



Autumn Conference
Friday 25th November 2022
ROYAL COLLEGE OF PHYSICIANS,
LONDON



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Monkeypox: what we've learned

Chair:

Dr Claire van Halsema

This educational event is supported by



Monkeypox
What we've learned from research

Jake Dunning
Royal Free Hospital, London
Pandemic Sciences Institute, University of Oxford

Conflict of Interest

In relation to this presentation, I declare that I have no financial conflicts of interest

I am an investigator on studies of vaccines and treatments for monkeypox (not funded by manufacturers)

I am a member of the WHO EC for monkeypox & the UKHSA Technical Advisory Group

Monkeypox before 2022 - Africa

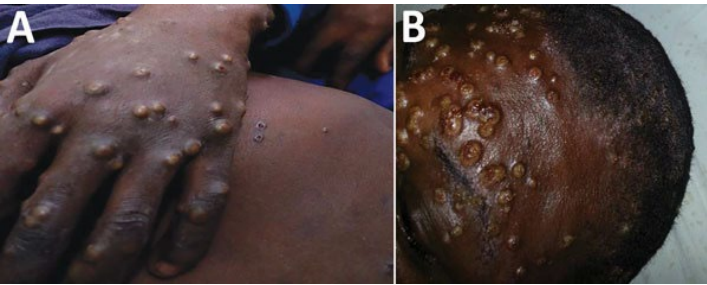


Emerg Infect Dis. 2018 Jun; 24(6): 1149–1151.
doi: 10.3201/eid2406.180017

PMCID: PMC6004876
PMID: 29619921

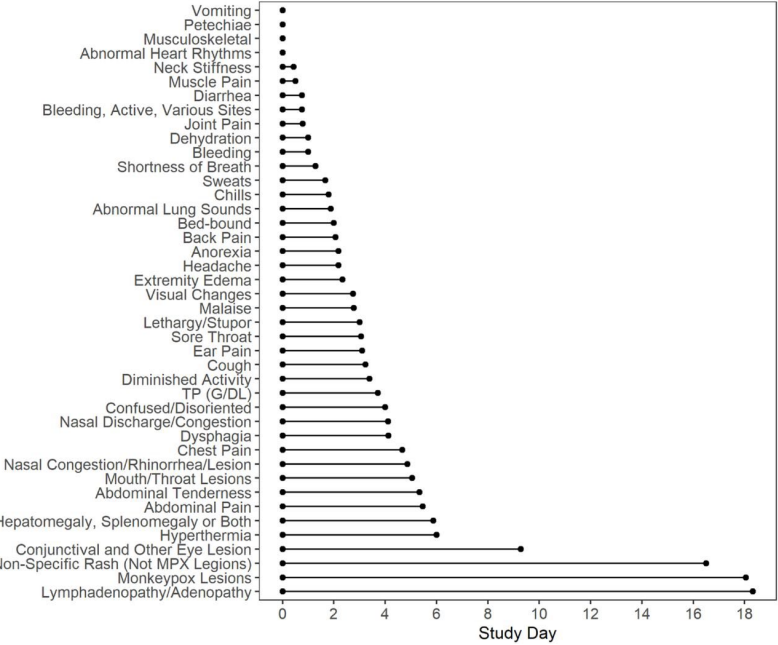
Reemergence of Human Monkeypox in Nigeria, 2017

Adesola Yinka-Ogunleye,¹ Olusola Aruna, Dimie Ogoina, Neni Aworabhi, Womi Eteng, Sikiru Badaru, Amina Mohammed, Jeremiah Agenyi, E.N. Etebu, Tamuno-Wari Numbere, Adolphe Ndorero, Eduard Nkuzimana, Yahyah Disu, Mahmood Dalhat, Patrick Nguku, Abdulaziz Mohammed, Muhammad Saleh, Andrea McCollum, Kimberly Wilkins, Ousmane Faye, Amadou Sall, Christian Happi, Nwando Mba, Olubumi Ojo, and Chikwe Ihekweazu



Clinical characterization of human monkeypox infections in the Democratic Republic of the Congo

Phillip R. Pittman, James W. Martin, Placide Mbala Kingebeni, Jean-Jacques Muyembe Tamfum, Qingwen Wan, Mary G. Reynolds, Xiaofei Quinn, Sarah Norris, Michael B. Townsend, Panayampalli S. Satheshkumar, Bryony Soltis, Anna Honko, Fernando B. Güereña, Lawrence Korman, John W. Huggins The Kole Human Monkeypox Infection Study Group



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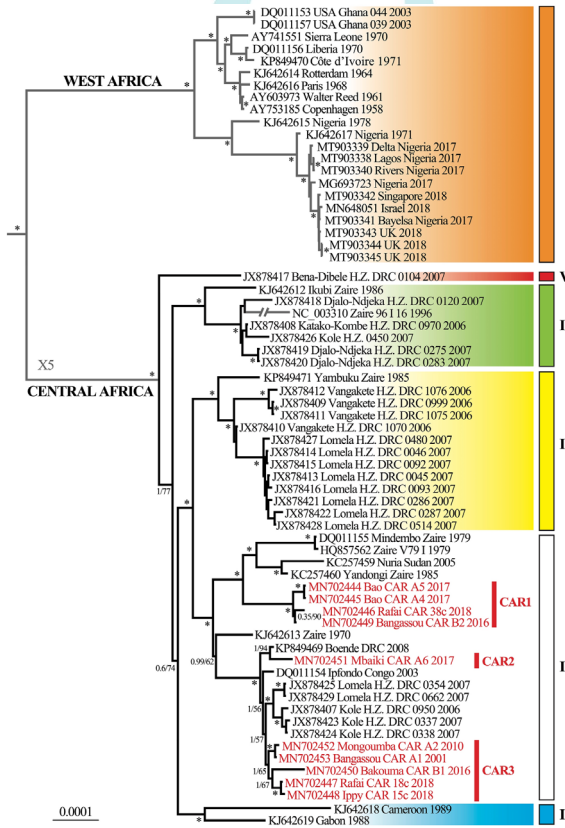
Article | Open Access | Published: 22 June 2021

Genomic history of human monkey pox infections in the Central African Republic between 2001 and 2018

Nicolas Berthet, Stéphane Descorps-Declère, Camille Besombes, Manon Curaudeau, Andrianiaina Andy Nkili Meyong, Benjamin Selekon, Ingrid Labouba, Ella Cyrielle Gonofio, Rita Sem Ouillibona, Huguette Dorine Simo Tchetsna, Maxence Feher, Arnaud Fontanet, Mirdad Kazanjii, Jean-Claude Manuguerra, Alexandre Hassanin, Antoine Gessain & Emmanuel Nakoune

