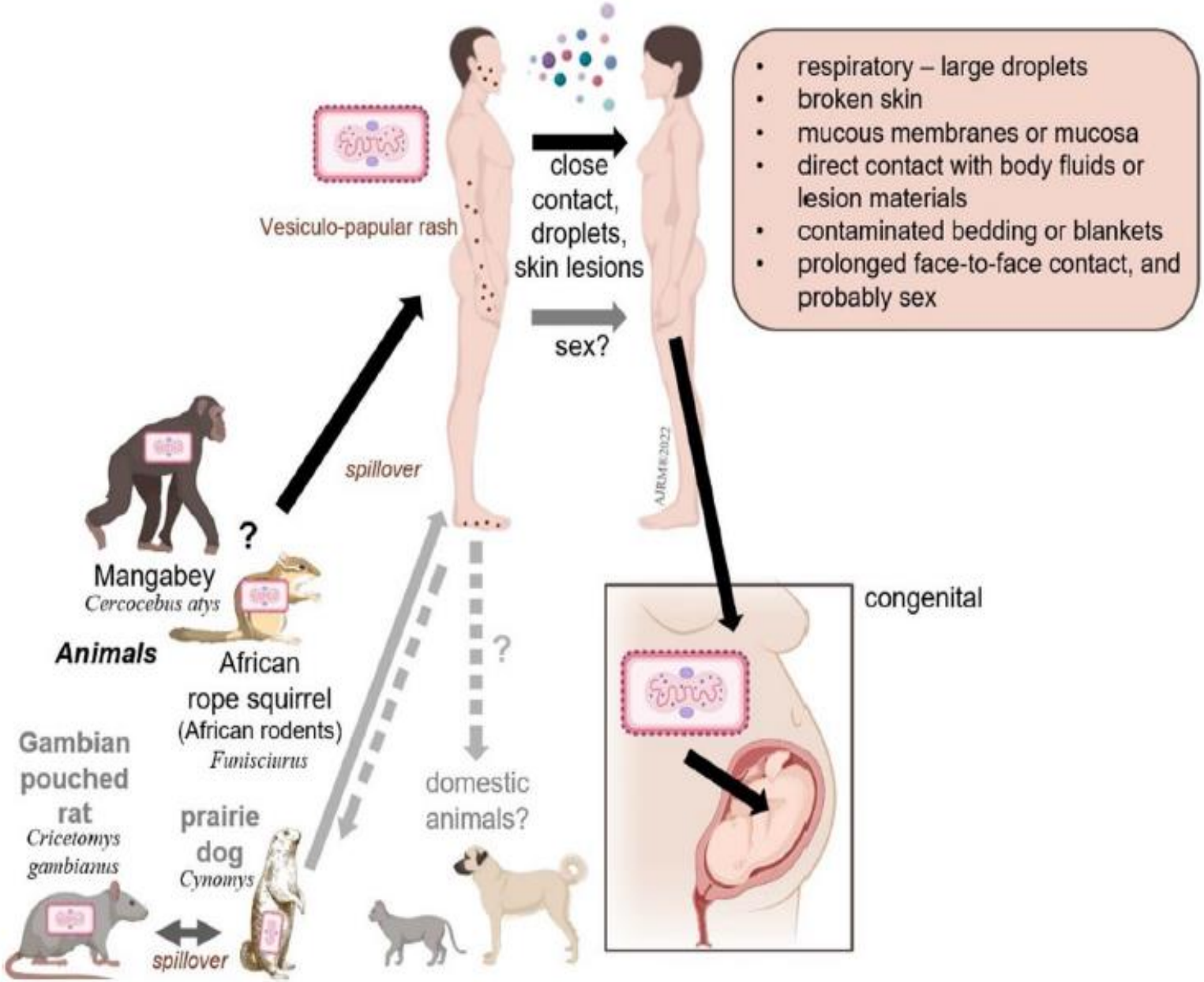


Fig. 1 Transmission routes associated with monkeypox infection

Bulletin of the World Health Organization, **66** (4): 459–464 (1988)

Clinico-epidemiological features of monkeypox patients with an animal or human source of infection

Z. JEŽEK,[1] B. GRAB,[1] M. SZCZENIOWSKI,[2] K. M. PALUKU,[2] & M. MUTOMBO[2]

Table 2. Distribution of the main characteristics of the exanthem in unvaccinated monkeypox patients, by presumed source of infection

Characteristics	Infection from animal source	Infection from human source
Occurrence:		
Monomorphic[a]	176 (79.3)[b]	57 (78.1)
Pleomorphic[a]	46 (20.7)	16 (21.9)
Total observed	222	73
Lesions:		
Discrete	124 (55.9)	48 (65.8)
Semiconfluent	70 (31.5)	23 (31.5)
Confluent	28 (12.6)	2 (2.7)
Haemorrhagic	0 (0)	0 (0)
Total observed	222	73
Body distribution:		
Centrifugal	192 (86.5)	54 (74.0)
Centripetal	8 (3.6)	5 (6.8)
Indefinite	22 (9.9)	14 (19.2)
Total observed	222	73
Presence of pocks:		
Facial	196 (88.3)	60 (82.2)
Palmar	157 (70.7)	49 (67.1)
Plantar	156 (70.3)	40 (54.8)

[a] Monomorphic = all lesions at the same stage; pleomorphic = more than one crop of lesions.
[b] Figures in parentheses are percentages.

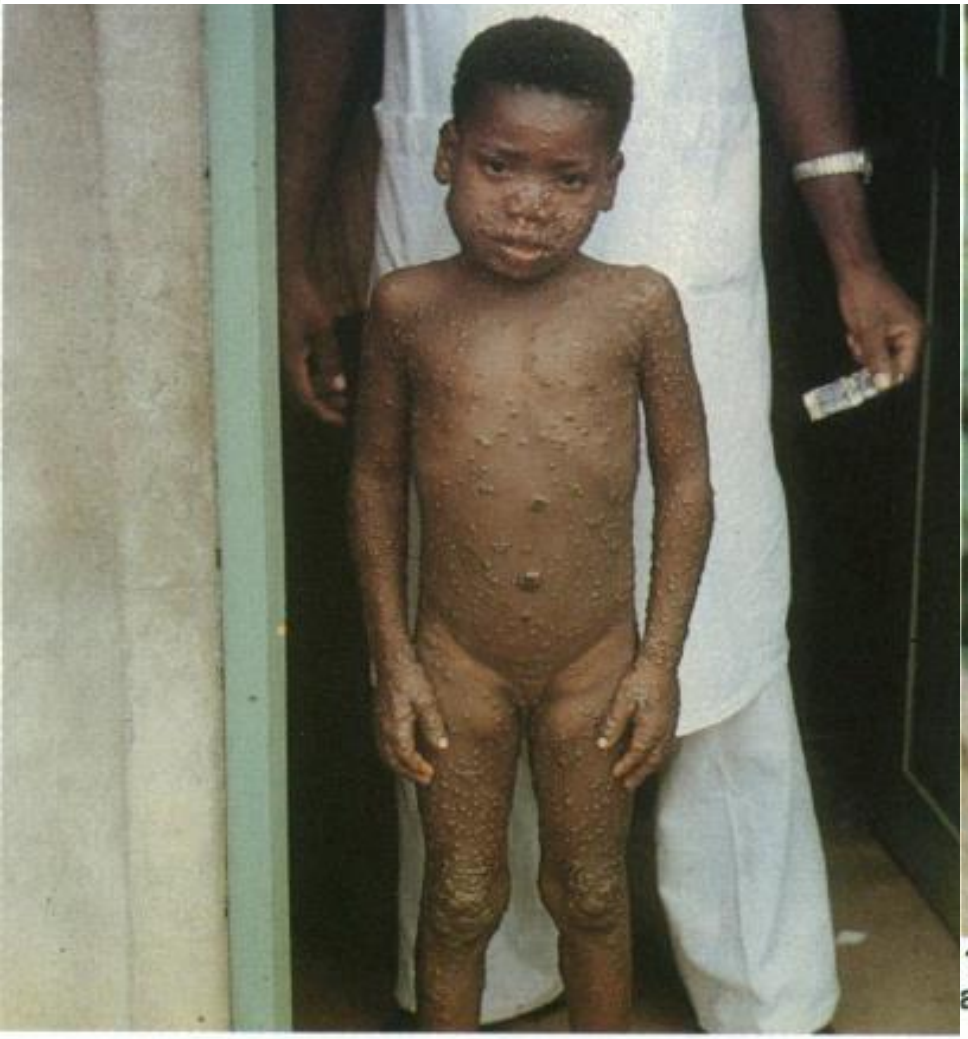
Table 3. Frequency of lesions on mucous membranes and of tonsillitis in unvaccinated monkeypox patients, by presumed source of infection

	Infection from animal source	Infection from human source
Total observed	222	73
Lesions on mucous membranes:[a]	175 (78.8)[b]	50 (68.5)
Oral	166 (74.8)	41 (56.2)
Conjunctival	45 (20.3)	12 (16.4)
Genital	74 (33.3)	14 (19.2)
Absent	47 (21.2)	23 (31.5)
Tonsillitis:		
Present	119 (53.6)	29 (39.7)
Absent	103 (46.4)	44 (60.3)

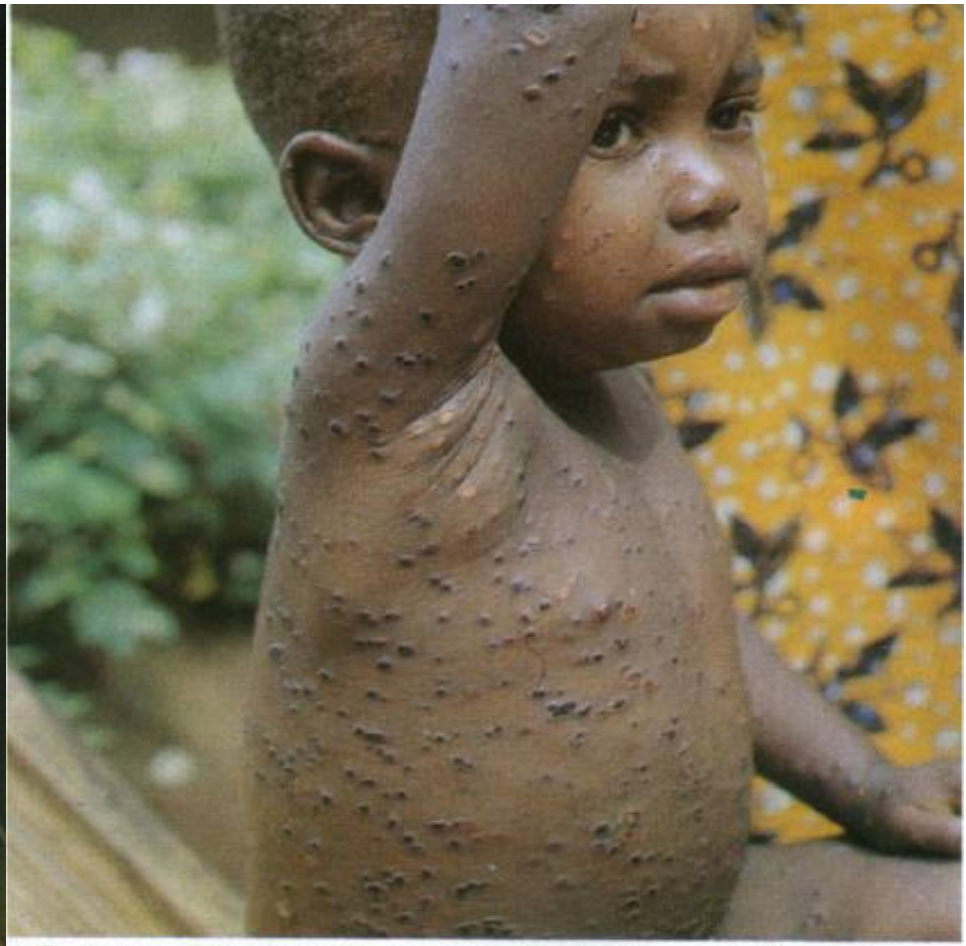
[a] For several patients more than one site was affected.
[b] Figures in parentheses are percentages.

