

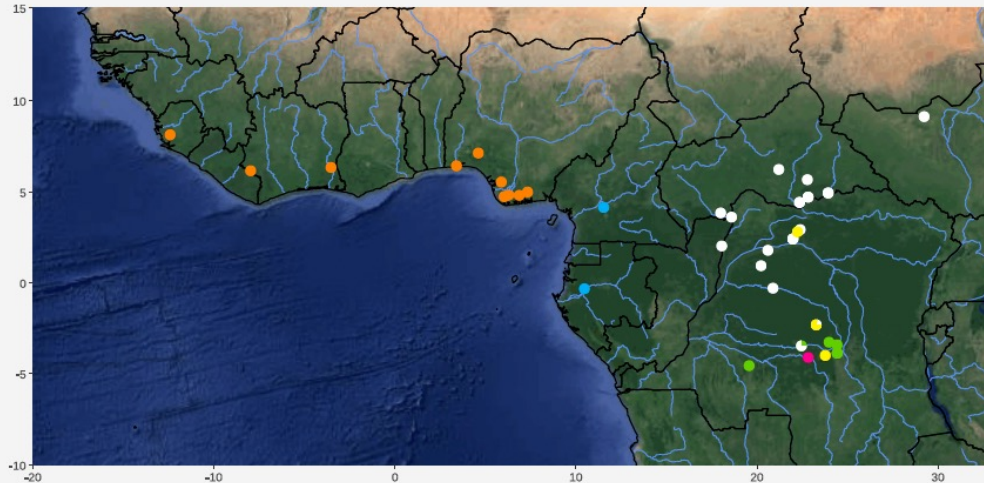
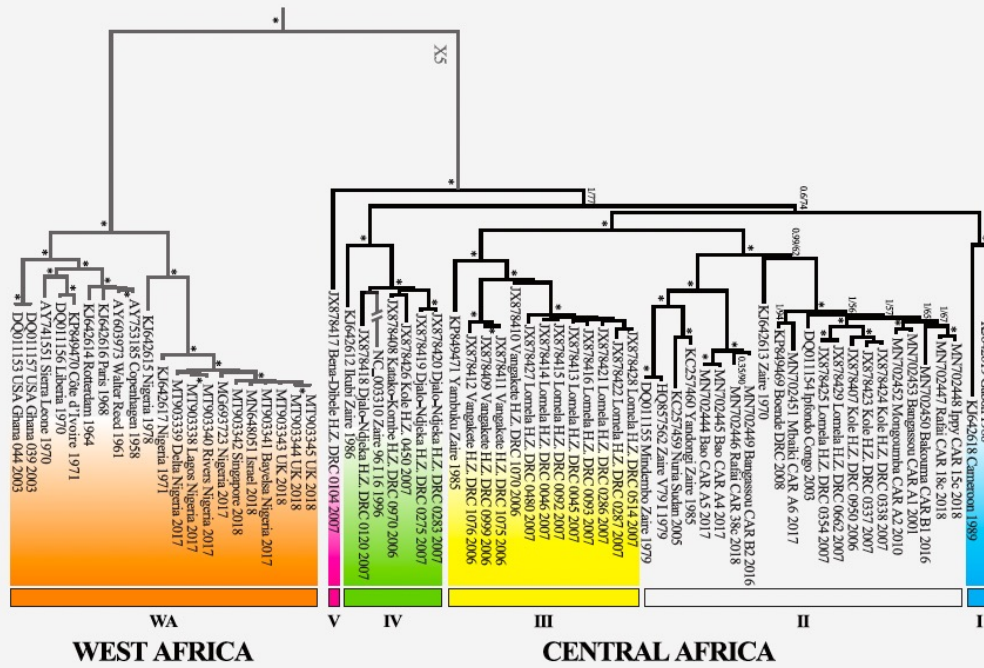
Monkeypox virus

Monkeypox is caused by a virus: Monkeypox virus (MPXV)

- Poxviridae, like smallpox (Fenner and Nakano, 1988)
- Specifically *Orthopoxvirus* (Fenner and Nakano, 1988)
- Double-stranded DNA genome
- 197kb genome and 186 ORFs



Phylogeny of Monkeypox virus



Berthet *et al.*, 2021

Whole genome phylogeny of Monkeypox cases

- Human cases
- Animal cases

2 main phylogenetic groups of MPXV

- West Africa
- Central Africa/Congo Basin
- Smaller groups within the two clades

All cases in African rainforests

→ **Which regions are suitable for the virus?**

What is Monkeypox virus animal reservoir?

1. MPXV belongs to *Orthopoxvirus*, a genus exclusive to mammals
 - MPXV reservoir is a **mammal**
 2. All human cases in African rainforests
 - MPXV reservoir is an **African rainforests-dwelling mammals**
 3. Isolated from seven wild species of African rainforests
 - All of them reservoirs?
 - Some of them intermediate hosts?
 - Some of them victims of the virus?
- **Exhaustive list of reservoirs**
- **Niches of African rainforests-dwelling mammals**