Scientific Reports 11, Article number: 13085 (2021) | Cite this article

8511 Accesses | 23 Citations | 36 Altmetric | Metrics



Monkeypox before 2022 – UK & elsewhere

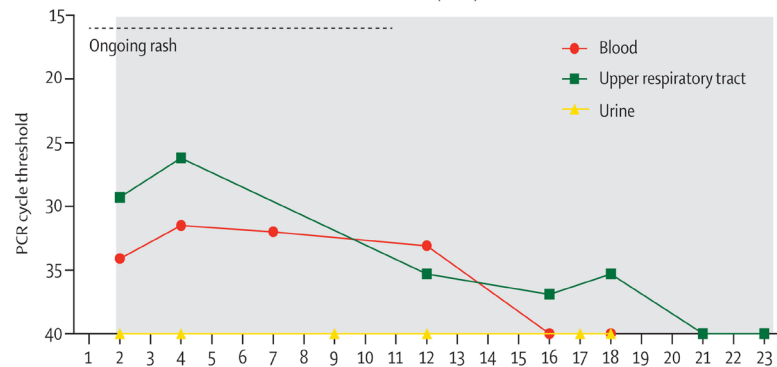
Articles

Clinical features and management of human monkeypox: a retrospective observational study in the UK

Hugh Adler, Susan Gould, Paul Hine, Luke B Swift, Watson Wong, Catherine F Howlman, Jane C Osborne, Tommy Rumping, Mike B Bendsworth, Christopher JA Duncan, Jake Dunning, Tom E Fletcher, Euan R Hunter, Michael Jacobs, Sage H Khoo, William Newsholme, David Porter, Robert J Parise, Libula Ratchiff, Matthieu L Schmid, Malcolm G Scarpie, Anne J Tunbridge, Tom Wingfield*, Nicholas M Price* on behalf of the NHS England High Consequence Infectious Diseases (Aikome) Network

oa

Patient 6 (2021)



EMERGING INFECTIOUS DISEASES*

EID Journal > Volume 26 > Number 4—April 2020 > Main Article

Volume 26, Number 4—April 2020

Dispatch

Human-to-Human Transmission of Monkeypox Virus, United Kingdom, October 2018

Aisling Vaughan¹, Emma Aarons, John Astbury, Tim Brooks, Meera Chand, Peter Flegg, Angela Hardman, Nick Harper, Richard Jarvis, Sharon Mawdsley, Mark McGivern, Dilys Morgan, Gwyn Morris, Grainne Nixon, Catherine O'Connor, Ruth Palmer, Nick Phin, D. Ashley Price, Katherine Russell, Bengu Said, Matthias L. Schmid, Roberto Vivancos, Amanda Walsh, William Welfare, Jennifer Wilburn, and Jake Dunning*

Author affiliations: Public Health England, London, UK (A. Vaughan, E. Aarons, J. Astbury, T. Brooks, M. Chand, A. Hardman, R. Jarvis, M. McGivern, D. Morgan, G. Morris, G. Nixon, C. O'Connor, N. Phin, K. Russell, B. Said, R. Vivancos, A. Walsh, W. Welfare, J. Wilburn, J. Dunning); NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, London (A. Vaughan, T. Brooks, D. Morgan, R. Vivancos, J. Dunning); Blackpool Teaching Hospitals NHS Foundation Trust, Blackpool, UK (P. Flegg, N. Harper, S. Mawdsley, R. Palmer); The Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, UK (D.A. Price, M.L. Schmid)

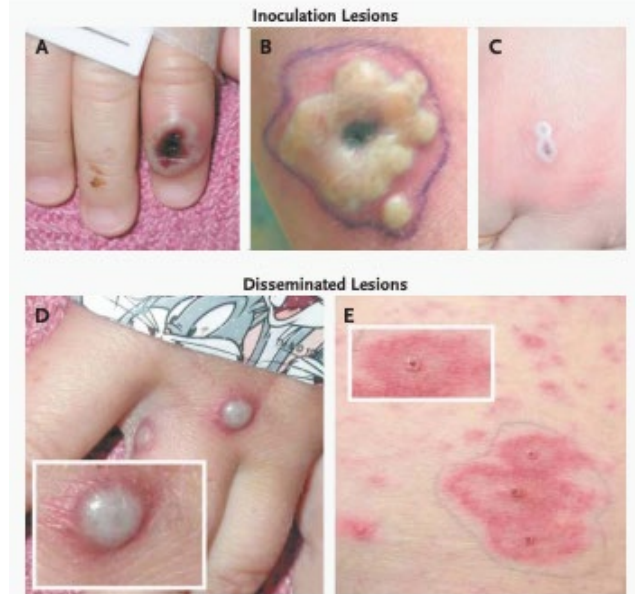


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

The Detection of Monkeypox in Humans in the Western Hemisphere

Kurt D. Reed, M.D., John W. Melski, M.D., Mary Beth Graham, M.D., Russell L. Regnery, Ph.D., Mark J. Sotir, Ph.D., M.P.H., Mark V. Wegner, M.D., M.P.H., James J. Kazmierczak, D.V.M., M.S., Erik J. Stratman, M.D., Yu Li, Ph.D., Janet A. Fairley, M.D., Geoffrey R. Swain, M.D., M.P.H., Victoria A. Olson, Ph.D., Elizabeth K. Sargent, B.S., Sue C. Kehl, Ph.D., Michael A. Frace, Ph.D., Richard Kline, M.S., Seth L. Foldy, M.D., Jeffrey P. Davis, M.D., and Inger K. Damon, M.D., Ph.D.



Clade IIb MPXV affecting mostly GBMSM in 2022

www.gov.uk/government/news/monkeypox-cases-confirmed-in-england-latest-updates

16 May 2022

Four more cases of monkeypox identified by UKHSA

The UK Health Security Agency (UKHSA) has detected 4 additional cases of monkeypox, 3 in London and one linked case in the North East of England.