Bulletin of the World Health Organization, 62 (5): 703 – 713 (1984)

The current status of human monkeypox: Memorandum from a WHO Meeting*



1.1. Case 25, age 7 years. Day 7 of rash in the acute stage. Note distinct bilateral inguinal lymphadenopathy. There is also submaxillar lymphadenopathy on the right side.



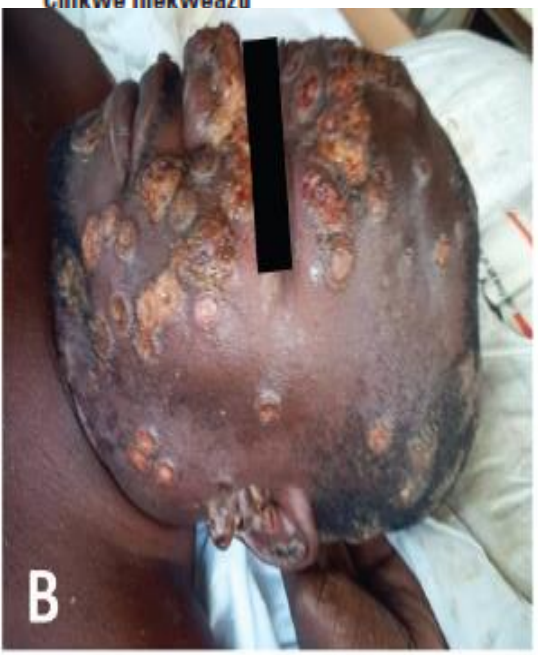
1.3 Case 81, age 3 years. Rash in scabbing stage, approximately day 12. Note lymphadenopathy in armpit.

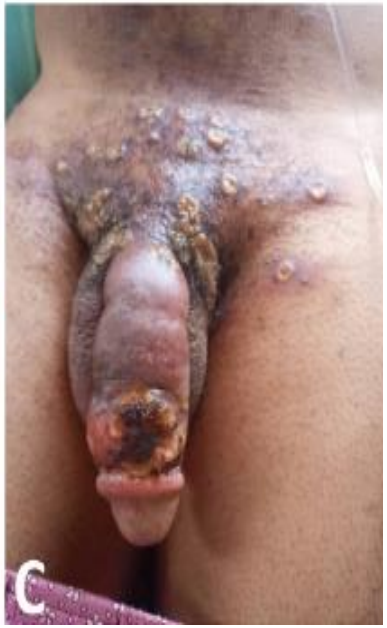
Clinical Infectious Diseases

BRIEF REPORT

Clinical Course and Outcome of Human Monkeypox in Nigeria

Dimie Ogoina,[1] Michael Iroezindu,[2] Hendris Izibewule James,[1] Regina Oladoku Adesola Yinka-Ogunleye,[4] Paul Wakama,[5] Bolaji Otike-odibi,[6] Liman Muhammed Usman,[7] Emmanuel Obazee,[6] Olusola Aruna,[8] and Chikwe Ihekweazu[4]





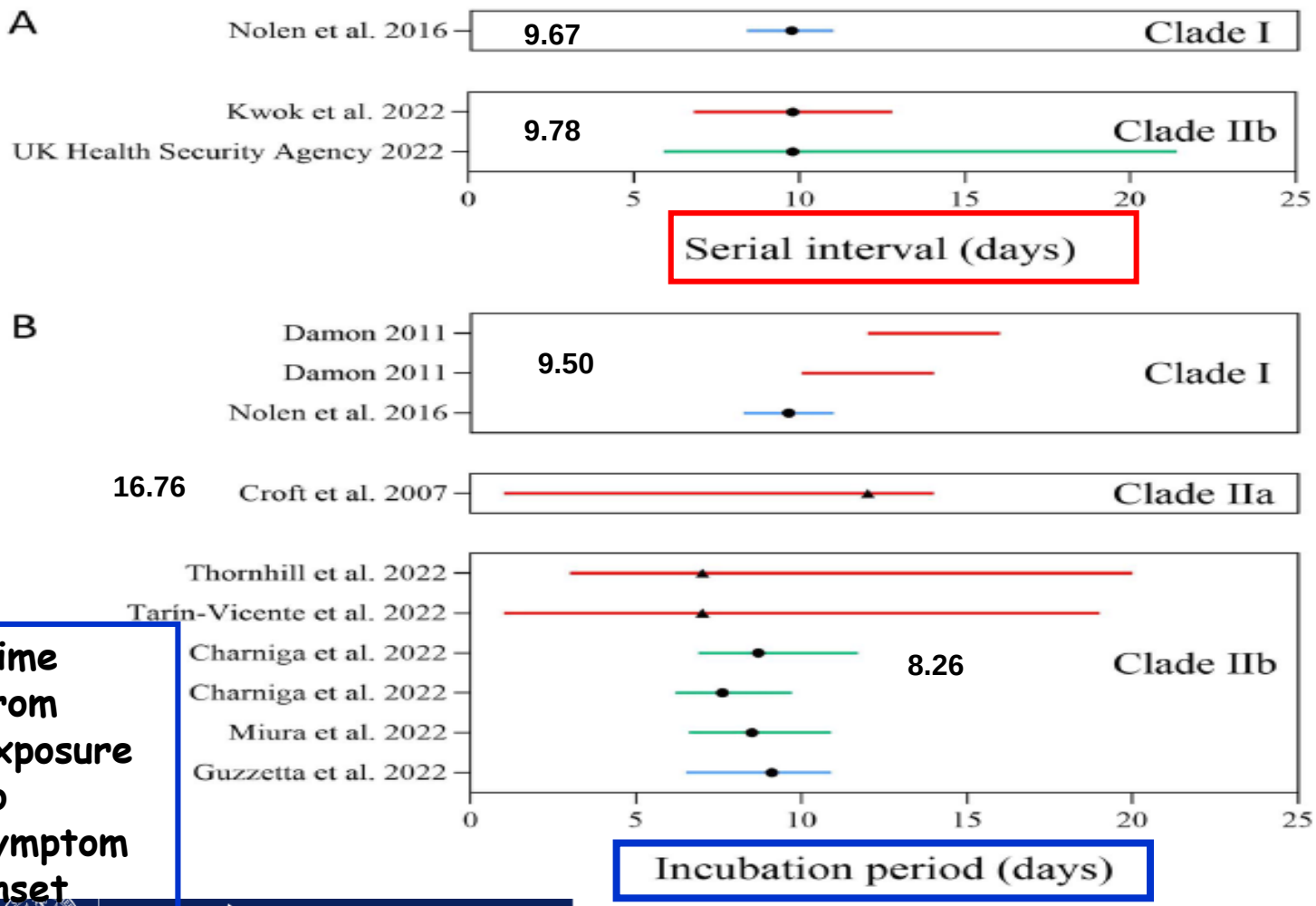
The demographic and clinical characteristics of the 40 cases in relation to their HIV status are summarized in Table 1. The cases were 28 days to 54 years of age (median, 32 years) and the majority (77.5%) were male.

The following clinical features were observed: skin rash (n = 40), fever (n = 36), lymphadenopathy (n = 35), genital ulcer (n = 25), body aches (n = 25), headache (n = 19), sore throat (n = 18), pruritus (n = 15), and conjunctivitis and photophobia (n = 9). Nasal congestion, cough, skin ulcers, and hemorrhagic skin lesions were observed in 5 cases each. Other less common features were nausea and vomiting (n = 3), hepatomegaly (n = 3), and scrotal edema (n = 2).

Of 35 cases who gave details of their first symptom, 23 (65.7%) had rash as the first symptom, while 12 (34.3%) had fever as first symptom. In 2 patients, genital rash associated with ulcer was the first symptom. Skin rashes were observed on the following sites: face (97.5%), trunk (92.5%), arms (87.5%), legs (85%), genitalia (67.5%), scalp (62.5%), palms (55%), soles (50%), mouth (37.5%), and eyes (25%).

Serial intervals and incubation periods of the monkeypox virus clades

Shuqi Wang, BSc[1,†], Fengdi Zhang, BDSc[2,†], Zhilu Yuan, PhD[3,*], Mingda Xu, MSc[4], Zhen Wang, PhD[1], Chao Gao, PhD[4], Renzhong Guo, PhD[3], and Zhanwei Du, PhD[5]



Time between symptom onset in the primary and secondary case

Time from exposure to symptom onset

J Travel Med 2022, in press

Table 3.1. Risk factors and clinical findings described as being associated with severe disease and poor outcomes (based on small, uncontrolled, observational studies)

Patient groups at higher risk of severe disease or complications	• Children, pregnant women, persons who are immunosuppressed such as persons living with HIV having poorly controlled disease *(5,6,10,11,13,26)*. • Though data are lacking, patients with chronic skin conditions (e.g. atopic dermatitis), acute skin conditions (i.e. burns) may also be at higher risk for complications, such as bacterial infection *(33)*.
Clinical signs and symptoms of complications	• Nausea and vomiting *(11,16)*, painful cervical lymphadenopathy causing dysphagia, poor oral intake, eye pain, vision abnormalities, hepatomegaly, sepsis, dehydration, respiratory distress/pneumonia, and/or confusion.
Laboratory abnormalities	• Elevated hepatic transaminases (AST and/or ALT), low blood urea nitrogen (BUN), low albumin, elevated white blood count (WBC), or low platelet count *(16)*.
Skin lesion severity score	• From smallpox experience *(28,94)*: – Mild (< 25 skin lesions) – Moderate (25–99 skin lesions) – Severe (100–250 skin lesions) – Very severe (> 250 skin lesions).