Primates



Shrews



Crocidura littoralis

Rodents



African squirrels as a potential reservoir of Monkeypox virus

Squirrels



Funisciurus anerythrus



Funisciurus bayoni



*Heliosciurus
rufobrachium*

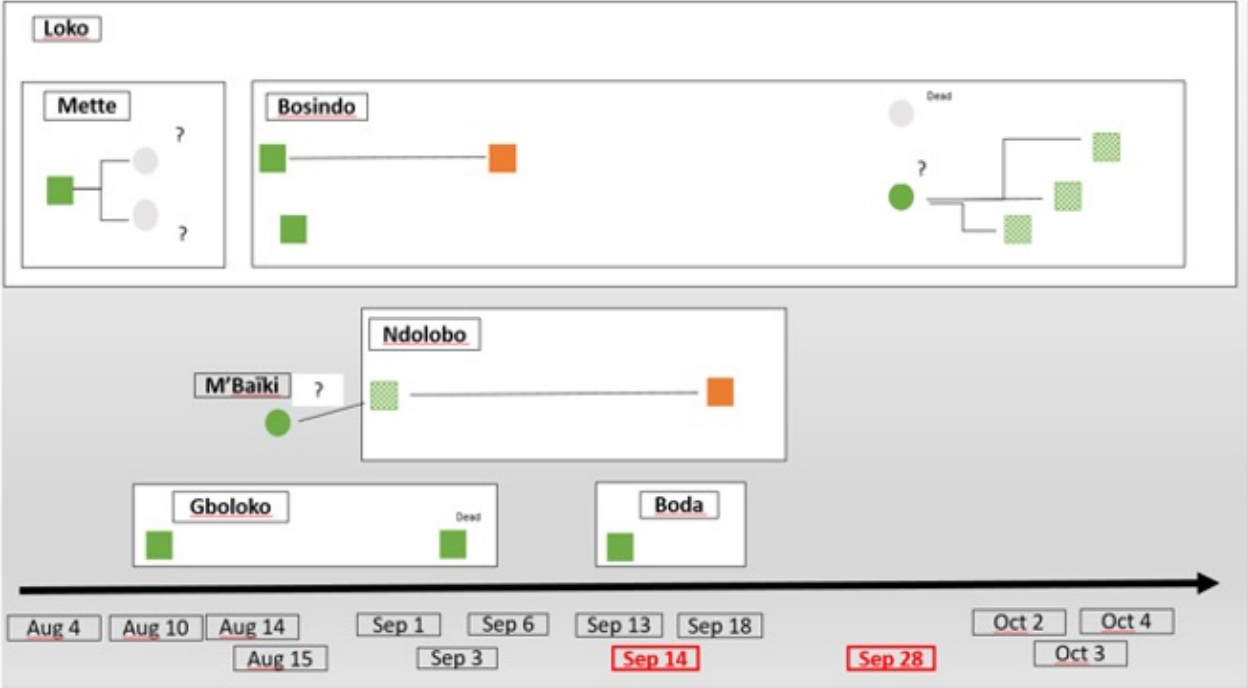
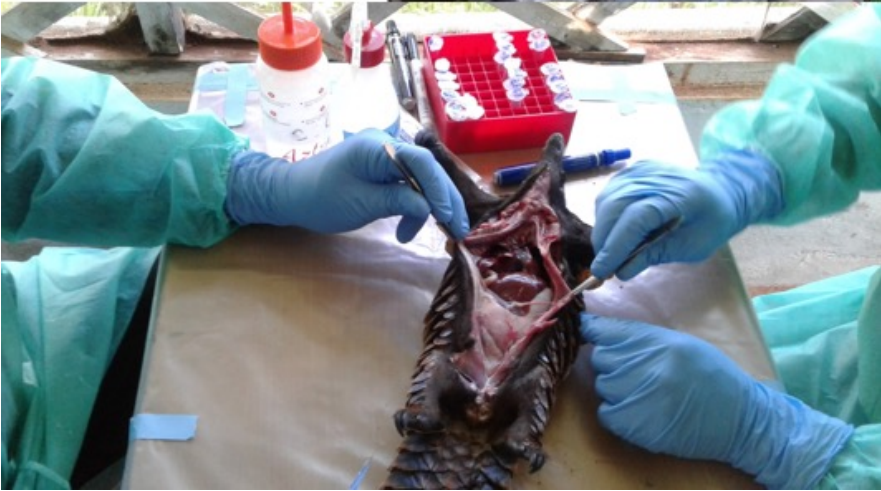
1. MMPXV isolated from two African squirrels
 - *Funisciurus anerythrus* (Khodakevich *et al.*, 1986)
 - *Funisciurus bayonii* (Mariën *et al.*, in review)
 2. MPXV DNA in African squirrel museum specimens (Tiee *et al.*, 2018)
 - Five species of *Funisciurus* including two new species
 3. Anti-OPXV antibodies in African squirrels (Khodakevich *et al.*, 1988)
 - *Funisciurus*
 - *Heliosciurus*
- **African squirrels are good candidates for the reservoir of Monkeypox virus**
- **Focus on African squirrels**

Monkeypox

- Monkeypox is a viral zoonotic disease
- Part of the *Orthopoxvirus* genus which includes variola virus (smallpox) and cowpox virus
- Endemic in 9+ African countries
- There are two main strains, one which typically has caused more severe illness (Congo clade) than the other (West African clade). Only the West African clade has been identified in the multi-country outbreak.
- The reservoir host is still unknown, although rodents incidental hosts and play a part in transmission, typically through hunting, preparation or consumption of meat (game)