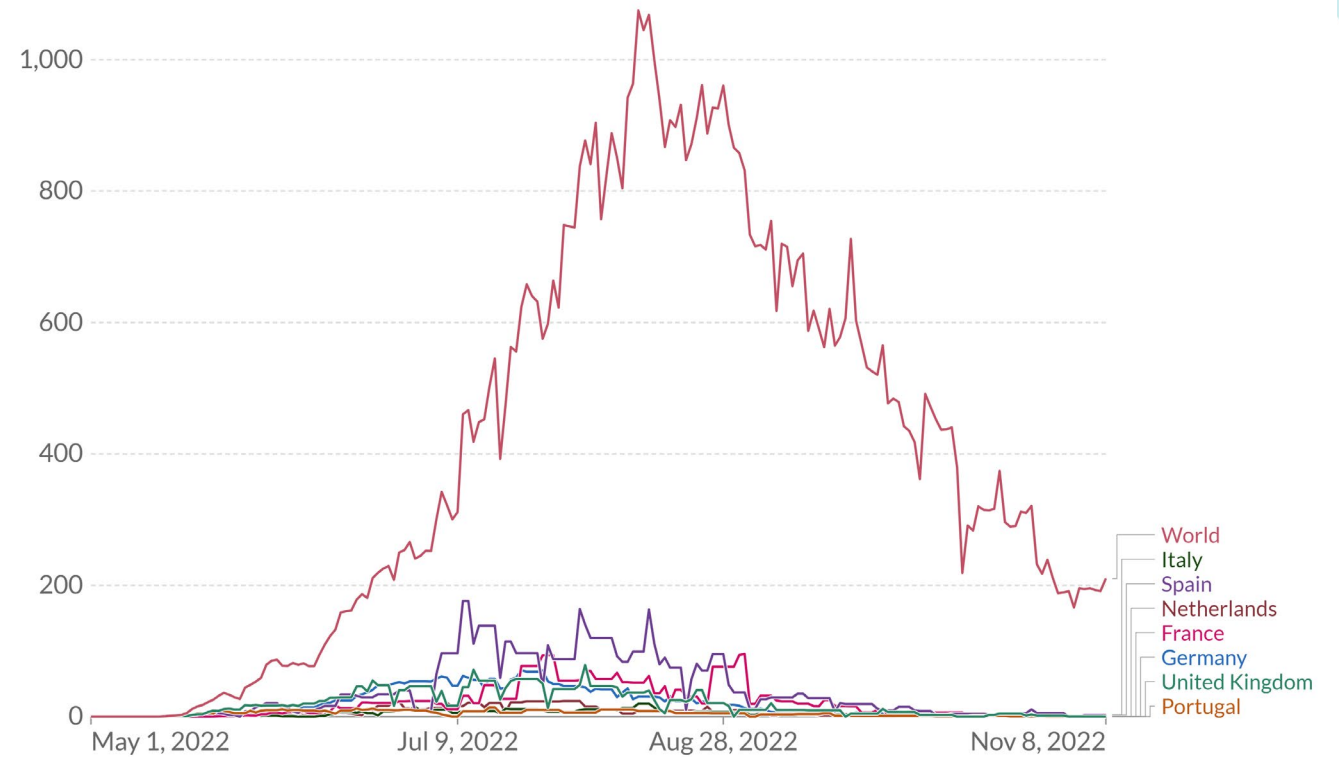
The 4 new cases do not have known connections with the previous confirmed cases [announced on 14 May](#) and the case [announced on 7 May](#).

Investigations are underway to establish links between the latest 4 cases, who all appear to have been infected in London. All 4 of these cases self-identify as gay, bisexual or other men who have sex with men (MSM).



Monkeypox: Daily confirmed cases

7-day rolling average



Source: World Health Organization

CC BY

UKHSA technical briefings

Research and analysis

Investigation into monkeypox outbreak in England: technical briefing 1

Updated 23 September 2022

Applies to England

Contents

[Potential levels of the outbreak in England](#)

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[Part 4. Transmission dynamics](#)

[Sources and acknowledgments](#)

The UK Health Security Agency (UKHSA) is working with the NHS and the public health agencies of the 4 nations to investigate the monkeypox outbreak in the past few weeks. This briefing is produced to share data useful to other public health investigators and academic partners undertaking related work. It includes early evidence and preliminary analyses which may be subject to change.

Potential levels of the outbreak in England

The outbreak can be considered to fall into one of 4 potential levels of transmission.

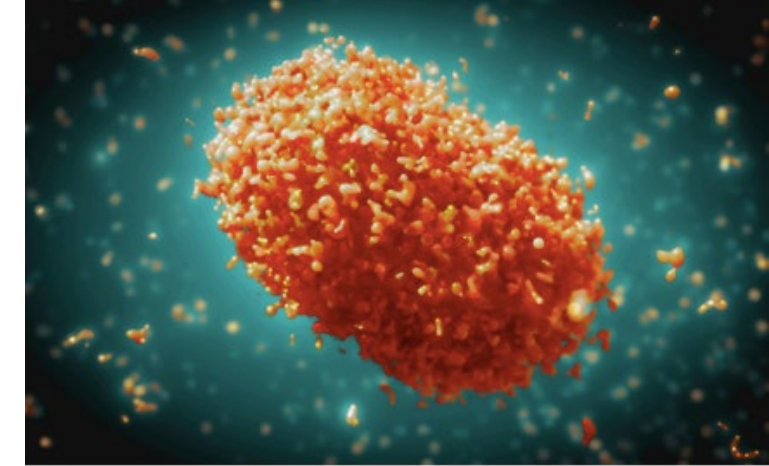
Devolved administrations	Confirmed cases
England	320
Northern Ireland	2
Scotland	11
Wales	3
Total	336

A high proportion of England cases were known to be London residents (81%, 224 of 276 with reported home address), see Table 3. Where gender information was available, 311 (99% of 314) confirmed cases were male, with 3 confirmed female cases. The median age of confirmed cases in the UK was 38 years old (interquartile range 32 to 44).

One hundred and fifty-two cases participated in more detailed questionnaires, implemented from 26 May 2022, and used retrospectively. In this data, 151 of the 152 men interviewed identified as gay, bisexual and other men who have sex with men (GBMSM), or reported same sex contact, and the remaining individual declined to disclose this information. Recent foreign travel, within 21 days prior to symptom onset, was reported by 75 cases (22%), with 59 of these reporting travel within Europe.

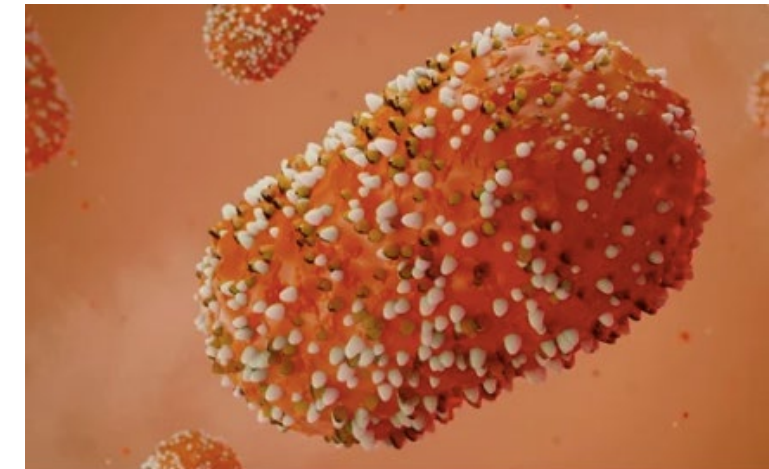
UKHSA R&D priorities

Research topic	Priority evidence gaps
Surveillance	Levels of undiagnosed disease Trends and growth Level of asymptomatic infection Wastewater surveillance
Transmission dynamics	Transmission risk to contacts Modes of transmission
Biological characterisation and virology	Genome sequencing and in-host variation Viral dynamics Virus characterisation, including biological significance of mutations
Clinical characterisation	Clinical presentation and outcomes. Groups at risk of worse outcomes
Vaccine response and immunology	Immune response to infection and vaccines Immunological correlates of protection Post-implementation effectiveness
Therapeutics	Post-exposure Prophylaxis with Tecovirimat Early treatment and risk of transmission Impact on disease protection
Diagnostics and evaluation	Best site to test Home sampling and testing Evaluation of Lateral Flow Devices Development of serology test
Evaluation of other interventions	Effectiveness of contact tracing
Behavioural and other social sciences	Public perception of risk Public understanding of disease Help seeking behaviour Vaccine acceptability Adherence to self-isolation Media coverage, behaviour and stigmatisation
Longer term consequences of infection	Are there longer-term consequences of infection?
Other	Reverse zoonosis risk



📅 2 – 3 June 2022

WHO monkeypox research: What are the knowledge gaps and priority research questions?



