Rita Cordeiro

Country: Portugal

Affiliation: Emergency Response and Biopreparedness Unit, Infectious Diseases Department, National Institute of Health Doutor Ricardo Jorge (INSA)

Function: Technical Laboratory Specialist

Main expertise: Diagnostics and surveillance of emerging and re-emerging pathogens, including highly pathogenic biothreat viruses, as well as biosafety and biosecurity management.

Session 3: Overview of the epidemiology and disease burden of VPI among adults in Portugal

3.1 Mpox outbreak management

- Mpox waves in Portugal
- Epidemiology and Genomic surveillance
- Transmission & vaccination modelling
- Serology & immunity
- Key findings & Lessons learned

Mpox outbreak in Portugal

- **Initial case alerts** emerged on **3 May 2022**, based solely on **clinical assessment**, without laboratory confirmation.
- The **first five laboratory-confirmed** cases were diagnosed on **18 May 2022** by the **Emergency Response and Biopreparedness Unit** of the **National Institute of Health Doutor Ricardo Jorge**.

Summary of Monkeypox cases

As of 24 Nov 2022

	Total Cases	Total cases per 1M inhabitants	Cases in the last week[1]	Cases in the preceding week	Weekly % change in cases[1]	Days since last report	Date of first reported case
European Region							
Spain	7,405	156	15	41	−63%	2	18 May 2022
France	4,104	63	2	5	−60%	2	19 May 2022
The United Kingdom	3,720	55	7	2	250%	2	07 May 2022
Germany	3,672	44	1	2	−50%	2	20 May 2022
Netherlands	1,248	72	7	3	130%	2	22 May 2022
Portugal	948	92	0	4	–	2	17 May 2022
Italy	917	15	2	17	−88%	2	19 May 2022
Belgium	789	68	1	0	–	2	19 May 2022
Switzerland	546	63	0	0	–	2	21 May 2022

- https://worldhealthorg.shinyapps.io/mpx_global/

Perez Duque M, et al. Ongoing monkeypox virus outbreak, Portugal, 29 April to 23 May 2022. *Euro. Surveill*. **2022** Jun;27(22):2200424. https://doi.org/10.2807/1560-7917.ES.2022.27.22.2200424

Cordeiro R, et al. Mpox Surveillance and Laboratory Response in Portugal: Lessons Learned from Three Outbreak Waves (2022–2025) *Infect. Dis. Rep.* **2025**, *17*(4), 86; https://doi.org/10.3390/idr17040086

Mpox outbreak in Portugal

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- The **first five laboratory-confirmed** cases were diagnosed on **18 May 2022** by the **Emergency Response and Biopreparedness Unit** of the **National Institute of Health Doutor Ricardo Jorge**.
- With these confirmations, Portugal became the **second country to report cases** during an outbreak that rapidly evolved into a global event.

- https://www.ecdc.europa.eu/en/news-events/monkeypox-cases-reported-uk-and-portugal

Perez Duque M, et al. Ongoing monkeypox virus outbreak, Portugal, 29 April to 23 May 2022. *Euro. Surveill*. **2022** Jun;27(22):2200424. https://doi.org/10.2807/1560-7917.ES.2022.27.22.2200424
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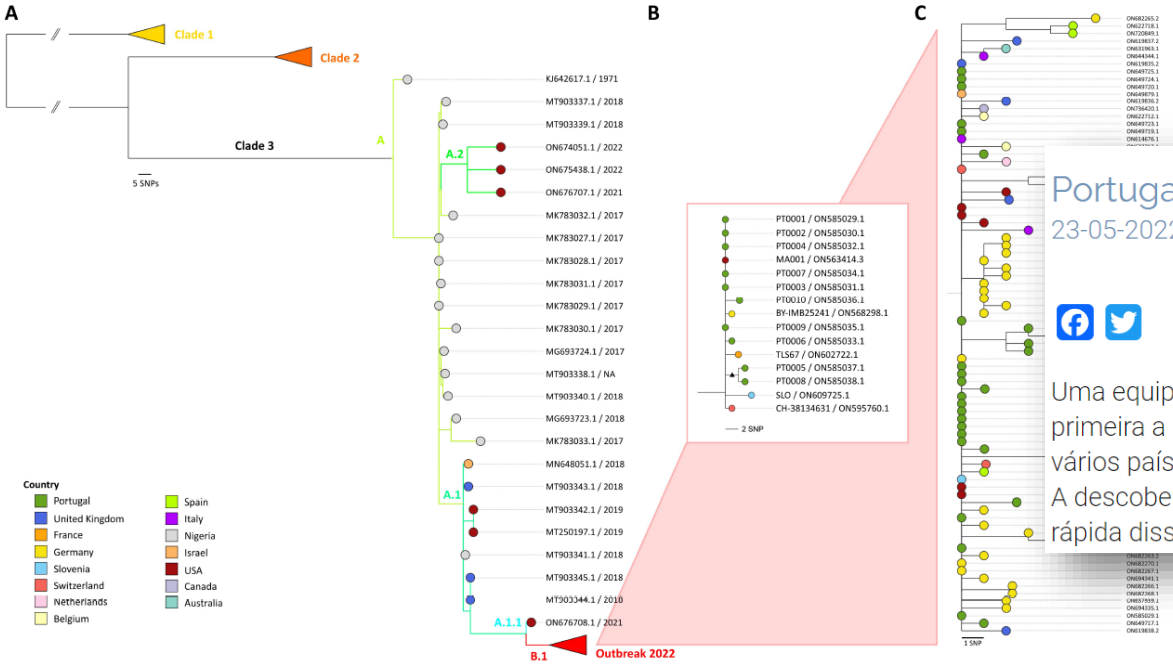
Mpox outbreak in Portugal