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

	Participants (n=181)
Age, years	37·0 (31·0–42·0)
Sex	
Female	6 (3%)
Male	175 (97%)
Ethnicity	
Spanish	79 (44%)
South and central American	82 (45%)
Other	19 (10%)
Missing data	1 (1%)
Sexual orientation	
Gay men, bisexual men, and other men who have sex with men	166 (92%)
Heterosexual men	9 (5%)
Heterosexual women	6 (3%)
History of smallpox vaccination	32 (18%)
HIV-positive	72 (40%)
Possible exposure to monkeypox	
Regular sexual partner with monkeypox	47 (26%)
Household contact with monkeypox	6 (3%)
Attendance at a Pride event	66 (36%)
Recent travel out of Spain	26 (14%)
Sexual risk factors	
Number of sexual partners in past 14 days	2·0 (1·0–5·0)
Number of sexual partners in past 3 months	6·5 (3·0–16·0)
Sexually transmitted infection in past 12 months	99 (55%)
Use of social media apps to identify sexual partners	107 (59%)
Sex outside of Spain in past 3 months	15 (8%)
Sex with a sex worker	8 (4%)
Use of recreational drugs during sex	57 (31%)

Tarin-Vicente EJ et al. Lancet, August 8, 2022

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

	Participants (n=181)
Incubation period, days*	7·0 (5·0–10·0)
Systemic features	
At least one systemic feature	160 (88%)
Systemic symptoms before the rash onset	87 (48%)
Influenza-like illness	147 (81%)
Fever	131 (72%)
Headache	96 (53%)
Sore throat	66 (36%)
Clinical features of the rash	
Approximate number of lesions	
>20	15 (8%)
3–20	145 (80%)
1–2	21 (12%)
Number of body regions involved	3 (2–4)
Lesion morphology	
Papular lesions	38 (21%)
Vesicular lesions	47 (26%)
Pustular lesions	162 (90%)
Lesion location	
Genital	100 (55%)
Perianal	66 (36%)
Oral ulcer	45 (25%)
Perioral	51 (28%)
Hands and feet	108 (60%)
Trunk and extremities	104 (57%)
Lymphadenopathies	
Any lymphadenopathy	153 (85%)
Lymphadenopathy by region	
Cervical	53 (29%)
Inguinal	110 (61%)
Axillary	2 (1%)
None	28 (15%)

Tarin-Vicente EJ et al. Lancet, August 8, 2022

Human monkeypox virus infection in women and non-binary individuals during the 2022 outbreaks: a global case series

Thornhill JP et al. Lancet 2022;400:1953-65

	Trans women (n=62)	Cis women and non-binary individuals (n=74)	Overall (n=136)
WHO region			
Region of the Americas	29/62 (47%)	36/74 (49%)	65/136 (48%)
European region	33/62 (53%)	35/74 (47%)	68/136 (50%)
African region	0/62	3/74 (4%)	3/136 (2%)
Age, years	N=62	N=74	N=136
Median (IQR)	34 (30–39)	33 (26–45)	34 (28–40)
Range	22–52	19–84	19–84
Living with HIV			
No or not known	31/62 (50%)	68/74 (92%)	99/136 (73%)
Yes	31/62 (50%)	6/74 (8%)	37/136 (27%)
PrEP use in those without HIV			
No or not known	13/31 (42%)	67/68 (99%)	80/99 (81%)
Yes	18/31 (58%)	1/68 (1%)	19/99 (19%)
Children in household			
No	50/62 (81%)	45/74 (61%)	95/136 (70%)
Yes	0/62	19/74 (26%)	19/136 (14%)
Not known	12/62 (19%)	10/74 (14%)	22/136 (16%)
Children infected with monkeypox			
No or not known	62/62 (100%)	72/74 (97%)	134/136 (99%)
Yes	0/62	2/74 (3%)	2/136 (1%)

Human monkeypox virus infection in women and non-binary individuals during the 2022 outbreaks: a global case series

Rash, including viral exanthem			
No	4/61 (7%)	6/73 (8%)	10/134 (7%)
Yes	57/61 (93%)	67/73 (92%)	124/134 (93%)
Not known or missing data	1	1	2
Duration of rash*, days	N=11	N=40	N=51
Median (IQR)	10 (10–22)	18 (13–21)	15 (10–21)
Range	7–56	2–30	2–56
Viral exanthem (rash all over body)			
No	53/60 (88%)	61/72 (85%)	114/132 (86%)
Yes	7/60 (12%)	11/72 (15%)	18/132 (14%)
Not known or missing data	2	2	4
Type of rash			
Vesiculopustular rash	45/52 (87%)	60/69 (87%)	105/121 (87%)
Multiple ulcers	1/52 (2%)	5/69 (7%)	6/121 (5%)
Single ulcer	3/52 (6%)	2/69 (3%)	5/121 (4%)
Macular	0/52	1/69 (1%)	1/121 (1%)
Other	3/52 (6%)	1/69 (1%)	4/121 (3%)
Not known	10	5	15
Number of lesions	N=56	N=70	N=126
Median (IQR)	10 (3–20)	10 (5–33)	10 (5–24)
Range	1–100	1–200	1–200
Any anogenital lesions†			
No	12/59 (20%)	22/70 (31%)	34/129 (26%)
Yes	47/59 (80%)	48/70 (69%)	95/129 (74%)
Not known	3	4	7

Thornhill JP et al. Lancet 2022;400:1953-65

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

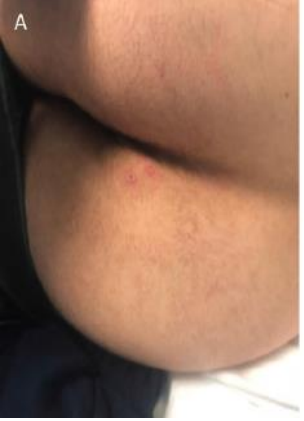
Complications	
Proctitis	45 (25%)
Tonsillitis	19 (10%)
Penile oedema	15 (8%)
Bacterial skin abscess	6 (3%)
Exanthem	8 (4%)

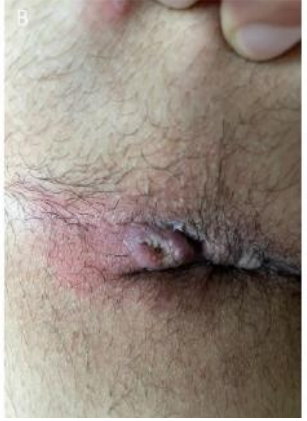
Investigations	
PCR of skin swab positive†	178/180 (99%)
Mean cycle threshold value of positive skin specimens	23 (4)
PCR of throat swab positive†	82/117 (70%)
Mean cycle threshold value of positive throat specimens	32 (6)
PCR of anal swab positive†	43/55 (78%)
Mean cycle threshold value of positive anal specimens	27 (7)

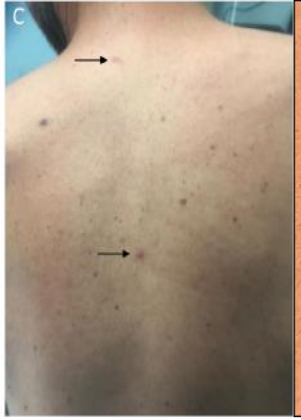
Concurrent sexually transmitted infection	
Any sexually transmitted infection	31 (17%)
HIV	1 (1%)
Chlamydia	10 (6%)
Gonorrhoea	6 (3%)
Herpes simplex virus	2 (1%)
Mycoplasma genitalium	2 (1%)
Syphilis	13 (7%)

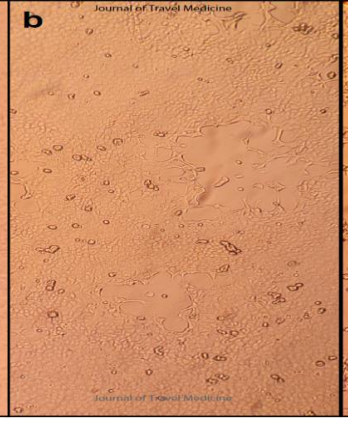
Outcomes	
Time to formation of dry crust, days	10·0 (7·0–12·5)
Admitted to hospital	
No	178 (98%)
Clinical management	2 (1%)
Social reasons	1 (1%)

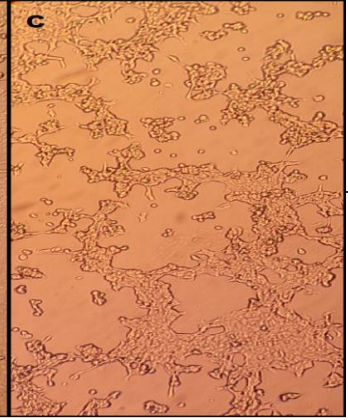
Tarin-Vicente EJ et al. Lancet, August 8, 2022