📅 2 August 2022 13:00 – 18:00 UTC Time

WHO Monkeypox Research - What study designs can be used to address the remaining knowledge...

When did outbreaks affecting GBMSM begin?

Human Monkeypox Virus outbreak among Men who have Sex with Men in Amsterdam and Rotterdam, the Netherlands: no evidence for undetected transmission prior to May 2022 in a retrospective study

Authors: Henry J. de Vries¹⁻⁴ (<http://orcid.org/0000-0001-9784-547X>), Hannelore M. Götz^{5,6}, Sylvia Bruisten¹, Annemiek A. van der Eijk⁷, Maria Prins^{1,3,8}, Bas B. Oude Munnink⁷, Matthijs R.A. Welkers^{1,9}, Marcel Jonges⁹, Richard Molenkamp⁷, Brenda M. Westerhuis^{1,9}, Leonard Schuele⁷, Arjen Stam^{1,9}, Marjan Boter⁷, Elske Hoornenborg^{1,3}, Daphne Mulders⁷, Mariken van den Lubben¹, Marion Koopmans⁷

medRxiv preprint doi: <https://doi.org/10.1101/2022.11.19.22282179>



Table 1: Test results for human Monkey Pox Virus of 401 samples from men who had sex with men visiting the Amsterdam and Rotterdam Centres for Sexual Health, February – May 2022.

sample type	sample period	location	test results		
			negative	positive	totals
anorectal samples of men without (anorectal) symptoms (1)	February 14 - May 9	Amsterdam	129	0	129
	April 1 - May 18	Rotterdam	64	0	64
anorectal samples of men with (anorectal) symptoms (1)	February 14 - May 9	Amsterdam	40	0	40
	April 1 - May 18	Rotterdam	29	1	30
positive ulcer samples (2)	February 14 - May 9	Amsterdam	79	0	79
	April 1 - May 18	Rotterdam	4	0	4
negative ulcer samples (3)	February 14 - May 9	Amsterdam	46	1	47
	April 1 - May 18	Rotterdam	8	0	8
Totals			399	2	401

(1) Rotterdam: any symptom, Amsterdam : anorectal symptoms (proctitis and/or skin lesions)

(2) Ulcer samples positive for either Herpes Simplex Virus, (Amsterdam & Rotterdam); *T. pallidum*, or *C. trachomatis*. (Amsterdam)

(3) Ulcer samples negative for either Herpes Simplex Virus, (Amsterdam & Rotterdam); *T. pallidum*, and *C. trachomatis*. (Amsterdam)

Has the virus 'evolved'?

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

Monkeypox | Evolution



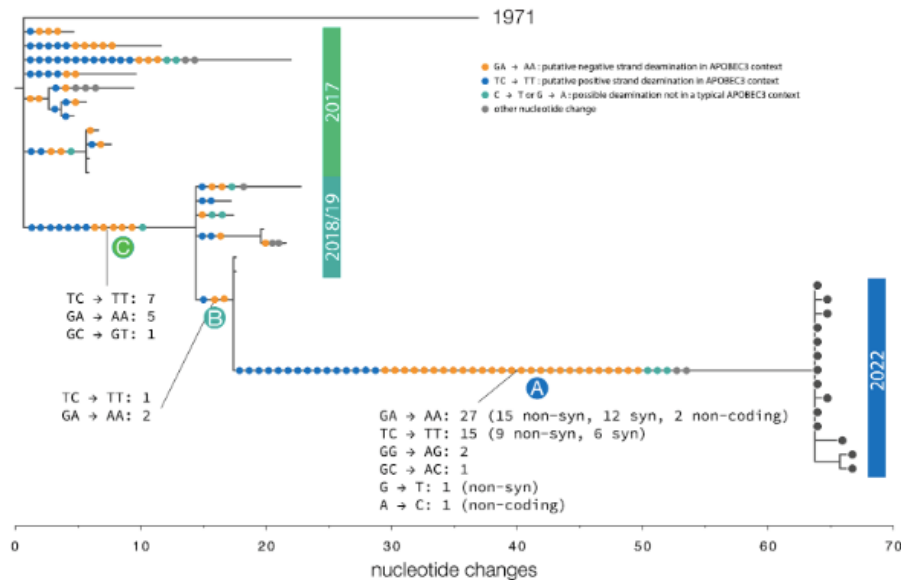
arambaut | ARTIC Network

9 May 30

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

This document is an initial report on the observation of an abundance of specific mutations in the 2022 MPXV outbreak and related virus genomes that can be ascribed to the action of APOBEC3 host enzymes. It should be considered work in progress and we plan to add additional analysis and interpretation. We also welcome discussion in the thread below. The analyses here are made possible by the groups and researchers who have shared MPXV genome sequence data (Table 1).

Áine O'Toole & Andrew Rambaut
Institute of Evolutionary Biology
University of Edinburgh
Edinburgh, UK



May 30

1/7

May 30

nature medicine

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Brief Communication | [Open Access](#) | [Published: 24 June 2022](#)

Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus

[Joana Isidro](#), [Vitor Borges](#), [Miguel Pinto](#), [Daniel Sobral](#), [João Dourado Santos](#), [Alexandra Nunes](#), [Verónica Mixão](#), [Rita Ferreira](#), [Daniela Santos](#), [Sílvia Duarte](#), [Luís Vieira](#), [Maria José Borrego](#), [Sofia Nuncio](#), [Isabel Lopes de Carvalho](#), [Ana Pelerito](#), [Rita Cordeiro](#) & [João Paulo Gomes](#) ✉

Abstract

The largest monkeypox virus (MPXV) outbreak described so far in non-endemic countries was identified in May 2022 (refs. [1,2,3,4,5,6](#)). In this study, shotgun metagenomics allowed the rapid reconstruction and phylogenomic characterization of the first MPXV outbreak genome sequences, showing that this MPXV belongs to clade 3 and that the outbreak most likely has a single origin. Although 2022 MPXV (lineage B.1) clustered with 2018–2019 cases linked to an endemic country, it segregates in a divergent phylogenetic branch, likely reflecting continuous accelerated evolution. An in-depth mutational analysis suggests the action of host APOBEC3 in viral evolution as well as signs of potential MPXV human adaptation in ongoing microevolution. Our findings also indicate that genome sequencing may provide resolution to track the spread and transmission of this presumably slow-evolving double-stranded DNA virus.