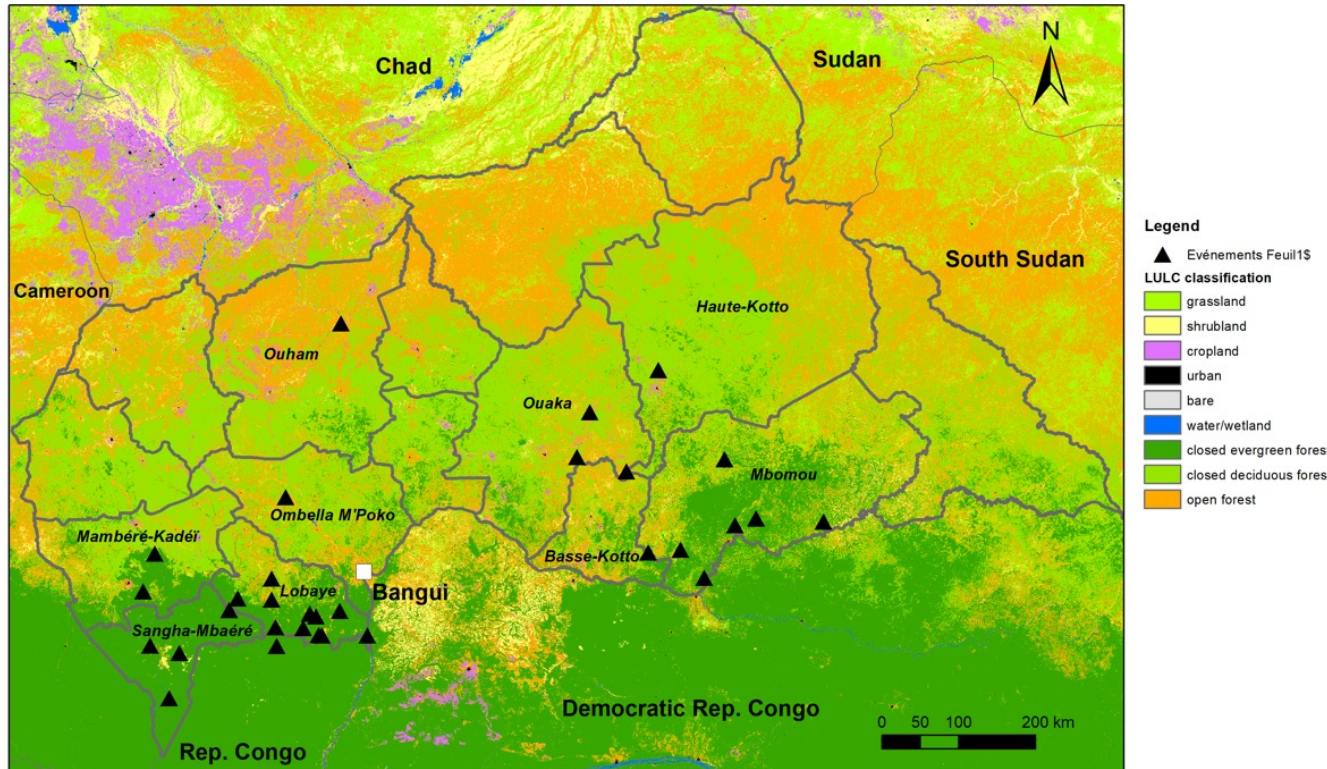
Monkeypox : Outbreak investigation



Pattern of monkeypox virus transmission hypothesized to have occurred during these outbreaks

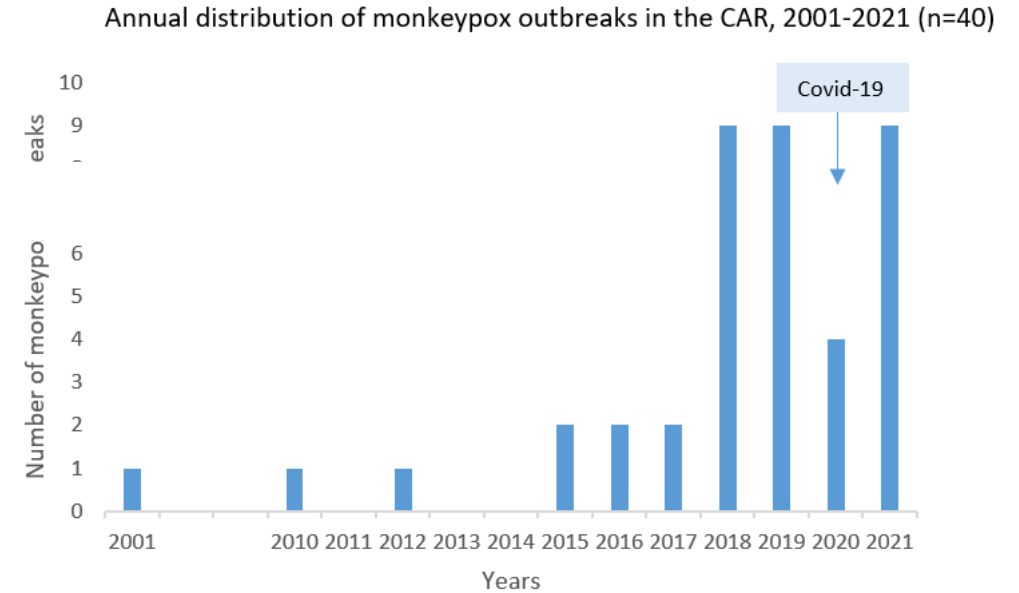


EPIDEMIOLOGY



Landuse/Landcover data source: Copernicus 2019 Global 100m Landcover

Buchhorn, M. ; Lesiv, M. ; Tsendbazar, N. - E. ; Herold, M. ; Bertels, L. ; Smets, B. Copernicus Global Land Cover Layers — Collection 2. Remote Sensing 2020, 12, Volume 108, 1044. DOI 10.3390/rs12061044



40 outbreaks, size range: 1 to 13 (1 to 25)
 99 confirmed cases, (160 with suspected cases)
 Case-fatality rate: 12/160 (7.5%)