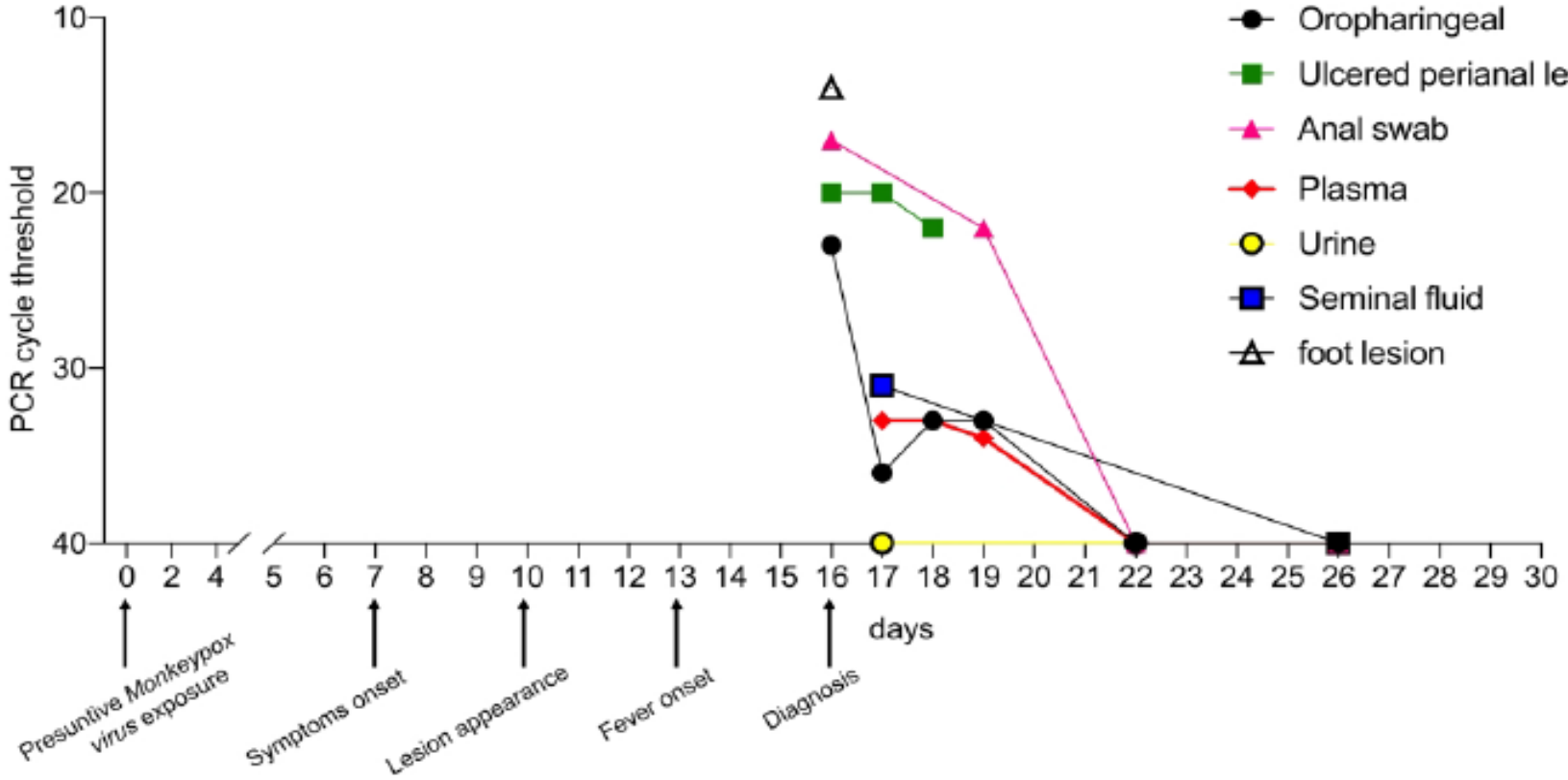












Mileto D et al. Travel Med Infect Dis 2022, 49:102386

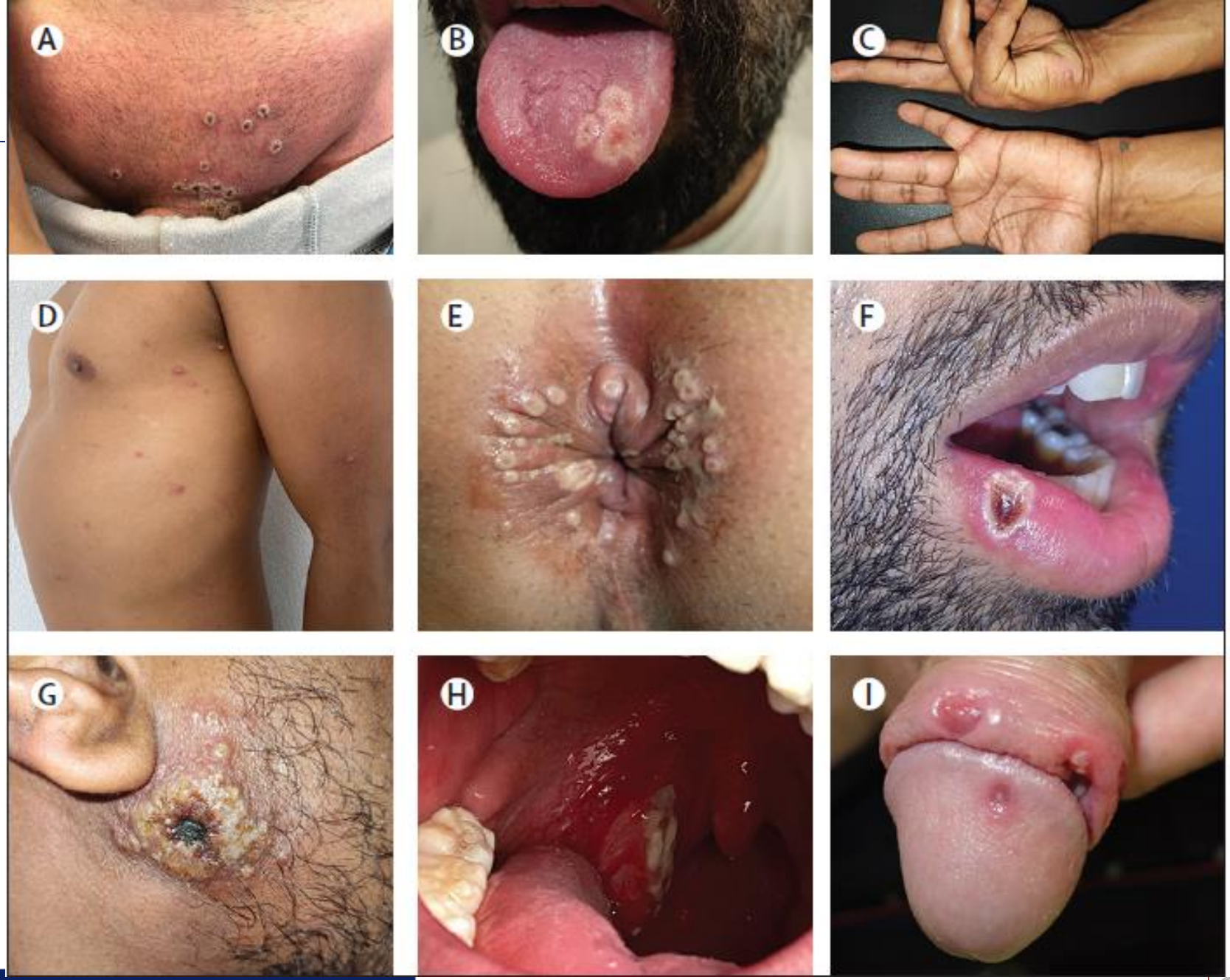
Casistica Dipartimento di Malattie Infettive
Ospedale L. Sacco, Milano

Caratteristiche epidemiologiche della coorte **Totale soggetti: 83** NA: soggetti per cui il dato non è disponibile o non è noto	
Età mediana in anni (RIQ1-3)	39 (34-44)
Sesso (%)	
- Maschi	82 (98.8)
- Femmine	1 (1.2)
Orientamento sessuale autodichiarato (%)	
- Omosessuale	77 (92.4)
- Eterosessuale	4 (4.8)
- Bisessuale	1 (1.2)
- NA	1 (1.2)
Vaccino per vaiolo (%)	
- No	74 (89.2)
- Sì	8 (9.6)
- NA	1 (1.2)
PrEP (% sul totale dei soggetti HIV negativi)	
- No	29 (63.0)
- Sì	12 (26.1)
- NA	5 (10.9)
Comorbidità (%)	
- Nessuna	39 (47.0)
- Presente/i	43 (51.8)
- NA	1 (1.2)
Infezione da HIV (%)	
- No	46 (55.4)
- Sì	37 (44.6)
MTS pregresse (%)	
- No	23 (27.7)
- Sì	58 (69.9)
- NA	2 (2.4)
MTS, diagnosi contestuale (%)	
- No	65 (78.3)
- Sì	18 (21.7)
Via di trasmissione (%)	
- Rapporto orale/bacio	8 (9.6)
- Rapporto sessuale	67 (80.7)
- NA	8 (9.6)
Transmission rank (%)	
- Caso isolato	57 (68.7)
- Caso indice	4 (4.8)
- Caso secondario	18 (21.7)
- NA	4 (4.8)
Storia recente di viaggi (%)	
- No	59 (71.7)
- Sì	21 (25.3)
- NA	3 (3.6)
Probabile nazione di acquisizione (%)	
- Italia	61 (73.5)
- Spagna	6 (7.2)
- Germania	4 (4.8)
- Francia	3 (3.6)
- Svizzera	1 (1.2)
- NA	8 (9.6)

Casistica Dipartimento di Malattie Infettive Ospedale L. Sacco, Milano

Caratteristiche cliniche della coorte **Totale soggetti: 83** NA: soggetti per cui il dato non è disponibile o non è noto	
Incubazione, mediana in giorni (RIQ1-3)	10 (6-13)
Durata della sintomatologia, mediana in giorni (RIQ1-3)	25 (18-29)
Sintomatologia (%)	
- Sistemica	73 (88.0)
- Febbre	62 (74.7)
- Linfoadenopatia	56 (67.5)
- Lesioni muco-cutanee	79 (95.2)
- Altro	51 (61.4)
Manifestazioni cutanee (%)	
- <5/>5	25 (30.1) /56 (67.5)
- <25/>25	73 (88.0) /8 (9.6)
- Monomorfe/Polimorfe	12 (14.5) /66 (79.5)
- Volto	45 (52.2)
- Cavo orale	9 (10.8)
- Genitali	47 (56.6)
- Anali	35 (42.2)
- Palmi delle mani	18 (21.7)
- Piante dei piedi	6 (7.2)
- Diffuse	59 (71.1)
Primo sintomo comparso, numero di soggetti (%)	
- Lesione mucocutanea	46 (55)
- Sintomo costituzionale	37 (45)
- Febbre	30 (36)
- Linfoadenopatia	20 (24)

Outcome (%)	
- Guarigione	80 (96.4)
- NA	3 (3.6)
Esiti a 90 giorni (%)	
- No	42 (50.6)
- Cicatrice non invalidante	23 (27.7)
- Cicatrice invalidante	2 (2.4)
- NA	16 (19.3)
Complicanze (%)	
- No	60 (72.3)
- Sì	22 (26.5)
- NA	1 (1.2)
Necessità di terapia specifica per la complicanza (% su numero totale di soggetti con complicanze)	
- No	1 (4.5)
- Sì	21 (95.5)
Terapia antivirale specifica (%)	
- No	77 (92.8)
- Sì	1 (1.2)
- NA	5 (6.)
Ricovero (%)	
- No	73 (88)
- Sì	7 (8.4)
- NA	3 (3.6)



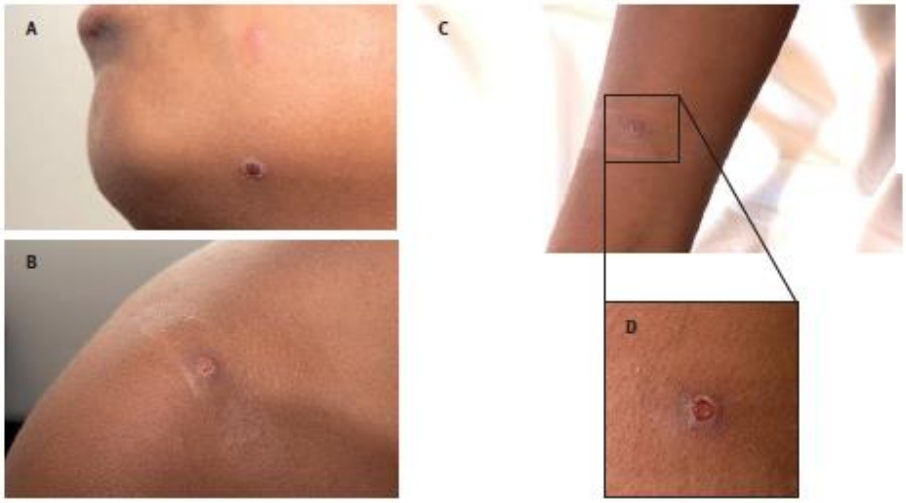
Tarin-Vicente EJ et al. Lancet, August 8, 2022

Paediatric monkeypox patient with unknown source of infection, the Netherlands, June 2022

A Marceline Tutu van Furth[1,2,*], Martijn van der Kuip[1,2,*], Anne L van Els[1,2], Lydia CR Fievez[3], Gini GC van Rijckevorsel[3,4], Anton van den Ouden[5], Marcel Jonges[6], Matthijs RA Welkers[6,7]

FIGURE 1

Monkeypox lesions, paediatric patient, the Netherlands, June 2022



Panel A: two solitary lesions on the left lower jaw and cheek; Panel B: right shoulder; Panel C: right forearm; Panel D: forearm zoomed in. Pictures were taken 10 days after appearance of the first lesion. Published with parental consent.