Community Clade IIb cases

THE LANCET

Submit Article

Journal of Infection 85 (2022) 334–363

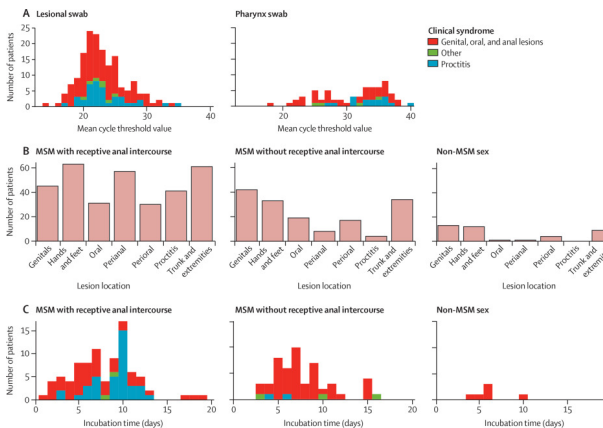
Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf



J Heskin et al.



EJ Tarín-Vicente et al.

The NEW ENGLAND JOURNAL of MEDICINE

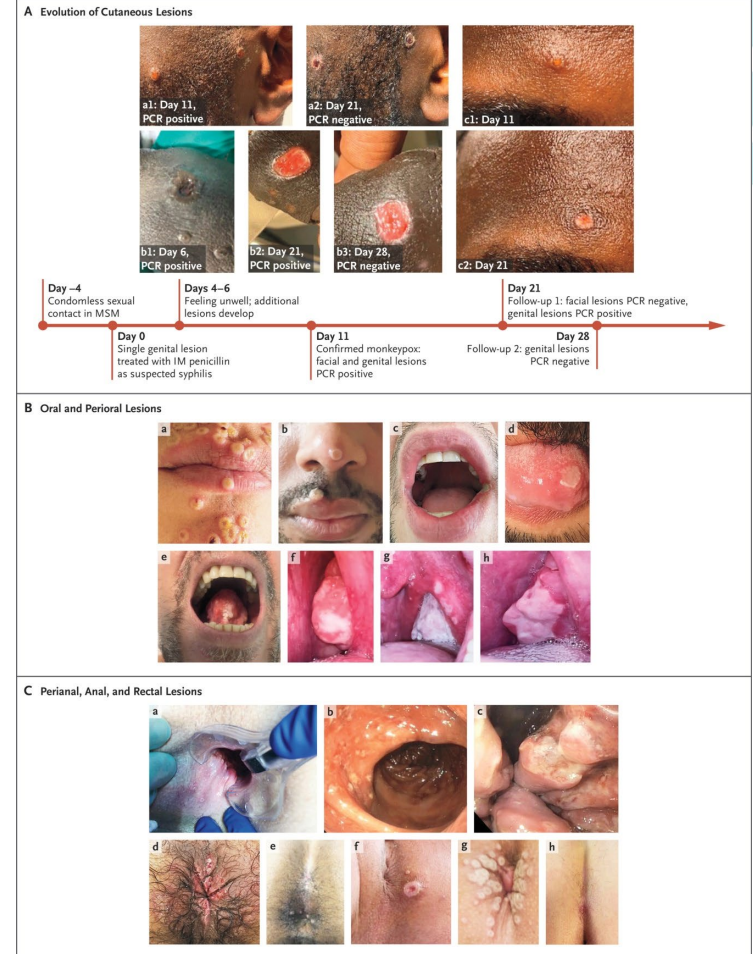
ESTABLISHED IN 1812

AUGUST 25, 2022

VOL. 387 NO. 8

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

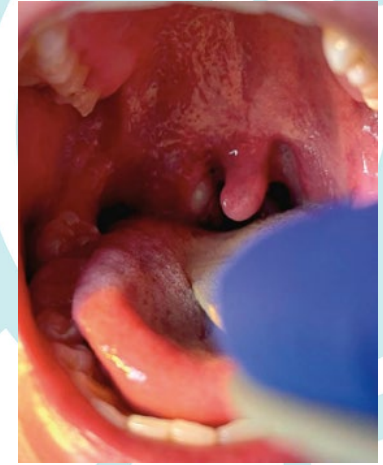
J.P. Thornhill, S. Barkati, S. Walmsley, J. Rockstroh, A. Antinori, L.B. Harrison, R. Palich, A. Nori, I. Reeves, M.S. Habibi, V. Apea, C. Boesecke, L. Vandekerckhove, M. Yakubovskiy, E. Sendagorta, J.L. Blanco, E. Florence, D. Moschese, F.M. Maltez, A. Goorhuis, V. Pourcher, P. Migaud, S. Noe, C. Pintado, 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 descriptions: UK inpatients

- Approximately 180 hospitalized for medical need
- Over 60 received tecovirimat in hospital
- No deaths
- Lots of pain and analgesic use
- Lots of secondary bacterial infections and antibiotic use
- Mostly genital & anorectal complications
- Also, oropharyngeal disease, eye disease and encephalitis
- Persistent, complex infection in HIV immunosuppression (rare in UK)

156 patient case-series **coming soon**
ISARIC CCP study: 106 recruited to date



T2 weighted magnetic resonance imaging scan of pelvis showing a 3.5 cm cavity in left mesorectum, adjacent to the rectal wall representing an area of localised perforation (arrow)

Images: Patel A et al. *BMJ* 2022; 378

Why did case numbers decrease?

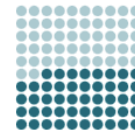
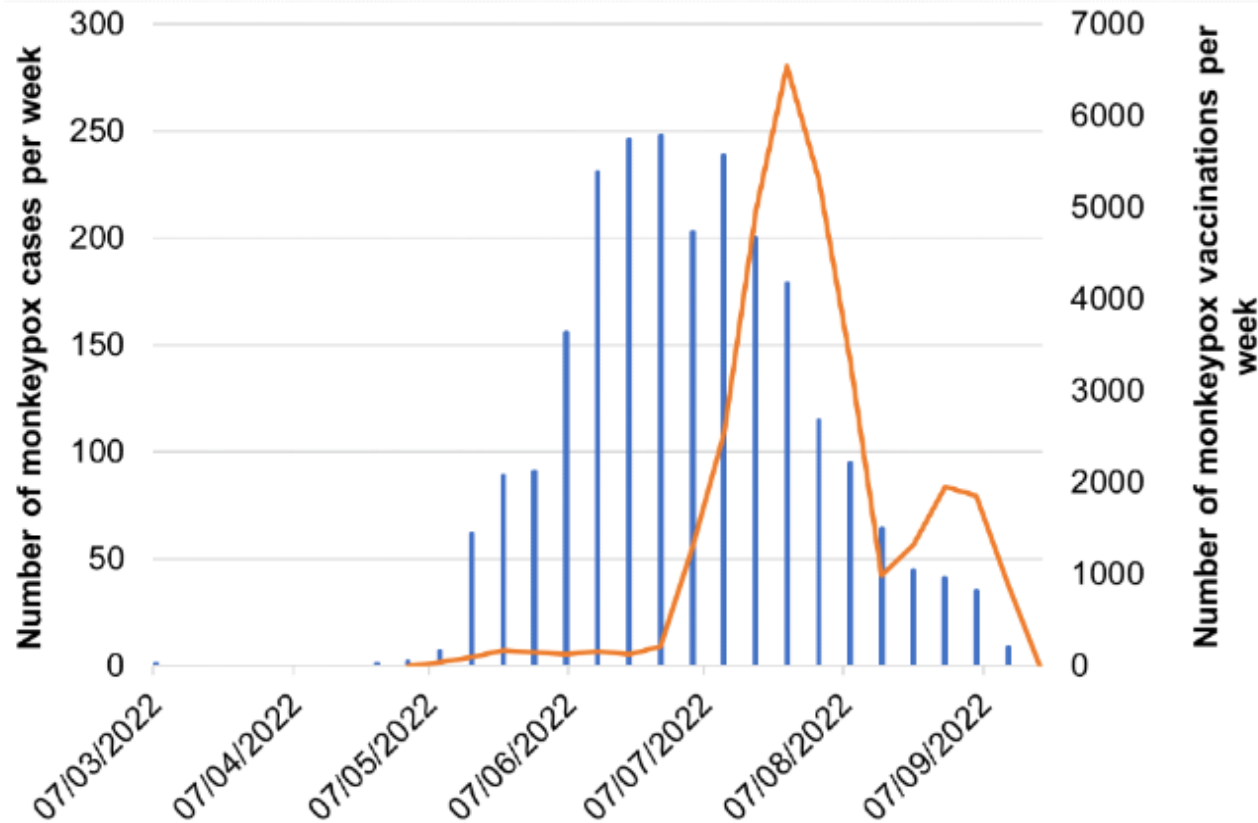
Impact of Monkeypox Outbreak on Select Behaviors