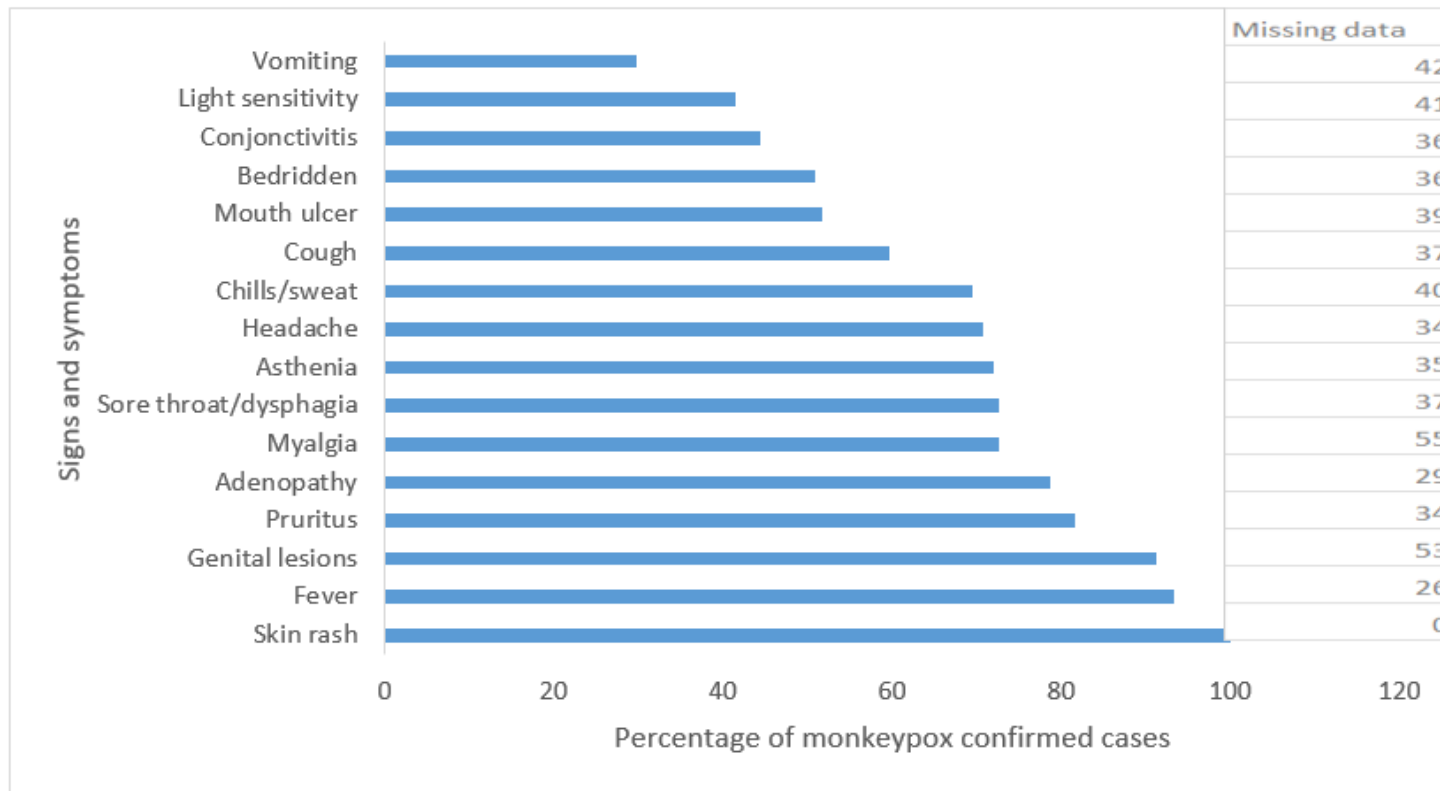
(Besombes et al, in preparation)

Clinical characteristics

Incubation= 7 days (IQR : 1-13, range : 0 - 17)

Genital lesions : 91,3% (n=42/46 with available information)

Figure 4: Frequency of signs and symptoms in people with confirmed monkeypox virus infection in the CAR, 2001-2021 (n=99)