Clinical case description

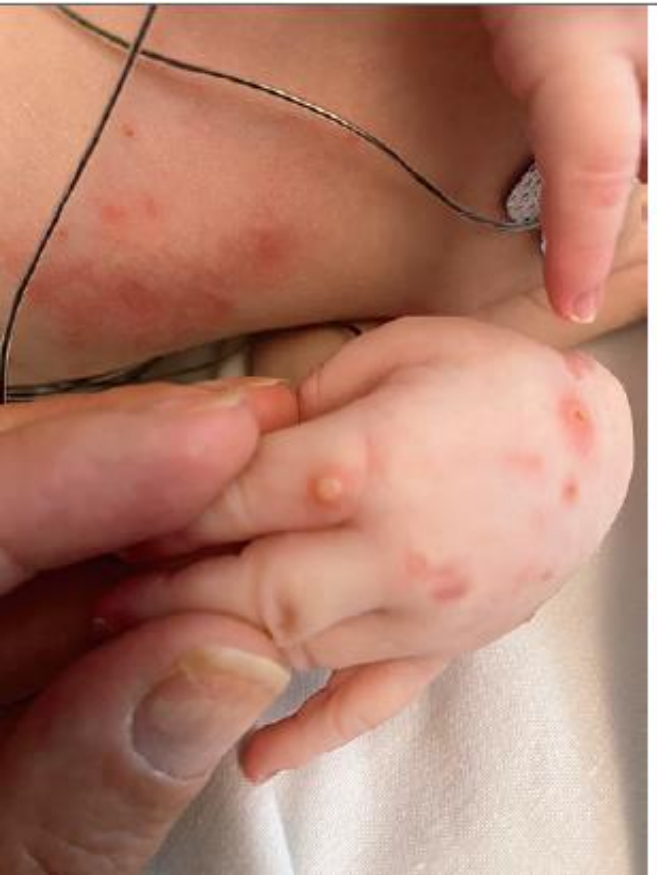
At the end of June 2022, a male child younger than 10 years without relevant medical history presented at a paediatric emergency room (ER) in Amsterdam, the Netherlands. He was vaccinated according to the Dutch national vaccination programme and had chicken pox when he was 5 years-old. Three weeks before his visit, he experienced a sore throat without fever that spontaneously resolved on the next day. A day later, he travelled to Turkey for a 1-week holiday. After his return, he noticed two small round skin lesions on his left lower jaw and cheek (Figure 1A). The general practitioner (GP) started with antifungal cream under the suspicion of a mild dermatomycosis. In the following days, more lesions appeared in the child's face. The GP was again consulted and antibiotic cream was started for suspected impetigo vulgaris. When ca 20 solitary lesions appeared on other body parts (Figure 1B-D) the child was referred to our hospital under the clinical suspicion of MPX. On physical examination, we observed an alert child in overall good health with stable vital parameters and without fever. There were no enlarged lymph nodes in the neck, armpits or groin region. The

Euro Surveill. 2022;27(29):pii=2200552.

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Neonatal Monkeypox Virus Infection



We report a case of perinatally acquired monkeypox virus infection and adenovirus coinfection in a 10-day-old infant. After the infant's uneventful birth in late April 2022, a rash developed on day 9 of life. The rash was initially vesicular, starting on the palms and soles and subsequently spreading to the face and trunk, and gradually became pustular (Fig. 1). Nine days before the birth, the infant's father had had a febrile illness, followed by a widespread rash; the rash resolved before the infant's birth. Four days after the infant's delivery, a similar rash developed in the mother. The family lived in the United Kingdom, and there was no history of travel to Africa or of contact with any travelers.

The infant was transferred to the regional pediatric intensive care unit on day 15 of life owing to evolving hypoxemic respiratory failure

secretions and blood. The infant's condition worsened, and invasive ventilation was initiated. A 2-week course of enteral tecovirimat (at a dose of 50 mg twice a day) was commenced in combination with intravenous cidofovir. After 4 weeks in intensive care, including 14 days of invasive

ventilation, the infant recovered and was discharged home. The timeline of intrafamilial in-

Ramnarayan P et al. N Engl J Med 2022, October 17

Severe disseminated clinical presentation of monkeypox virus infection in an immunosuppressed patient: first death report in Brazil

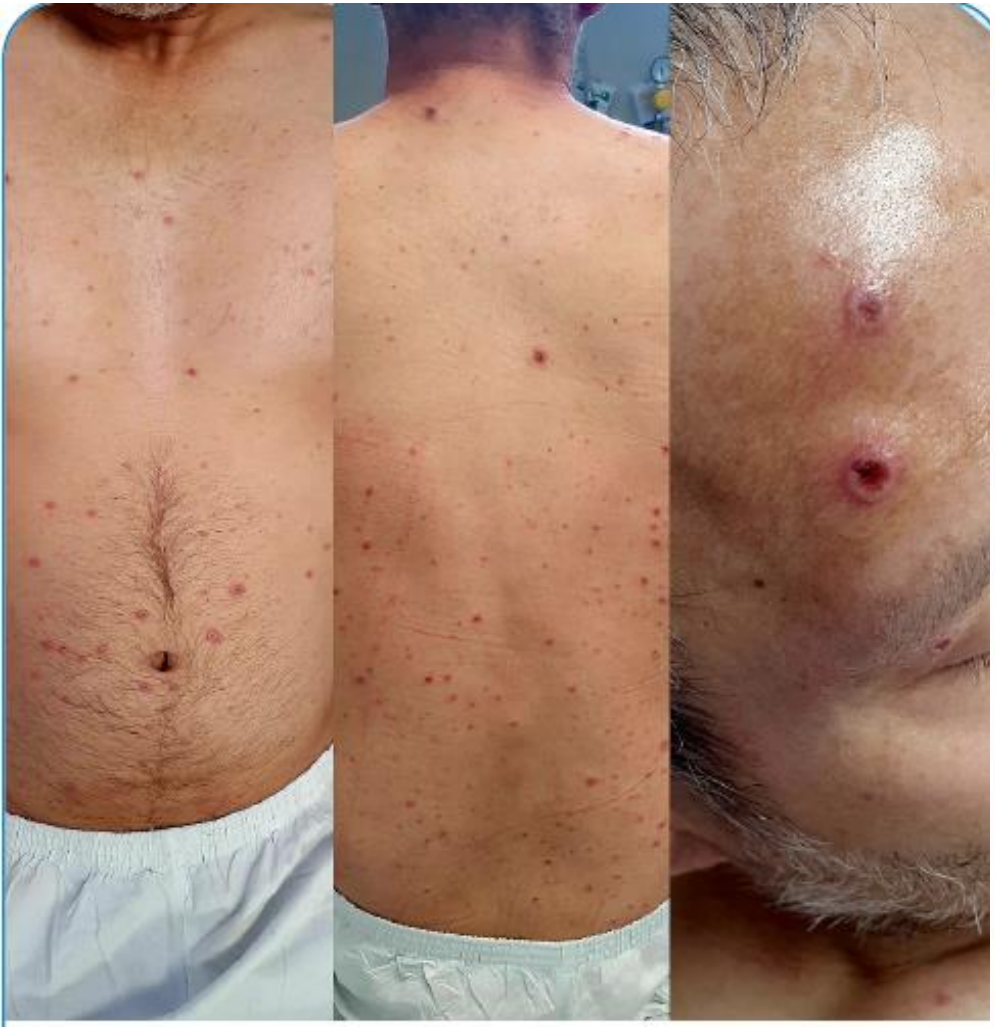


FIGURE 1: Hospital admission on July 15, 2022.

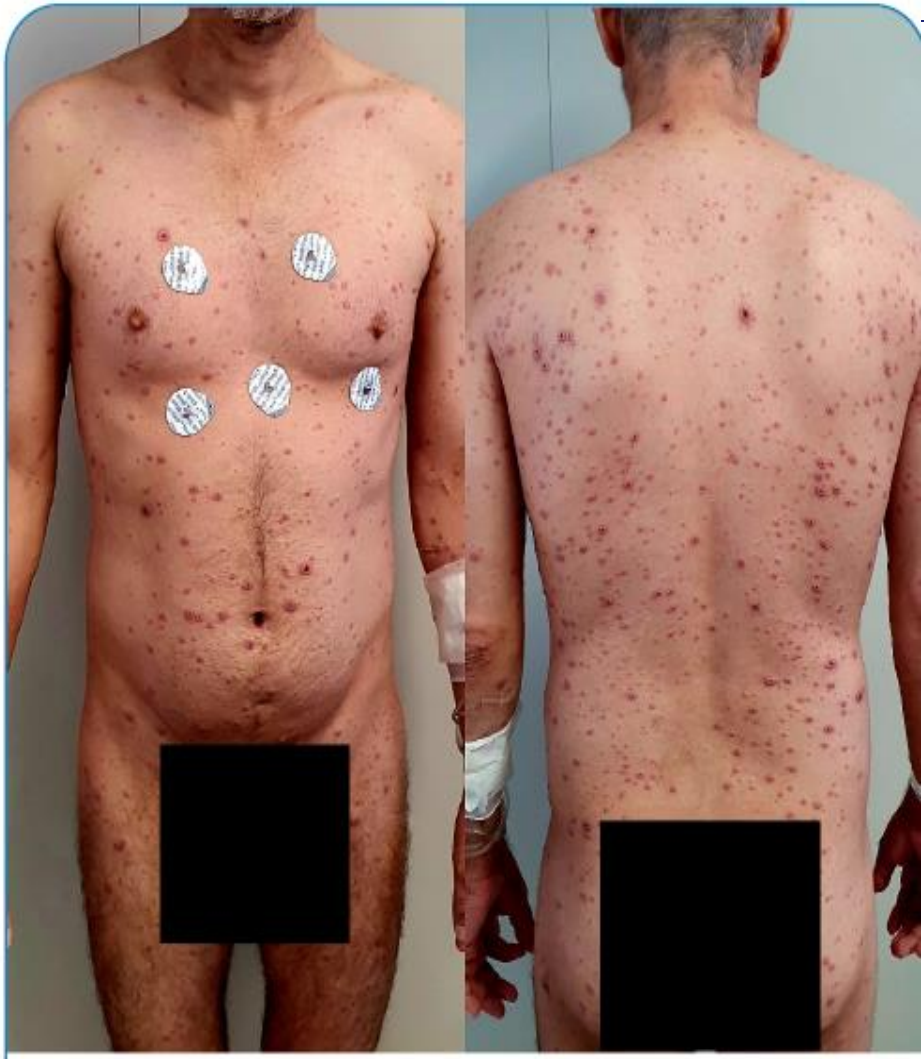


FIGURE 2: July 18, 2022.

Severe disseminated clinical presentation of monkeypox virus infection in an immunosuppressed patient: first death report in Brazil

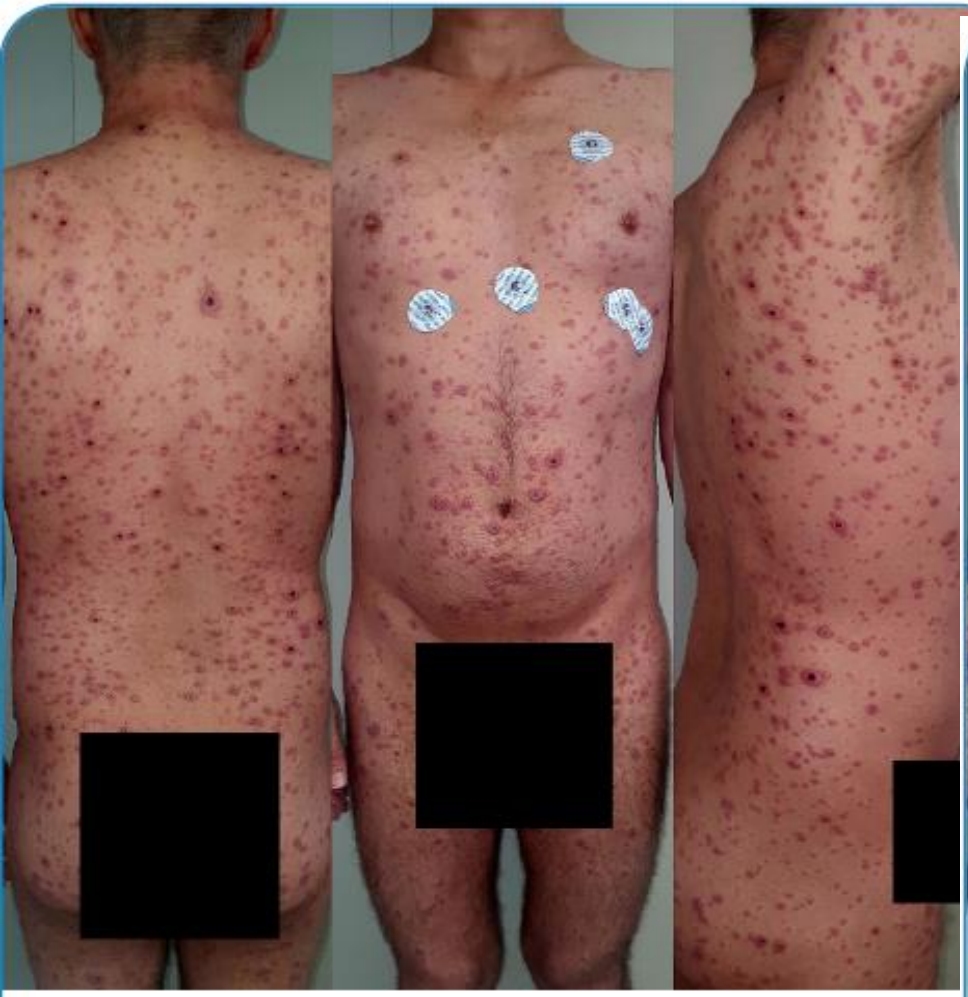


FIGURE 3: July 21, 2022.