Updated August 22, 2022 [Print](#)



Gay, bisexual, and other men who have sex with men are taking steps to protect themselves and their partners from monkeypox.

Figure 8b. London



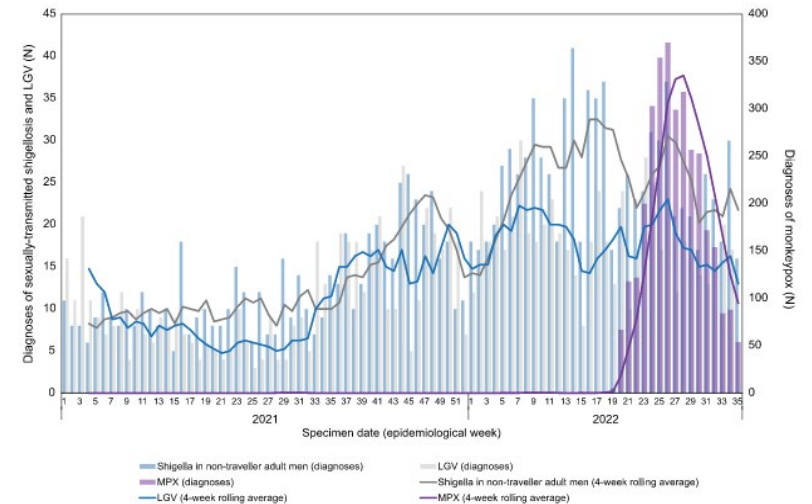
48%
 reduced number of sex partners



50%
 reduced one-time sexual encounters



50%
 reported reducing sex with partners met on dating apps or at sex venues



MVA (Imvanex) vaccine effectiveness

GOV.UK

Home > Health and social care > Public health > Health protection > Immunisation

Press release

UKHSA finds vaccination offers strong protection against monkeypox

GBMSM, 4 July to 3 November 2022
363 monkeypox cases in this period
8 had been vaccinated at least 14 days before
32 had been vaccinated between 0 to 13 days before
The rest (323) were not vaccinated
Est. VE of 78%, 14 or more days after one dose



Africa Has Not Received a Single Dose of Monkeypox Vaccine – Even Though Virus is Endemic and Often More Deadly

Medicines & Vaccines 25/08/2022 · Paul Adepoju

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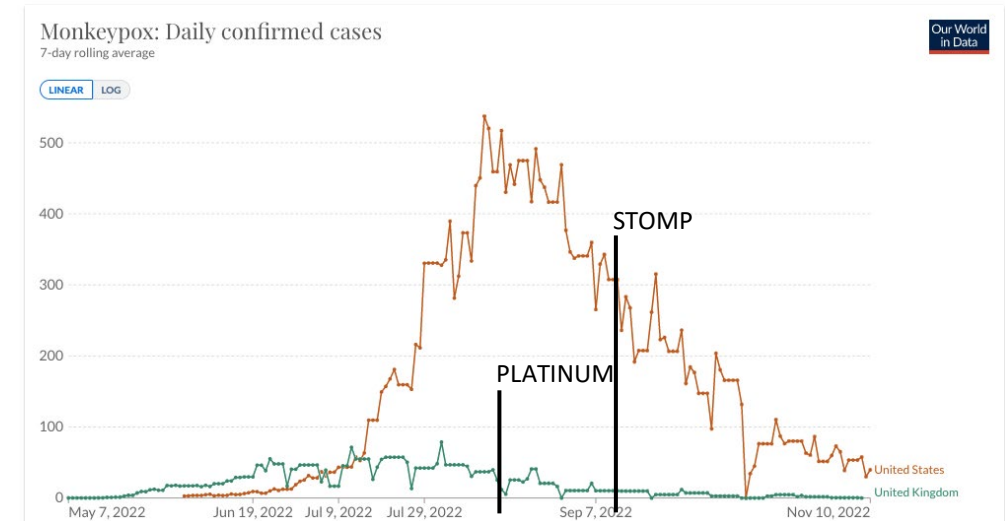
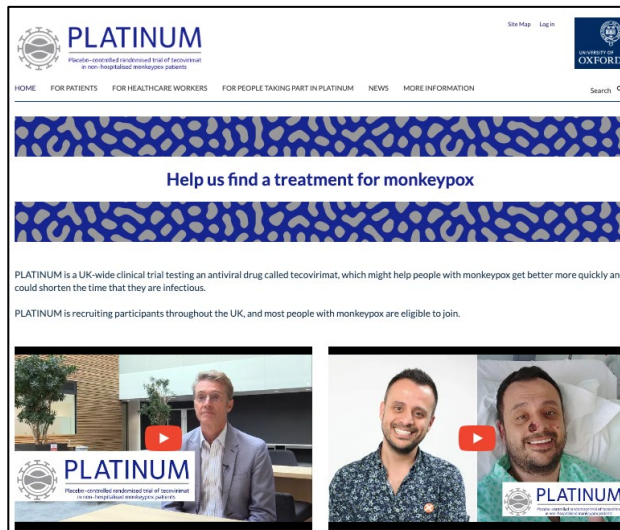
WHO African Regional Director, Dr Matshidiso Moeti

Another COVID rerun: WHO and Africa CDC officials lament the complete lack of access to monkeypox vaccines on the continent where the virus is endemic – as well as often more