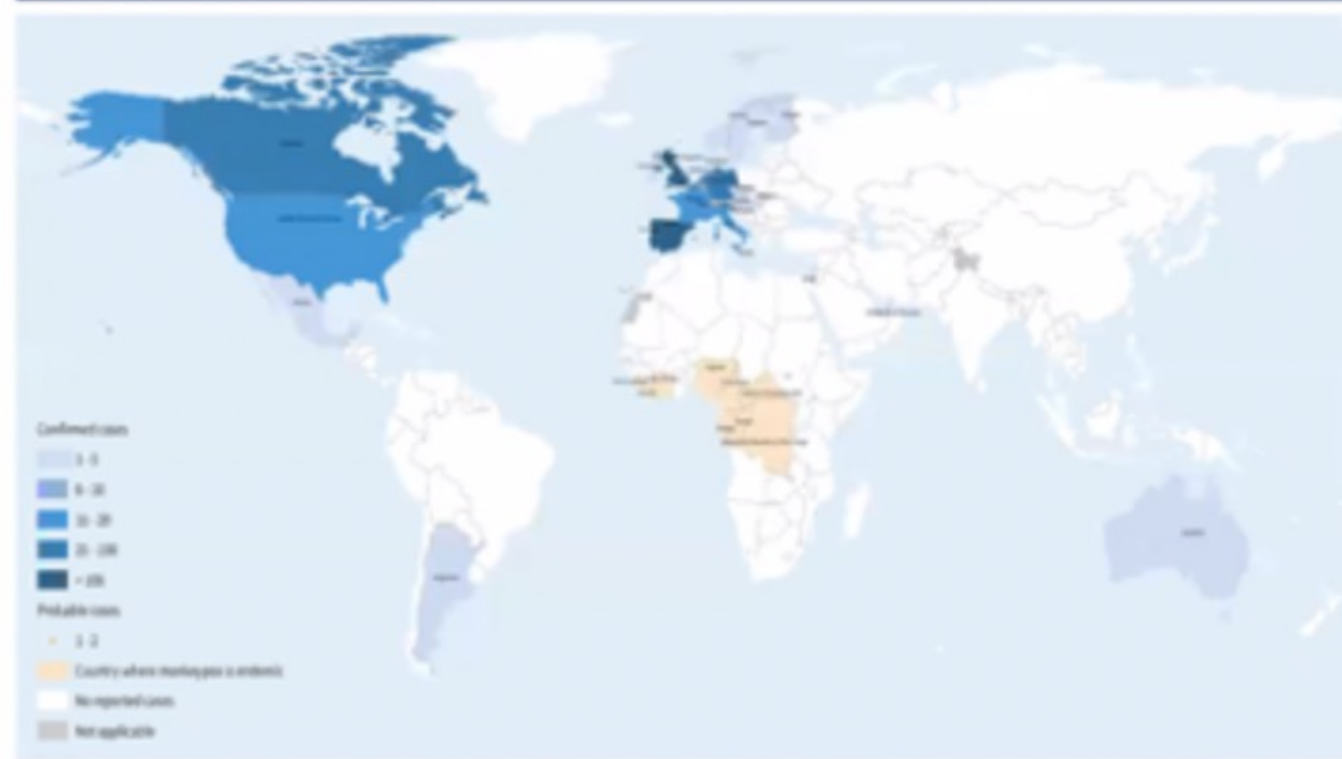


Cases of monkeypox in non-endemic countries

13 May to 1 June 2022

Region	Country	Confirmed	Probable
AMRO	Argentina	2	
	Canada	26	
	Mexico	1	
	United States of America	18	
EMRO	United Arab Emirates	4	
EURO	Austria	1	
	Belgium	10	2
	Czechia	5	
	Denmark	2	
	Finland	1	
	France	17	
	Germany	44	
	Hungary	1	
	Ireland	4	
	Israel	2	
	Italy	14	
	Malta	1	
	Netherlands	26	
	Norway	1	
	Portugal	119	
	Slovenia	2	
	Spain	142	
	Sweden	4	
	Switzerland	4	
The United Kingdom	190		
WPRO	Australia	2	
Total	26 countries	643	2

Confirmed and probable cases of monkeypox in non-endemic countries
(since 13 May 2022, as of 1 June 2022 16:00 CEST)



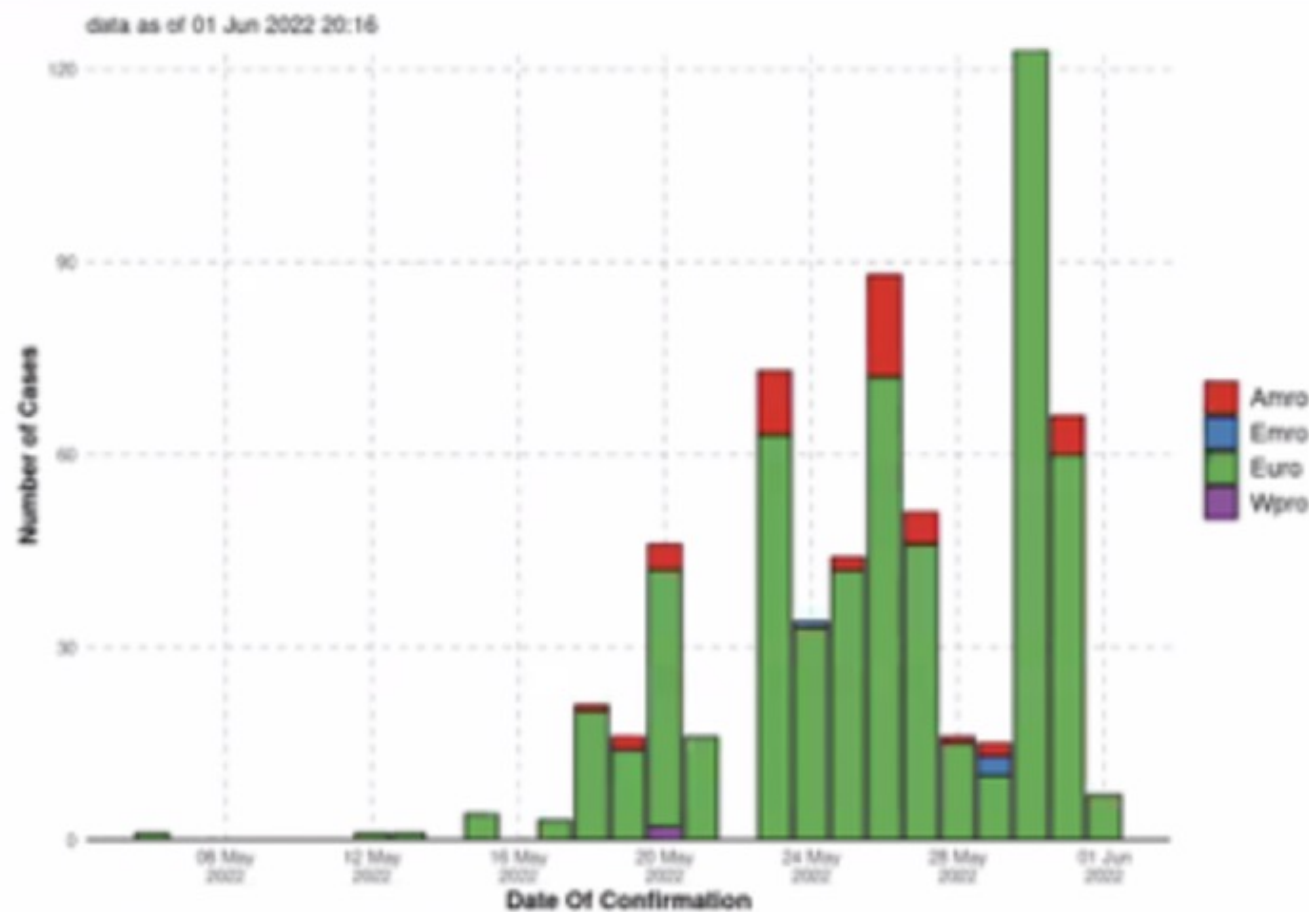
The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: WHO Health Emergencies Programme
Map Date: 1 June 2022