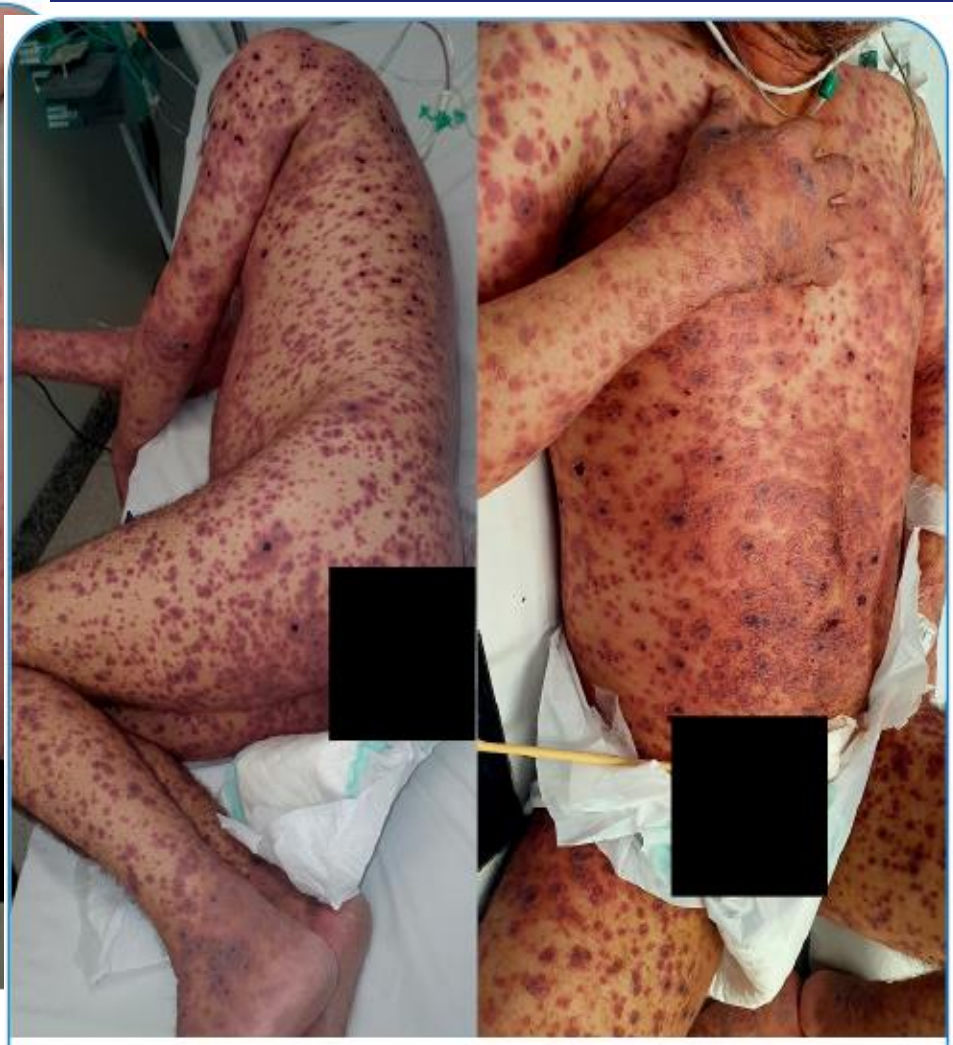
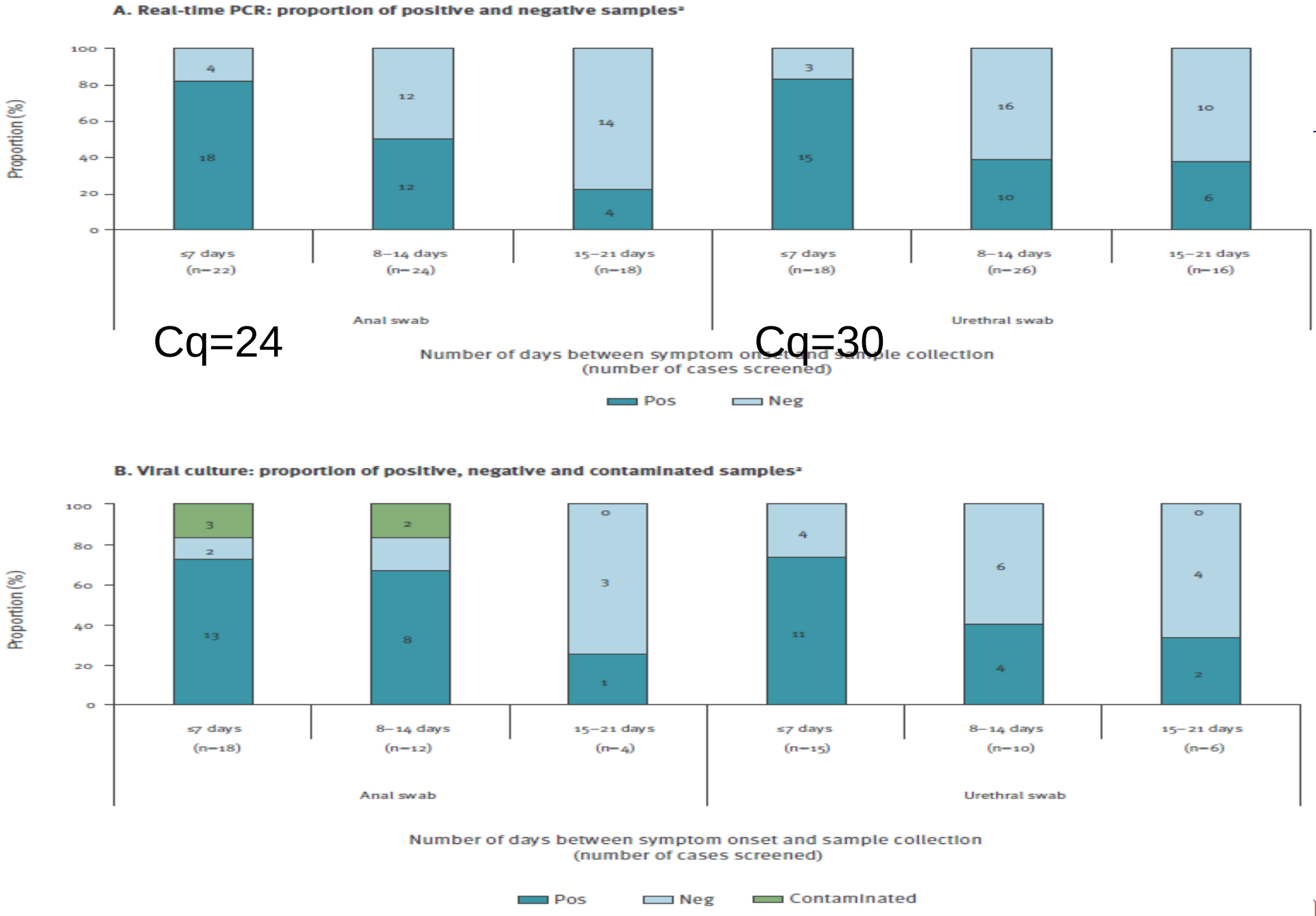


FIGURE 4: July 27, 2022.



Moschese D et al Euro Surveill 2022; 27:36:pii=2200675

Viral loads in clinical samples of men with monkeypox virus infection: a French case series

Palich R et al. Lancet Infect Dis 2023;23:74-80

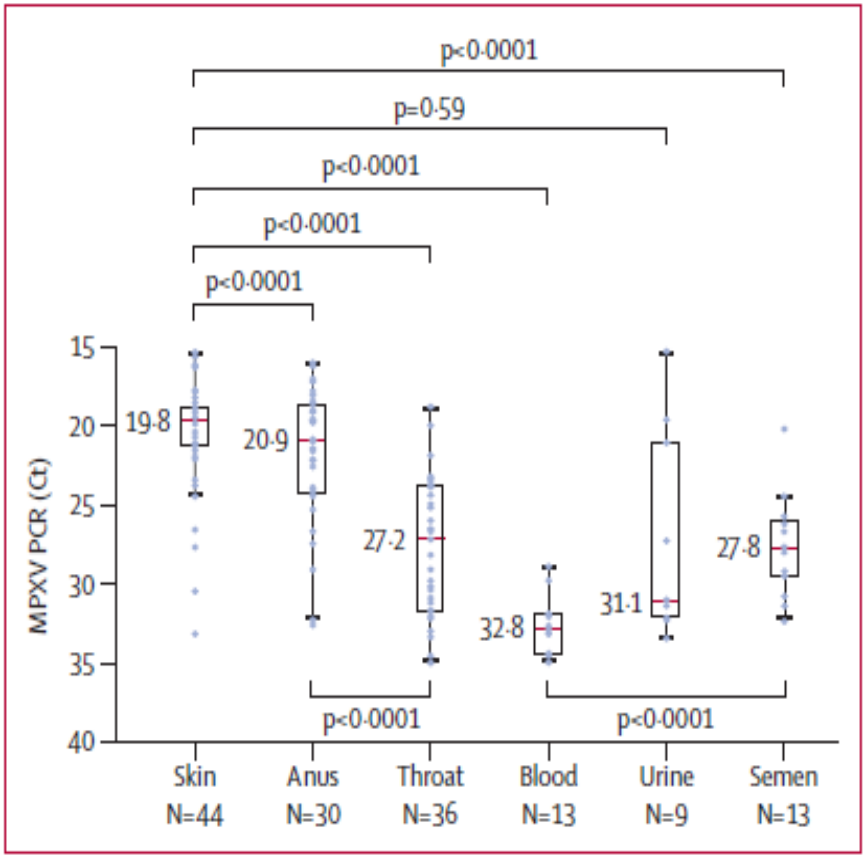


Figure 2: MPXV viral loads given as cycle thresholds, according to sampled sites

Clinical features and management of individuals admitted to hospital with monkeypox and associated complications across the UK: a retrospective cohort study

