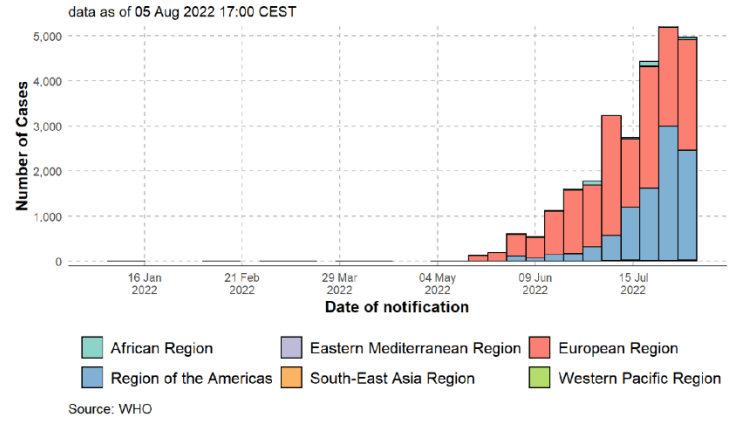
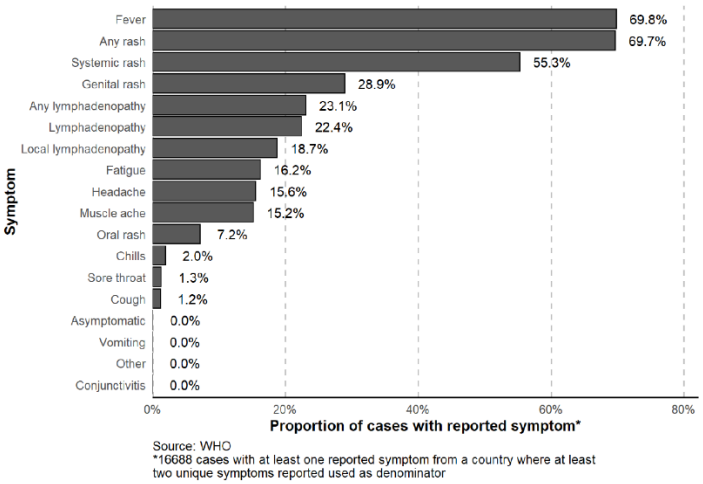
Episode 281 Monkeypox update

Epidemiology

Ep 281-1 Recent WHO data:



3.5.1. Bar chart - Symptoms 3.5.2. Table - Symptoms



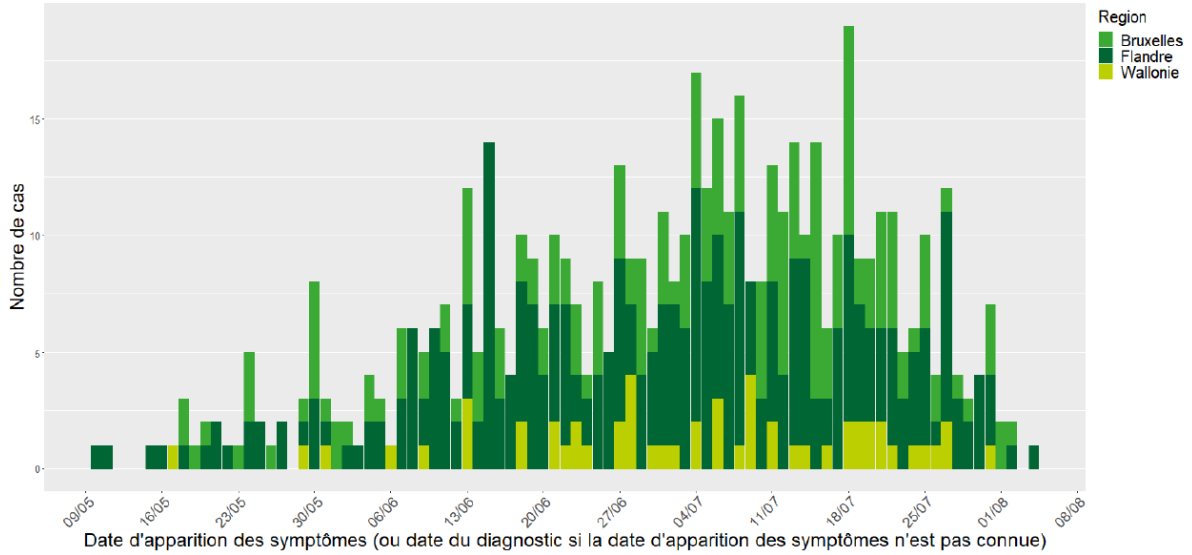
Ep 281-2: Sciensano Belgium

Dutch https://epidemio.wiv-isp.be/ID/Documents/Monkeypox/Info%20HCW_NL.pdf

French: https://epidemio.wiv-isp.be/ID/Pages/MonkeyPox.aspx

Sorry, not in English

Figure 1 : Nombre de cas par région en fonction de l'apparition des symptômes, depuis le 10 mai 2022, Belgique



Are we “over the top” or will Amsterdam and Antwerp pride give a “boost”?

Ep 281-3: Christophe Van Dijck medRxiv Modeling of Belgian epidemic

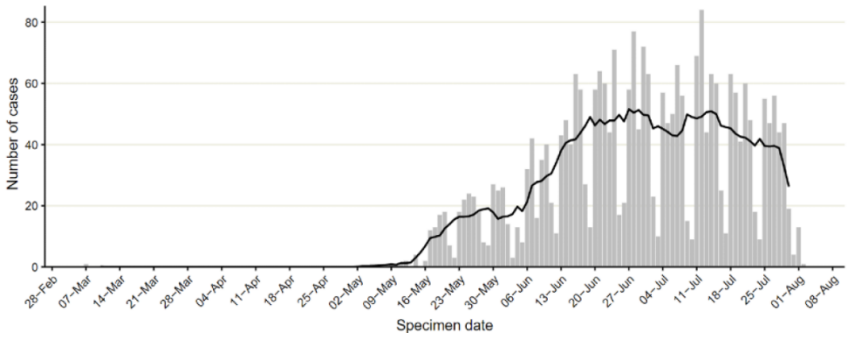
A network model to simulate a monkeypox epidemic among men who have sex with men suggest

- *that **unrecognized infections** have an important impact on the epidemic,*
- *that **vaccination of individuals at highest risk** of infection reduces epidemic size more than post-exposure prophylaxis of sexual partners*

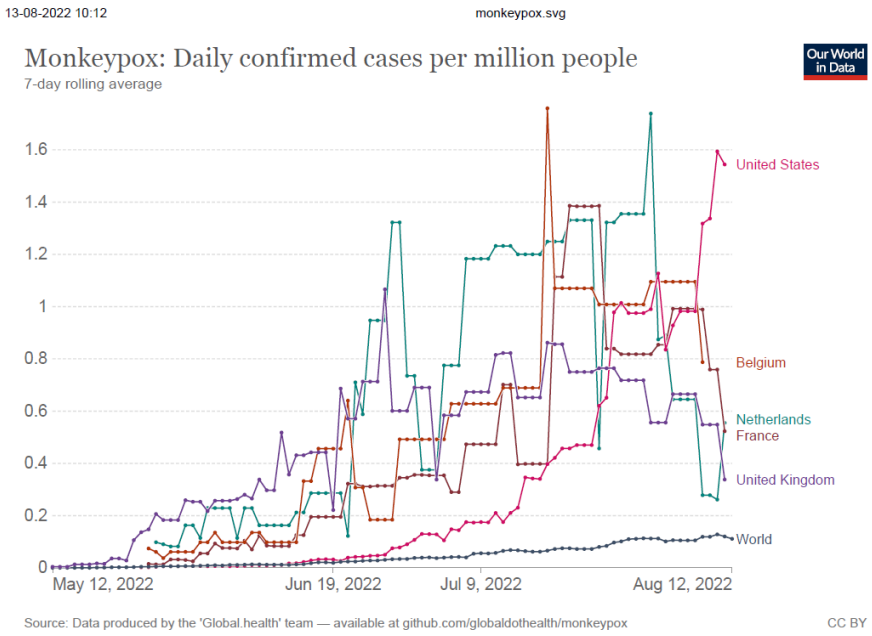
Ep 281-4: Technical briefing from UK Health Service Agency

Route of transmission

*Whilst the primary reported route is through **close or sexual contact**, monkeypoxvirus has been detected in air and environmental samples in the hospital room of infected patients. There are no confirmed instances of airborne transmission. **Limited household transmission** has been described in the UK. Detailed investigations of some cases have found small numbers with no known route of acquisition, due to reporting no sex or other potential exposures during their incubation. Assessment (confidence): transmitting primarily through close or sexual contact(moderate).*



CASES RELATIVE TO POPULATION



While new cases tend to drop in European countries, they increase in the US.