Epidemic Curve by region and date of confirmation

(public database)



Source: global health incident - official reporting only
where dates are not available, showing date of database entry



World Health
Organization

HEALTH
EMERGENCIES
programme

Epidemiological update as of 1 June 2022



- 373 cases in the EU/EEA since 18 May:
Austria (1), Belgium (10), Czechia (5), Denmark (2), Finland (1), France (17), Germany (44), Hungary (1), Ireland (2)*, Italy (14), Malta (1), the Netherlands (26), Portugal (100), Slovenia (2), Spain (142)* and Sweden (4).
- Almost all cases have no travel history to endemic countries.
- The majority of cases are in young men, self-identifying as MSM.
- Most cases presented with lesions on genitalia or peri-genital area, indicating that transmission likely occurs during close physical contact during sexual activities.
- **No deaths** have been reported.
- First time that chains of transmission are reported in Europe **without known epidemiological links to West or Central Africa.**

AFRIPOX

A One Health approach of monkeypox in the Central African Republic

Emmanuel Nakouné & Arnaud Fontanet

2-3 June 2022 – WHO monkeypox research webinar



One health – monkeypox - CAR

ZOOLOGY

Animal reservoir and intermediate hosts
identification – proliferation - contacts

ECOLOGY

Environnement, ecotopes,
ecological changes

ZOOLOGY

ECOLOGY

VIROLOGY

ANTHROPOLOGY

ANTHROPOLOGY

illness, changing ecologies,
wildlife

VIROLOGY

Molecular field diagnostic test
Sequencing & phylogeny
Serological test

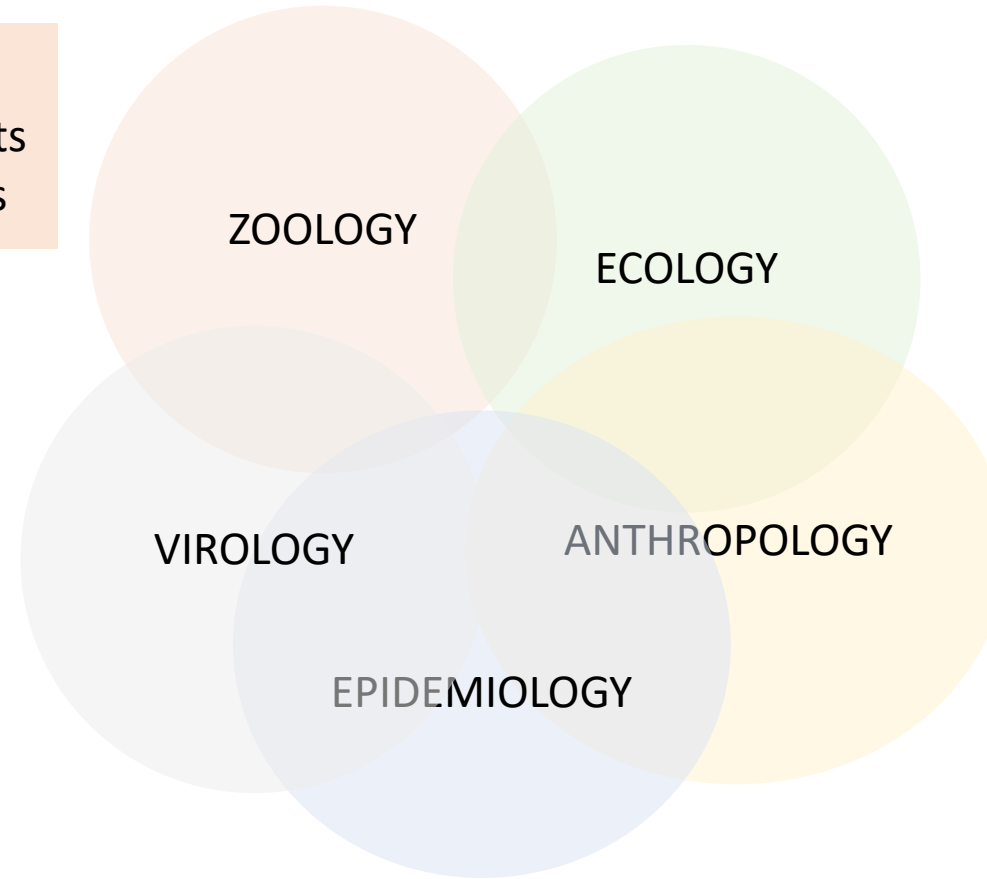
EPIDEMIIOLOGY

EPIDEMIIOLOGY

Surveillance, outbreak investigation,
modeling, transmission, natural history

CLINICAL RESEARCH

with University of Oxford:
clinical trial of tecovirimat



VIROLOGY – diagnostic tools

Molecular field diagnostics

- Monoplex (RT-LAMP) and multiplex (RT-LAMP QUASR) rapid tests
Integrated test cartridges (Withings) (MPX lineage, VZV)
- Detection by isothermal amplification / RPA strip technology

Serological diagnostic tests

- Multiplex test based on a library of more than 7891 viral peptides representative of the proteome of human pathogenic OPXV (MPXV, VACV, CPXV, VARV) (PhiP-Seq)
- Multiplex assay based on a combination of a selection of 10 MPXV proteins and peptides (MMIA)