- And also, was the **first country to sequence** and **publish** the MPXV genome related to the 2022 outbreak.

Genomics and Bioinformatics Unit



Portugal é o primeiro país a sequenciar genoma do vírus Monkeypox

23-05-2022

Uma equipa de investigadores do Instituto Nacional de Saúde Doutor Ricardo Jorge (INSA) foi a primeira a identificar a sequência genética do vírus *Monkeypox*, atualmente em circulação em vários países como Portugal, Reino Unido, Espanha, Suécia, Bélgica e Estados Unidos da América. A descoberta poderá ser fundamental para compreender a origem do surto e as causas para a rápida disseminação da doença.

Isidro, J et al. Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus. *Nat. Med.* **2022** *28, 1569–1572*; https://doi.org/10.1038/s41591-022-01907-y

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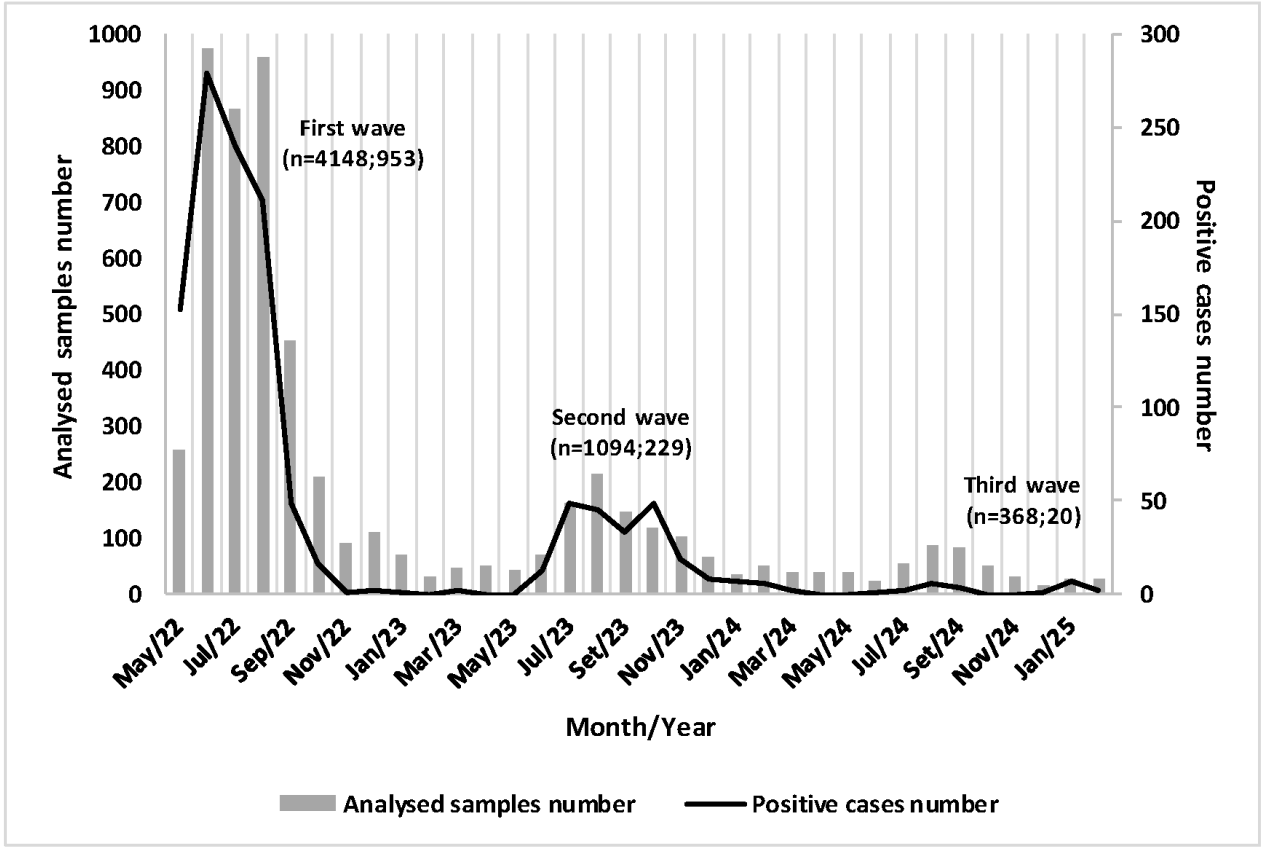
Mpox outbreak in Portugal

- Between May 2022 until now, **three distinct mpox outbreak waves** were identified in Portugal:
  - The **first wave**, which occurred between **May 2022 and March 2023**, accounted for the majority of confirmed cases, with **956 cases**;
  - The **second wave**, from **June 2023 and March 2024**, recorded **240 cases**, reflecting a significant decrease compared to the previous wave;
  - The **third wave** began in **June 2024** and recorded **90 cases** until **15 November 2025** (19 new cases in the last month);
  - Overall, **1286 confirmed cases** were reported in Portugal.