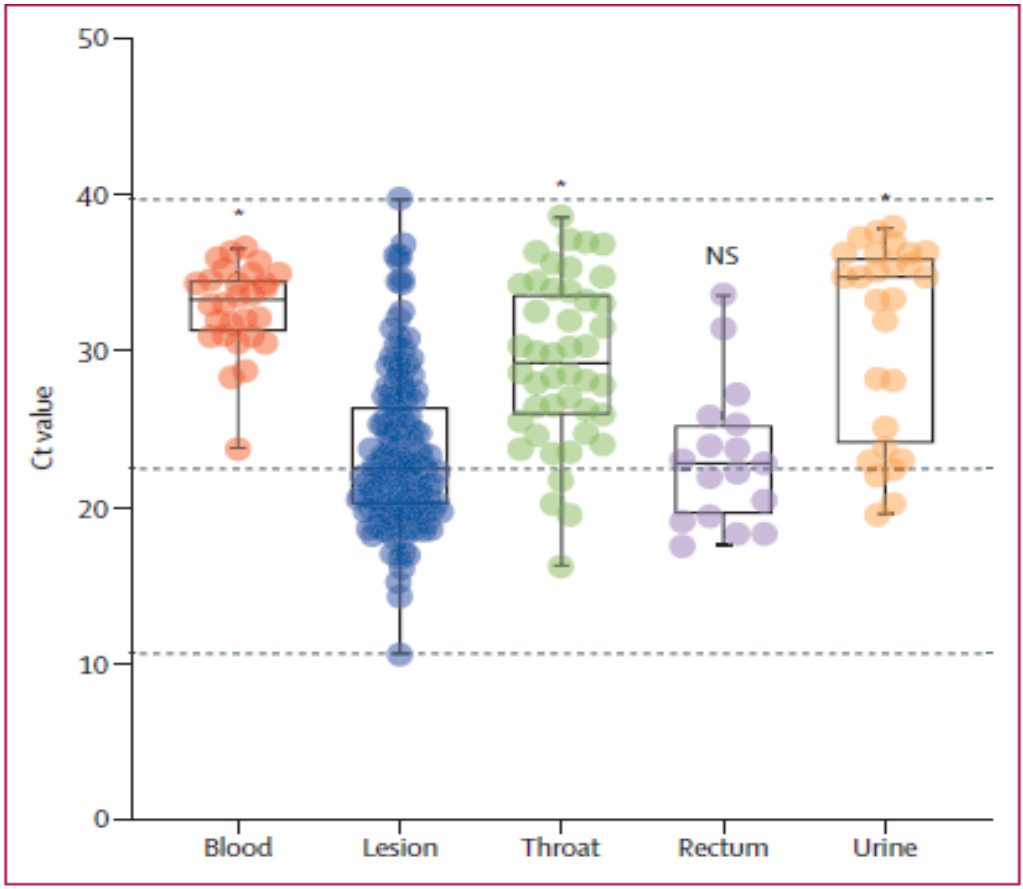


Figure 2: Orthopox PCR cycle threshold values by anatomical site

Fink DL et al.Lancet Infect Dis 2022, Dec 22

Hospitalisation for monkeypox in Milan, Italy

Davide Moschese [a], Andrea Giacomelli [b], Martina Beltrami [b,c], Giacomo Pozza [b,c], Davide Mileto [d], Serena Reato [b,c], Martina Zacheo [b,c], Mario Corbellino [b], Giuliano Rizzardini [a], Spinello Antinori [b,c,*]

Up to July 18, 2022, 34 confirmed cases of MPXV infection were diagnosed at the Department of Infectious Diseases of Luigi Sacco Hospital in Milan, Italy. Overall, 4 patients (11.7%) required hospitalisation (Table 1) but only in three cases (8.8%) it was directly due to clinical worsening of MPX infection and bacterial superinfections. Patient # 1

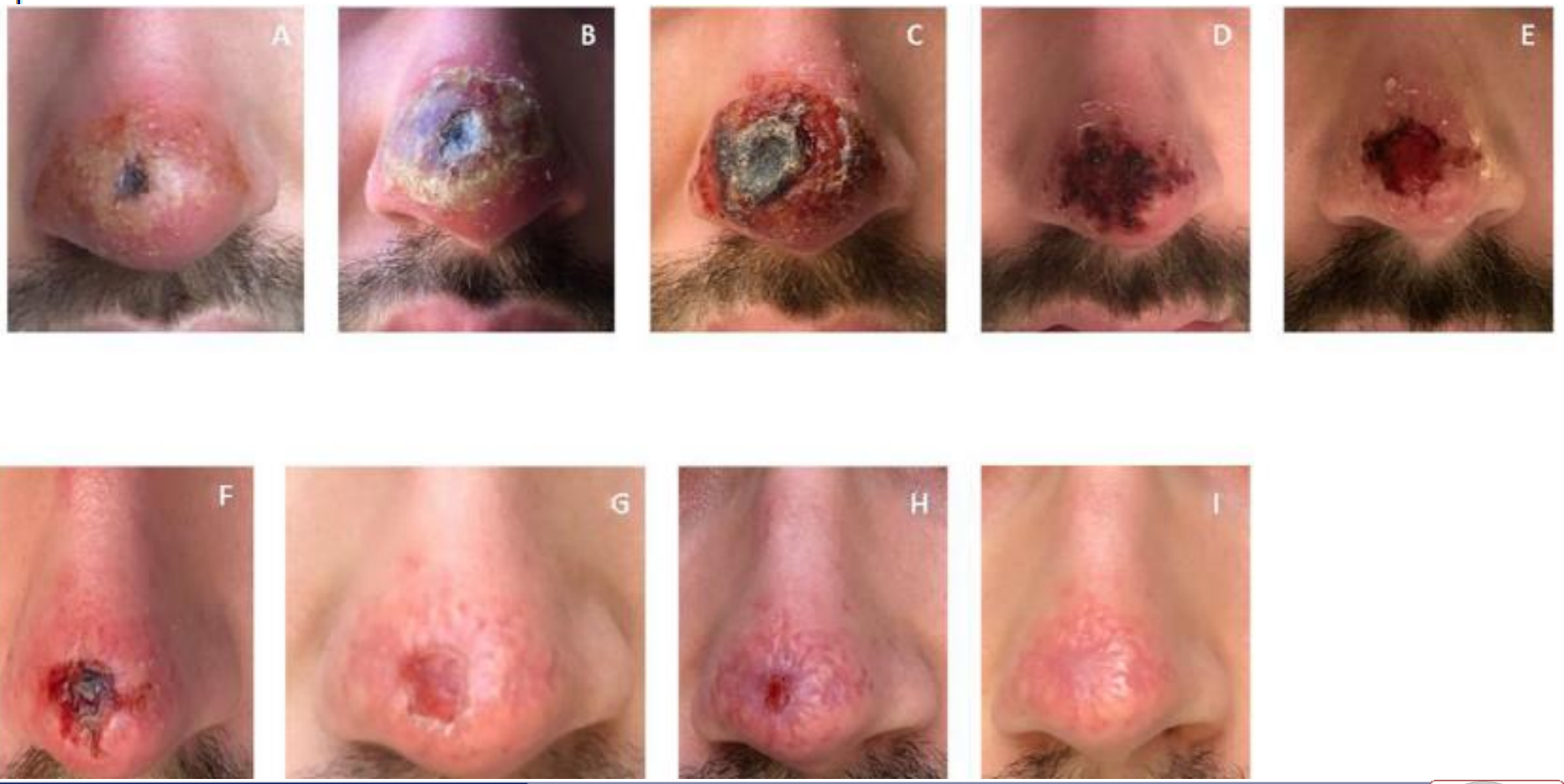
Characteristics of hospitalised subjects with monkeypox.

Gender/Age	M/26y	M/35y	M/34y	M/37y
HIV status	Negative	Negative	Positive	Positive
Clinical manifestations	Lesion on the nose followed by high fever (39.3 °C), chills, sweats, lymphadenopathy	Vesicular rash on mouth, head, limbs, trunk followed by fever (38 °C), lymphadenopathy	Perianal lesion followed by fever (38.3 °C), lymphadenopathy	Skin lesion of inguinal areas, shaft of penis, scrotum followed by fever (38 °C), headache, lymphadenopathy
Location of skin lesions	Nose, limb	Head, limbs, trunk	Perianal, foot, face, arm	Inguinal, penis, scrotum, face
Samples positive for MPXV PCR	Vesicule (skin, nose), anal swab, pharynx, seminal fluid	Vesicule, pharynx	Vesicule, pharynx, anal swab	Vesicule, pharynx, anal and uretral swab
Cause of hospitalisation	Worsening nasal lesion with suspected bacterial infection	Severe anal pain	Inability to self isolate	Bacterial infection (*S. aureus*, *Streptococcus pyogenes*)
Time of hospitalisation (days)	8	5	8	13
Abnormalities of laboratory findings	Increased C-reactive protein (45.1 mg/L)	Increased white blood cells (11,440/μL, N 40% L50%), increased C-reactive protein (12 mg/L)	Mild thrombocytopenia (146,000/μL), increased C-reactive protein (30 mg/L)	Increased C-reactive protein (23,1 mg/L), increased D-dimer (1930 ng/mL)
Treatment	Amox/clav 3 g/d for 8 days; Cidofovir 5 mg/kg day 1 and 7	Analgesic therapy	None	Ceftriaxone 2 g/d for 7 days + daptomycin 500 mg/d for 5 days
Outcome	Recovery	Recovery	Recovery	Recovery

N, neutrophils; L, lymphocytes; Amox/clav, amoxicillin/clavunalic acid; C-reactive protein normal value 10 mg/L.