VIROLOGY - sequencing

- Use of capture probes for long DNA fragments
- Microfluidic technology and droplet generation for targeted enrichment of droplets containing viral genome fragments
- Direct Illumina sequencing, or direct and real-time MinION sequencing on samples

www.nature.com/scientificreports/

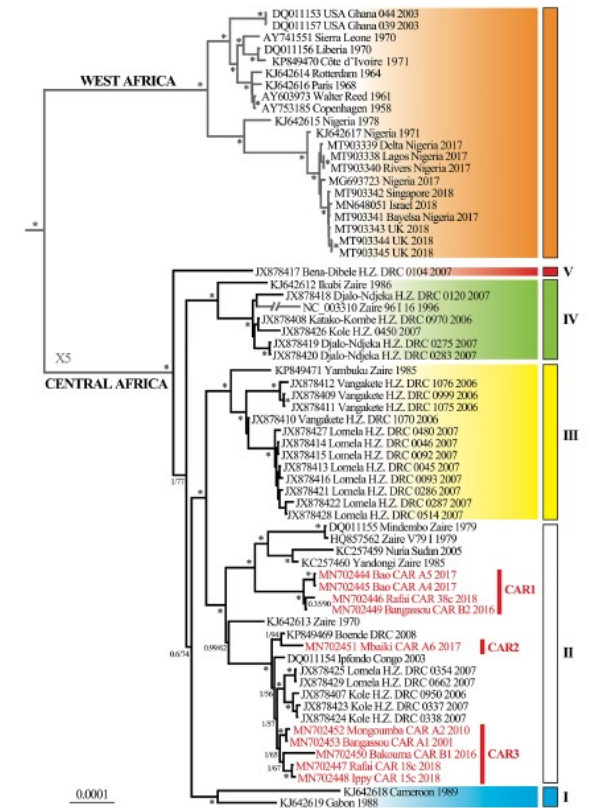
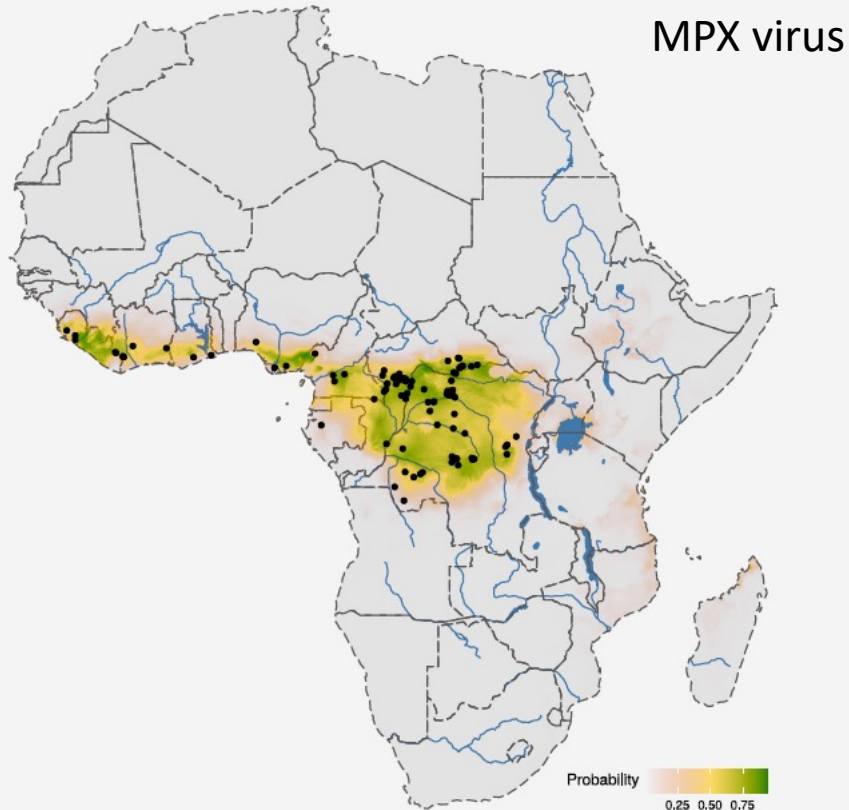


Figure 2. Phylogeny of monkeypox viruses (MPXV) based on complete genomes. The Bayesian tree was

(Berthet et al, Scientific Reports, 2021)