Studies of antiviral treatments are ongoing

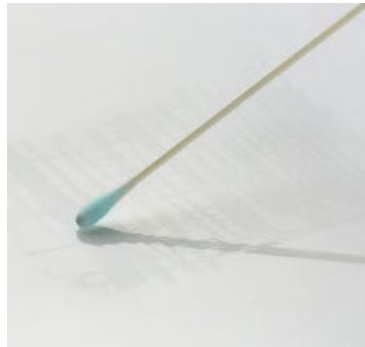
Tecovirimat – FDA, EMA and MHRA exceptional approvals for smallpox & monkeypox based on animal rule

UK inpatients: pan-European MOSAIC observational study, linked to ISARIC CCP



- WHO CORE PROTOCOL – proposed adaptive RCT of treatments
- Central African Republic (Clade I) Tecovirimat Extended Access Protocol Observational study – recruiting
- PALM007 tecovirimat RCT in the Democratic Republic of the Congo (clade I) - recruiting

Virus contamination of specific environments



THE LANCET
Microbe

ARTICLES | ONLINE FIRST

Air and surface sampling for monkeypox virus in a UK hospital: an observational study

Susan Gould, MRCP [✉] • Barry Atkinson, PhD ^{*} • Okechukwu Onianwa, PhD • Antony Spencer, BSc • Jenna Furneaux, MSc • James Grieves • Caroline Taylor, BSc • Iain Milligan, FRCPath • Allan Bennett, MSc • Tom Fletcher, PhD • Jake Dunning, PhD •
on behalf of the NHS England Airborne High Consequence Infectious Diseases Network [†] • Show less •

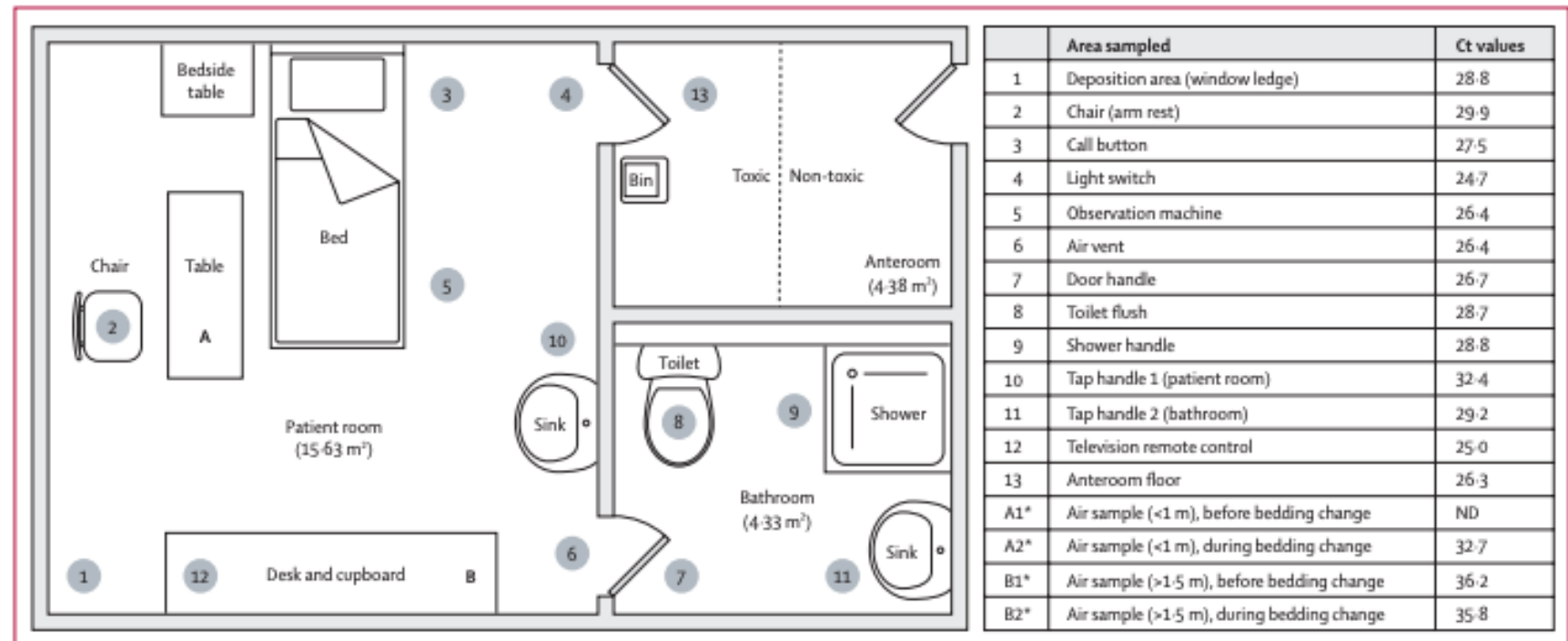


Figure: Plan of room A representing the sites of samples and Ct values

*Air samples were collected over a period of 10 min at a rate of 50 L/min (500 L total). Ct=quantitative PCR crossing threshold value of monkeypox DNA detected.

Viral Dynamics in Patients with Monkeypox Infection: A Prospective Cohort Study in Spain

36 Pages • Posted: 14 Oct 2022 SSRN preprint

Clara Suñer

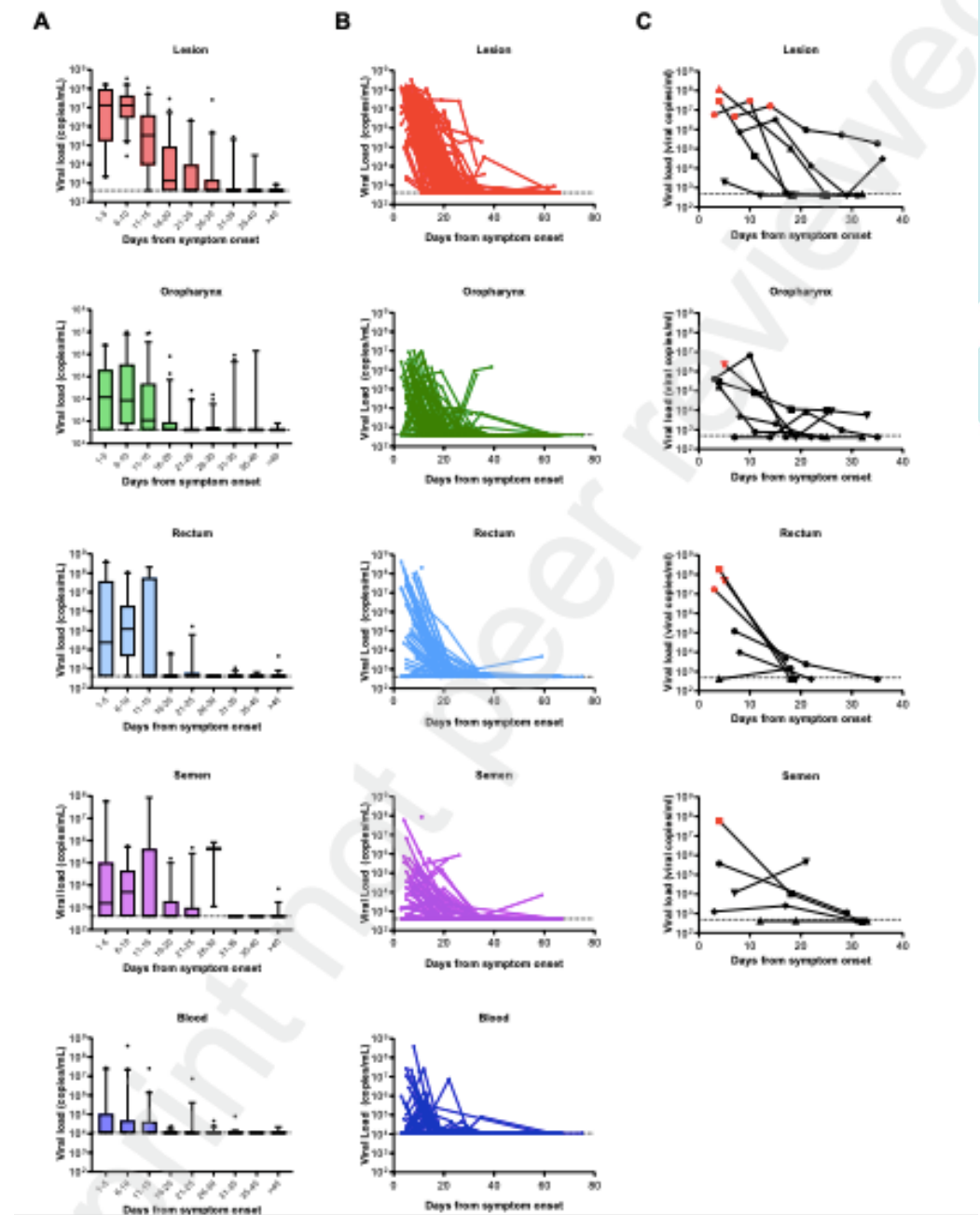
Hospital Universitari Germans Trias i Pujol - Skin Neglected Diseases and Sexually Transmitted Infections Section