THERAPY

Ep 281-5: Gaelle Frenois-Veyrat bioRxiv 20 July : Tecovirmat has nanomolar activity, while cidofovir has only micromolar activity in vitro against MPX

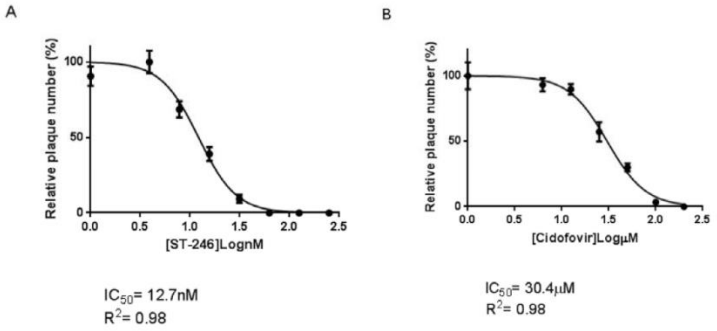


Figure 2: ST-246 and Cidofovir inhibits plaque formation of the MPXV MPXV/France/IRBA2211/2022 isolate. A) Vero cells are infected with MPXV/France/IRBA2211/2022 and treated with indicated concentrations of ST-246 (A) or Cidofovir (B) for 72h. Lysis plaque inhibition is expressed in % normalized over CTL conditions. IC_{50} and R^2 are indicated.

According to https://pubmed.ncbi.nlm.nih.gov/19195323/ resistance to Tecovirimat is associated with particular mutations in the FL13L or VP37 protein: positions F25V, H194N, G277C, I372N and insertion SVK at 303-305

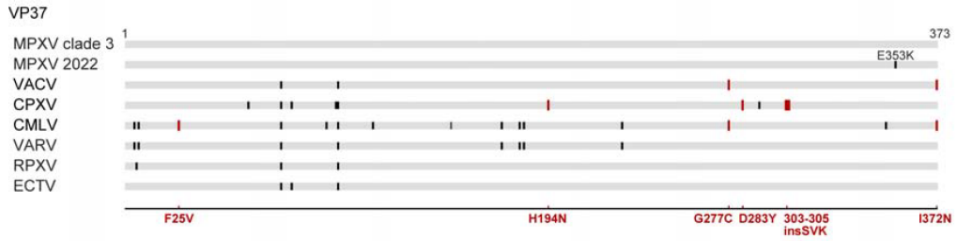


Figure S2: VP37 (F13L homologs) amino acid alignment to MPVX clade 3 shows multiple differences, marked with black vertical bars, with other orthopoxviruses susceptible to tecovirimat. The E353K mutation in VP37 is a signature substitution of MPXV lineage B.1 (2022). Experimentally generated and verified mutations associated with resistance to ST-246 are marked in red below the alignment and well as in the corresponding OPV species in which they have been experimentally tested (vertical red bars). Importantly, these mutations (in red) are annotated in the alignment in the corresponding positions, while they do not exist in the original sequences.

Conclusions:

These results support the use of tecovirimat in the clinical response to the 2022 MPXV outbreak, in particular for immunosuppressed patients. Of note, tecovirimat is not recommended for pregnant women due the absence of safety data.

Considering that resistance mutations to tecovirimat under artificial culture pressure have been described for various orthopoxviruses 17 (Figure S2), attention to adherence to treatment will be needed, especially in the context of milder clinical forms, and it will be important to monitor of the evolution of the virus during its outbreak circulation.