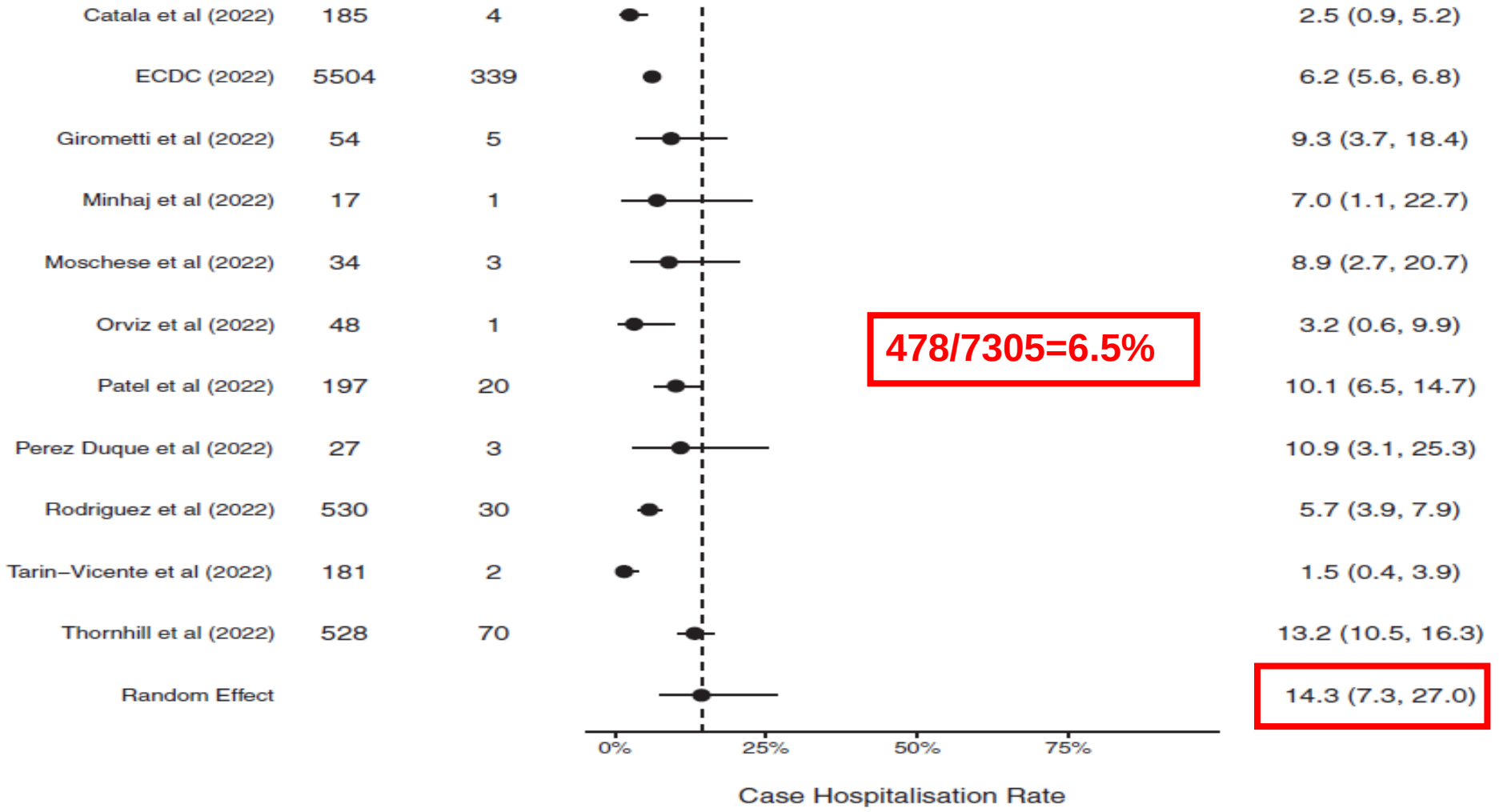
Hospitalisation for monkeypox in Milan, Italy

Davide Moschese [a], Andrea Giacomelli [b], Martina Beltrami [b,c], Giacomo Pozza [b,c], Davide Mileto [d], Serena Reato [b,c], Martina Zacheo [b,c], Mario Corbellino [b], Giuliano Rizzardini [a], Spinello Antinori [b,c,*]



Global monkeypox case hospitalisation rates: A rapid systematic review and meta-analysis

Michael E. DeWitt,[a,b,*] Christopher Polk,[a,b,c] John Williamson,[a,b] Avinash K. Shetty,[a,b,d] Catherine L. Passaretti,[b,c] Candice J. McNeil,[a,b] Robert T. Fairman,[b,c,e] Mindy M. Sampson,[a,b,c] Cynthia Dalton,[a] and John W. Sanders[a,b]



eClinicalMedicine
2022;54: 101710

Management of mild or uncomplicated monkeypox

10 June 2022

WHO recommends:

- Patients with suspected or confirmed MPX with mild, uncomplicated disease and not at high risk for complications can be isolated at home, for the duration of the infectious period, as long as a home assessment determines infection prevention and control (IPC) conditions are fulfilled at home setting.
- A home assessment should be conducted when deciding to isolate and care for a person with suspected or confirmed MPX with mild uncomplicated disease in a home setting.
- A patient with mild, uncomplicated MPX cared for at home should be isolated in an area separate from other household members and away from shared areas of the home (i.e. a separate room or area with a curtain or screen).
- Caution should be taken when handling and cleaning linens, household surfaces and during waste disposal.
- Patients with MPX be given symptomatic treatment such as antipyretics for fever and analgesia for pain.
- Patients with MPX be assessed for their nutritional status and given adequate nutrition and appropriate rehydration.
- Counsel patients with mild MPX about signs and symptoms of complications that should prompt urgent care.
- Conservative treatment of rash lesions should be performed dependent of their stage with aims to relieve discomfort, speed healing and prevention of complications, such as secondary infections or exfoliation.
- Antibiotic therapy or prophylaxis not be used in patients with uncomplicated MPX. However, lesions should be monitored for secondary bacterial infection (i.e. cellulitis, abscess) and if present treated with antibiotics with activity against normal skin flora, including *Streptococcus pyogenes* and methicillin-sensitive *Staphylococcus aureus* (MSSA).

Table 2. Potential Treatment Options for Monkeypox Infection

Therapy	Mechanism of Action	Typical Dosing	Formulation	FDA Approval Status	Side Effects and Adverse Events
Cidofovir	Blocks viral DNA synthesis through competitive inhibition of DNA polymerase	5 mg/kg per dose once weekly for ≥2 doses (with concomitant probenecid)	IV; off-label: topical, intravesicular	CMV retinitis in patients with AIDS [82] (1996)	Nephrotoxicity; neutropenia; decreased intraocular pressure, nausea, vomiting
Brincidofovir	Lipid conjugate prodrug of cidofovir	4 mg/kg once weekly for 2 doses (max 200 mg/dose)	Oral	Smallpox (2021) [83]	Abdominal pain, nausea, vomiting, diarrhea, elevated liver transaminases and bilirubin
Tecovirimat	Inhibits activity of the protein VP37, which prevents creation of virions that can be released from an infected host cell, thereby preventing replication and dissemination within the host	IV: 35 to <120 kg: 200 mg q12 hours ≥120 kg: 300 mg q12 hours Oral: 40 to <120 kg: 600 mg q12 hours ≥120 kg: 600 mg q8 hours All regimens for 14 days	IV and oral (off-label topical) [84]	Smallpox (2018) [85]	IV: pain and swelling at infusion site; extravasation at infusion site; headache [86] Oral: headache, abdominal pain, nausea, vomiting
VIGIV	Passive immunity through OPXV-specific antibodies collected from pooled human plasma of persons immunized with smallpox vaccine	6000 units/kg as a single dose (up to 9000 units/kg) Dose can be repeated depending upon symptoms	IV	Complications of vaccinia vaccination (progressive vaccinia, severe generalized vaccinia, etc) (2005) [87]	Infusion reaction; local injection-site reaction (contraindicated in persons with IgA deficiency and possible IgA hypersensitivity)

Abbreviations: AIDS, acquired immunodeficiency syndrome; CMV, cytomegalovirus; DNA, deoxyribonucleic acid; FDA, US Food and Drug Administration; IgA, immunoglobulin A; IV, intravenous; Max, maximum; VIGIV, vaccinia immunoglobulin intravenous.

Clinical features and management of individuals admitted to hospital with monkeypox and associated complications across the UK: a retrospective cohort study

	Number of participants (n=156)
Indication for admission	
Severe rectal or perianal pain	44 (28%)
Oropharyngeal symptoms	
Upper respiratory tract disease affecting swallowing or airways	16 (10%)
Throat pain without affecting swallowing or airways	2 (1%)
Secondary bacterial infection	
Non-genital cellulitis	5 (3%)
Genital cellulitis	16 (10%)
Tonsillitis	9 (6%)
Other or not recorded	10 (6%)
Sepsis	0
Urological not secondary to secondary infection	
Difficulty passing urine or urinary obstruction	9 (6%)
Severe genital pain	8 (5%)
Genital oedema	8 (5%)
Ocular or periocular disease	5 (3%)
Encephalitis	0
Extensive and progressive cutaneous disease	14 (9%)

	All (n=156)	Secondary bacterial infection (n=82)	No secondary bacterial infection (n=74)
Received any antibiotics	119 (76%)	81 (99%)	38 (51%)
Received intravenous antibiotics	79 (51%)	65 (79%)	14 (19%)
Single dose	6/79 (8%)	2/65 (3%)	4/14 (29%)
<48 h duration	19/79 (24%)	18/65 (28%)	1/14 (7%)
>48 h duration	54/79 (68%)	45/65 (69%)	9/14 (64%)
Received oral antibiotics	106 (68%)	71 (87%)	35 (47%)
Single dose	4/106 (4%)	0	4 (5%)
<48 h duration	10/106 (9%)	6 (7%)	4 (5%)
>48 h duration	92/106 (87%)	65 (79%)	27 (36%)
Received tecovirimat	38 (24%)	23 (28%)	15 (20%)
Surgical procedures	10 (6%)	9 (11%)	1 (1%)
Duration of admission, days	5 (2–9)	7 (3–10)	4 (2–8)

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	Pre-exposure indications	Post-exposure indications*	Administration	Common side-effects	Serious adverse events	Contraindications
Replication-competent vaccinia virus, second-generation (ACAM2000)	Research laboratory personnel working with orthopoxviruses; clinical laboratory personnel doing diagnostic testing for orthopoxviruses; designated response team members; health care-personnel who administer ACAM2000 or care for patients infected with orthopoxviruses; and not recommended for the general population as of June, 2022	Unprotected direct contact with an active orthopoxvirus lesion or fluid or a contaminated item; being within 2 m of an individual with an active orthopoxvirus case for 3 h or more	Single percutaneous dose with bifurcated needle	Pruritus, lymphadenopathy, administration site soreness, fever, headache, myalgia, rash, fatigue, and bacterial infection at the administration site	Myopericarditis and pericarditis, encephalitis, progressive vaccinia, erythema multiforme major, eczema, vaccinatum, generalised vaccinia, post-vaccinial encephalitis or encephalomyelitis, blindness due to autoinoculation, and fetal death in pregnant women	Atopic dermatitis†, active exfoliative skin conditions†, immunosuppression†, pregnancy†, age <1 year†, breastfeeding, serious vaccine component allergy, underlying heart disease, and ≥3 major cardiac risk factors
Attenuated, minimally replication-competent vaccinia virus, third-generation (LC16m18, available in Japan)	Same as above; preferred for those with contraindications for replicating vaccines, immune deficiencies, immunosuppression, or atopic dermatitis; not recommended for the general population as of June, 2022	Same as above; preferred for those with contraindications for replicating vaccines, immune deficiencies, or atopic dermatitis; preferred for pregnant women if modified vaccinia virus Ankara-Bavarian Nordic not available; licensed in Japan for use in children	Single percutaneous dose with bifurcated needle	Pruritus, lymphadenopathy, administration site soreness, fever, headache, myalgia, rash, and fatigue	None noted in clinical trials	Serious vaccine component allergy
Replication-deficient modified vaccinia Ankara, third-generation (JYNNEOS)	Same as above; preferred for those with contraindications for replicating vaccines, immune deficiencies, immunosuppression, or atopic dermatitis	Same as above; preferred for those with contraindications for replicating vaccines, immune deficiencies, or atopic dermatitis; preferred for pregnant women	Two subcutaneous doses, 28 days apart	Injection site reactions, myalgia, headache, fatigue, nausea, and chills	None	Serious vaccine component allergy

*Post-exposure vaccination is ideally provided within 4 days of exposure to prevent infection; however, vaccination within 4–14 days of exposure can reduce disease severity if infection were to occur. †Including household contacts with the condition.

Table 1: **Indications, administration, side-effects, and contraindications for smallpox and monkeypox vaccination**[32-37]

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