Maria Ubals

Hospital Universitari Germans Trias i Pujol - Skin Neglected Diseases and Sexually Transmitted Infections Section

More...

- 1,486 longitudinal samples from 74 participants
- 97% male, 51% PLWH
- Viral clearance: Skin 25d, pharynx 16d, rectal 14d, semen 11d, blood 5d
- MPXV DNA not detectable in skin lesions by day 41 (34-50) in 90%
- MPXV VL: skin > rectum > blood > pharynx > semen
- Marked decrease in VL all samples over time
- Viable virus from all sample types except blood, but only from samples collected within 15 days of the onset of symptoms with high DNA levels



Asymptomatic infection?

Brief Communication | [Open Access](#) | [Published: 12 August 2022](#)

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

[Irith De Baetselier](#) , [Christophe Van Dijck](#) , [Chris Kenyon](#), [Jasmine Coppens](#), [Johan Michiels](#), [Tessa de Block](#), [Hilde Smet](#), [Sandra Coppens](#), [Fien Vanroye](#), [Joachim Jakob Bugert](#), [Philipp Gierl](#), [Sabine Zange](#), [Laurens Liesenborghs](#), [Isabel Brosius](#), [Johan van Griensven](#), [Philippe Selhorst](#), [Eric Florence](#), [Dorien Van den Bossche](#), [Kevin K. Ariën](#), [Antonio Mauro Rezende](#), [Koen Vercauteren](#)  & [Marjan Van Esbroeck](#) 
[for the ITM Monkeypox study group](#)



Nature Medicine **28**, 2288–2292 (2022) | [Cite this article](#)

3 cases of 224 tested asymptomatic at testing & were asymptomatic before and following (3-5w)

- Challenges of identifying subtle disease
- Pathogenic infection vs. transient carriage?
- Implications of asymptomatic infection

Letters | October 2022

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 FREE

[Valentine Marie Ferré](#), PharmD , [Antoine Bachelard](#), MD, [Meryem Zaidi](#), BSc, ... [View all authors](#) 

[Author, Article, and Disclosure Information](#)

<https://doi.org/10.7326/M22-2183>

200 samples - 13 asymptomatic men had positive test results and only 2 of them later presented to the clinic with symptoms.

Monkeypox and People Living with HIV



- PLWH are common in clade IIb outbreak ‘outpatient’ cohorts
 - e.g. Thornhill et al NEJM (90% European): 41% PLWH; CD4 680, 95% VL<50
- Hospitalised cohorts – more severe disease
 - 156 UK hospitalized cases (unpublished): 30% PLWH; CD4 510, 85% VL<50
 - Nine CD4 <350; three CD4 <200 (52, 141, 163)
 - All recovered from acute illness, including 10 with immunosuppression
- Few complex MPXV infections in UK PLWH – seen in untreated advanced HIV late in outbreak
- Nigeria 2017-2018: 122 cases, 7 deaths (6%) including 4 in PLWH

Severe Monkeypox in Hospitalized Patients — United States, August 10–October 10, 2022

Weekly / November 4, 2022 / 71(44);1412–1417

- Description of 57 patients (95% male) hospitalized Aug 10 – Oct 10
- **82%** (47) were **PLWH**
- **72%** (31 of 43) with known CD4 count had **CD4 <50**
- **68% patients were non-Hispanic Black; 23% homeless**
- 17 (30%) patients went to ICU
- 12 (21%) have died
 - MPX cause of death or contributing factor in five of these death
 - MPX unrelated to death in one case
 - Six remain under investigation
 - Progressive severe MPX +/- superinfections described
- Tecovirimat, cidofovir, IV anti-vaccinia immunoglobulin

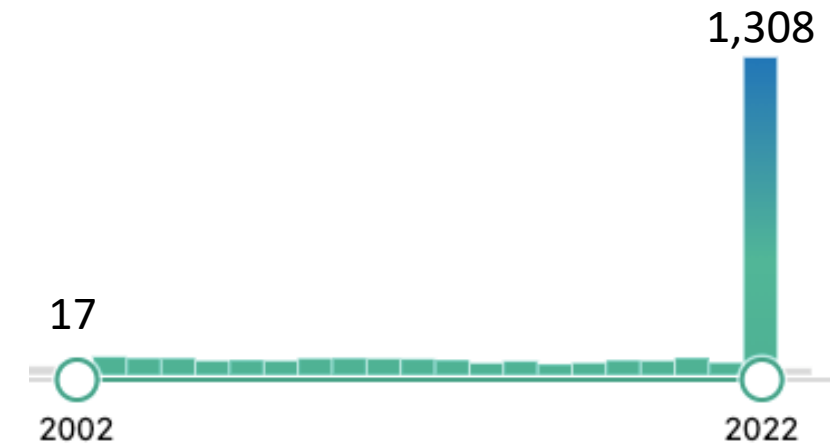




Research response so far

- Not bad at all
- Could have done better e.g., more rapid drug trials
- More infections to come in GBMSM?
- 2022 outbreaks have increased interest
- Africa should be focus of efforts
- Research questions & priorities may differ
- More social science research needed
- Not a 'gay disease', not an 'African disease'
- A global health problem requiring global efforts

MPX publications on PubMed





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