VACCINATION

Ep 281-6: Patrick Smits collected info on various strategy throughout Europe

Ep 281-7: Michael Thy medRxiv 4 August 2022 Breakthrough infections after post-exposure MPX vaccination

From 276 post-exposure vaccinated individuals, 12 (4%) had a MPX breakthrough infection with no severe infection. 10/12 patients developed MPX in the five days and 2 had a BTI at 22 and 25 days after vaccination

Ep 281-8: Flavia Chiuppesi medRxiv 11 August 2022 Synthetic modified vaccinia Ankara vaccines confer potent monkeypox immunity in non- human primates and healthy adults

A vaccine carrier, Modified Vaccinie Ankara (non-replication competent), developed as (experimental) SARS-CoV-2 vaccine, also induces high neutralizing Ab and T cells in non-human primates

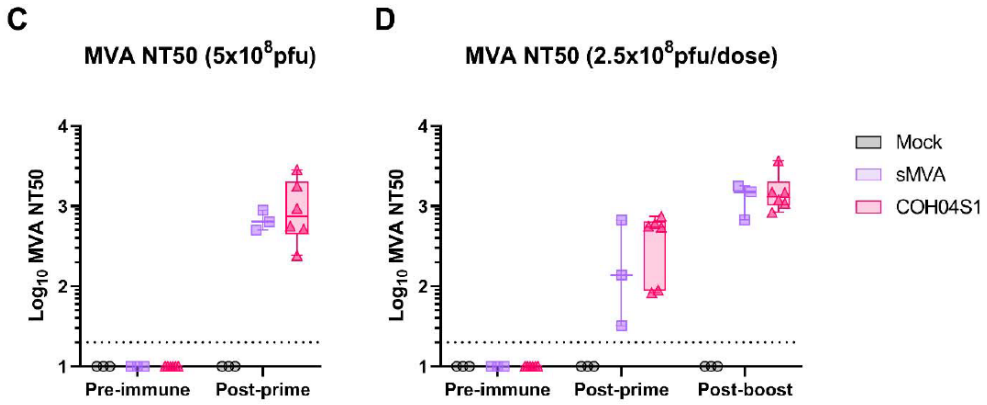


Figure 1. MVA-specific humoral responses in sMVA- and COH04S1-vaccinated NHP. N

Human data

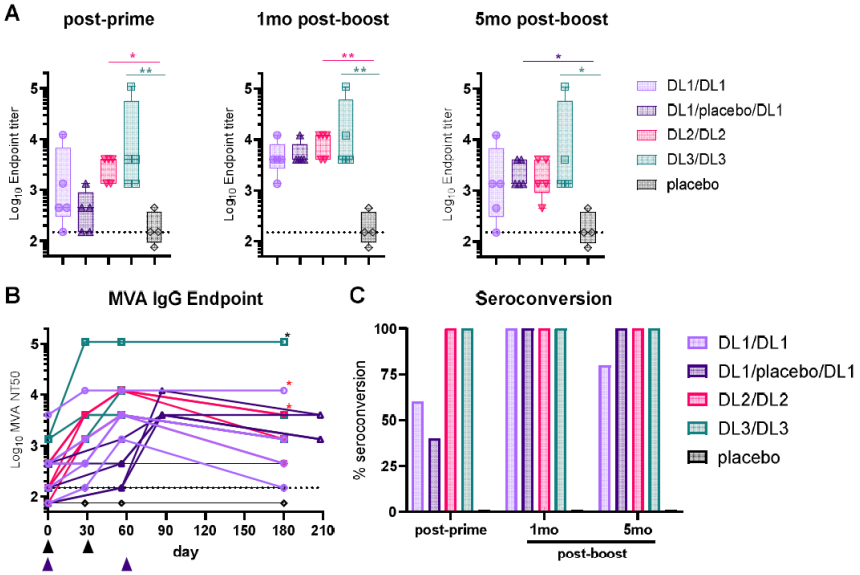
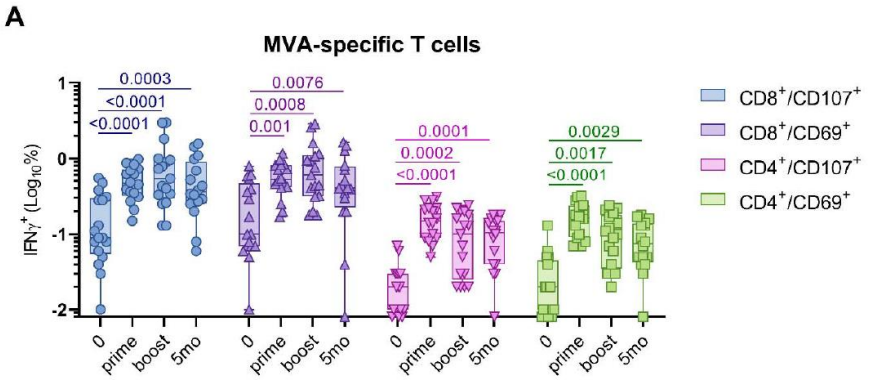