ZOOLOGY – Ecological niche



Curaudeau *et al.*, in prep

Ecological Niche Modelling with MaxEnt in R

African squirrels as a potential reservoir of Monkeypox virus

Squirrels



Funisciurus anerythrus



Funisciurus bayoni



Heliosciurus rufobrachium

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ZOOLOGY – Field work



Animal samples: 250

2019 Toma outbreak

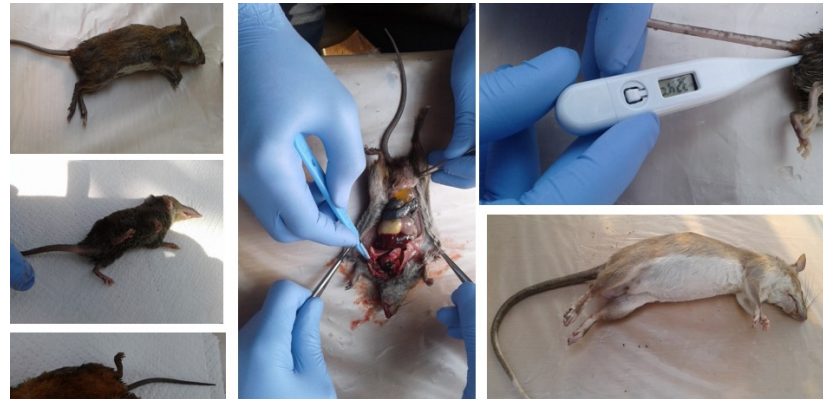
2021 Moloukou outbreak

2021 Grima outbreak

Rodents, duikers, squirrels,
bats, pangolins

PCR

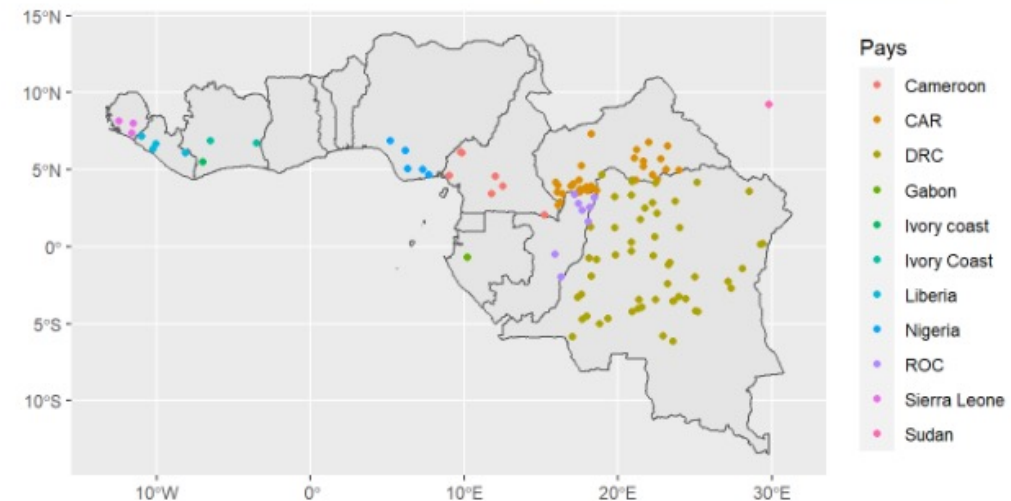
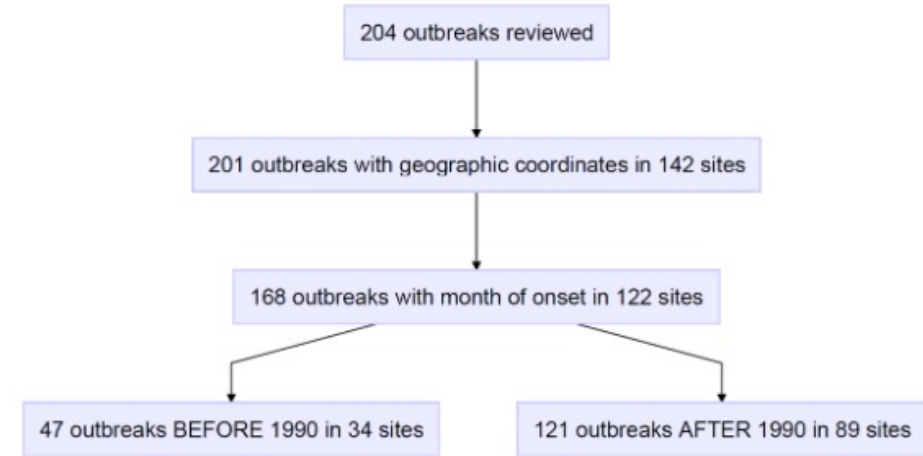
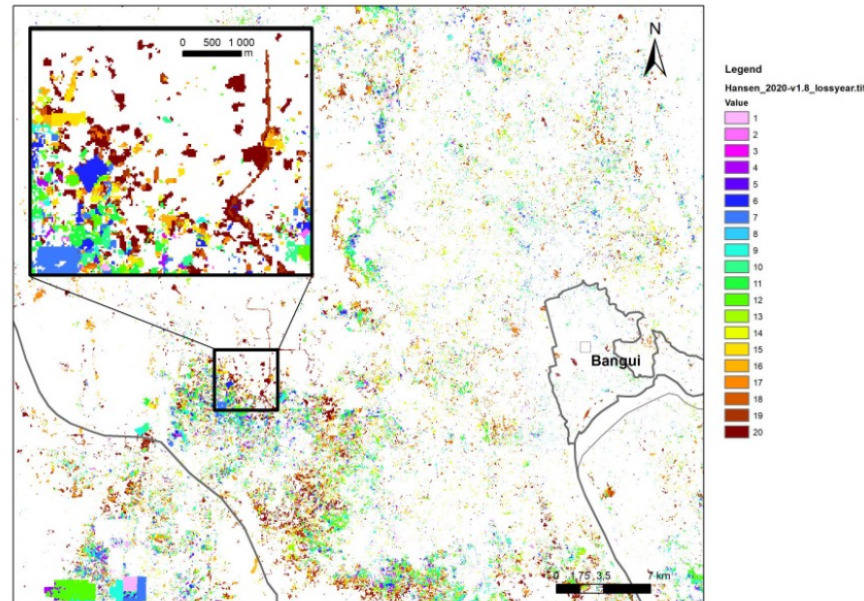
Serological assay



ECOLOGY

Environmental atlas
Climate profile
Human activities

DEFORESTATION



ANTHROPOLOGY

- **Anthropological investigation** of monkeypox illness, diagnosis & treatment pathways, care: formal health care workers, traditional healers, former patients
- **Participatory investigation of « local epidemiologies »** (local understandings of origins, emergence, transmission)
- **Ethnohistorical** study of local ecological (forest, wildlife) & social changes implied in monkeypox emergence in the CAR since 1970
- **Ethnoecology:** local conceptions and observations of wildlife; current practices with wildlife



Collaborators

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