Figure 2. MVA-specific binding IgG in COH04S1 vaccinees. **A-B**. Binding antibodies. M\

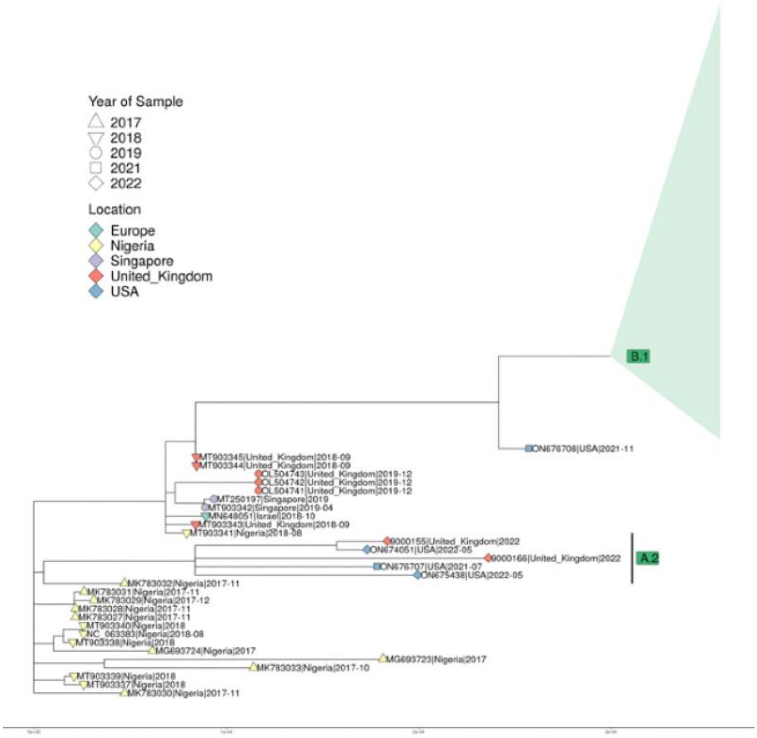


Intesting data, but still a long way to go with clinical trials

GENOMIC INFORMATION

Ep 281-4:

Most UK genomes fall in the known outbreak lineage **B.1**, but 2 are designated as lineage A.2, which may be co-circulating internationally.



B1 contains 105 distinct point mutations when compared to reference ON563414.3.
79 of the mutations (75.24%) are consistent with the action of human apolipoprotein B mRNA editing enzyme catalytic polypeptide 3 (**APOBEC3**) (also known to produce hypermutation in HIV, and copunteracted by HIV Vif).

Remarkably: evidence of genetic **variation within individual lesion** samples, which could be either acquired (by APOBEC3) or transmitted diversity

Ep 281-9: Tery Jones medRxiv 11 August 2022: Important genetic variability in first European isolates

- *Identical non-synonymous amino acid changes in six genes and the signature of APOBEC editing match other sequences from the European outbreak.*
- *Non-synonymous changes that were present in one to three sequences were found in 34 other genes.*

Conclusion: The relatively sustained and widespread human-to-human transmission is new and may lead to a new viral evolution. *The consequence of changes in poxvirus genes in a new host … is unpredictable.*

Ep 281-10: WHO on renaming MPX

*Consensus was reached to now refer to the former Congo Basin (Central African) clade as Clade one (I) and the former West African clade as Clade two (II). Additionally, it was agreed that the Clade II consists of two subclades clade II A and **II B,** the latter referring to the group of variants circulating in the **2022 global outbreak**.*