Samples analysed and confirmed cases at INSA between 17 May 2022, and 28 February 2025.

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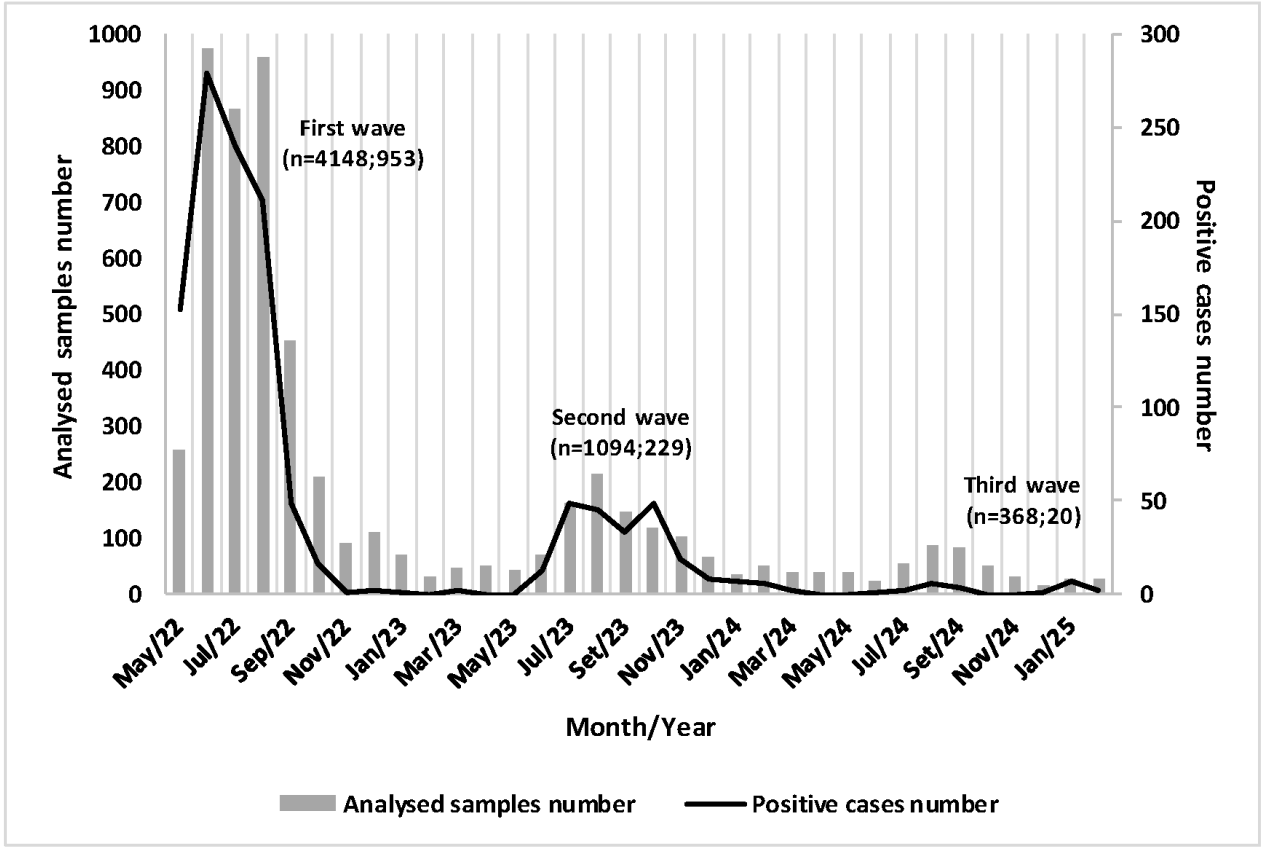
Infect. Dis. Rep. **2025**, *17*(4), 86; https://doi.org/10.3390/idr17040086

Mpox outbreak in Portugal

Epidemiological data

- The Portuguese outbreaks waves followed **demographic and clinical patterns similar** to those reported in other countries, primarily affecting **men who have sex with men (MSM)** and **young adults**:
  - The majority of cases were **male,** predominantly within the **20–29** and **30–39 age groups**, with most cases occurring among MSM.
  - Only a few cases were reported in **females**, indicating a marked gender disparity.
  - No cases were reported in children aged **0–9 years**, and a small number of cases were reported in individuals **over 60 years of age**.



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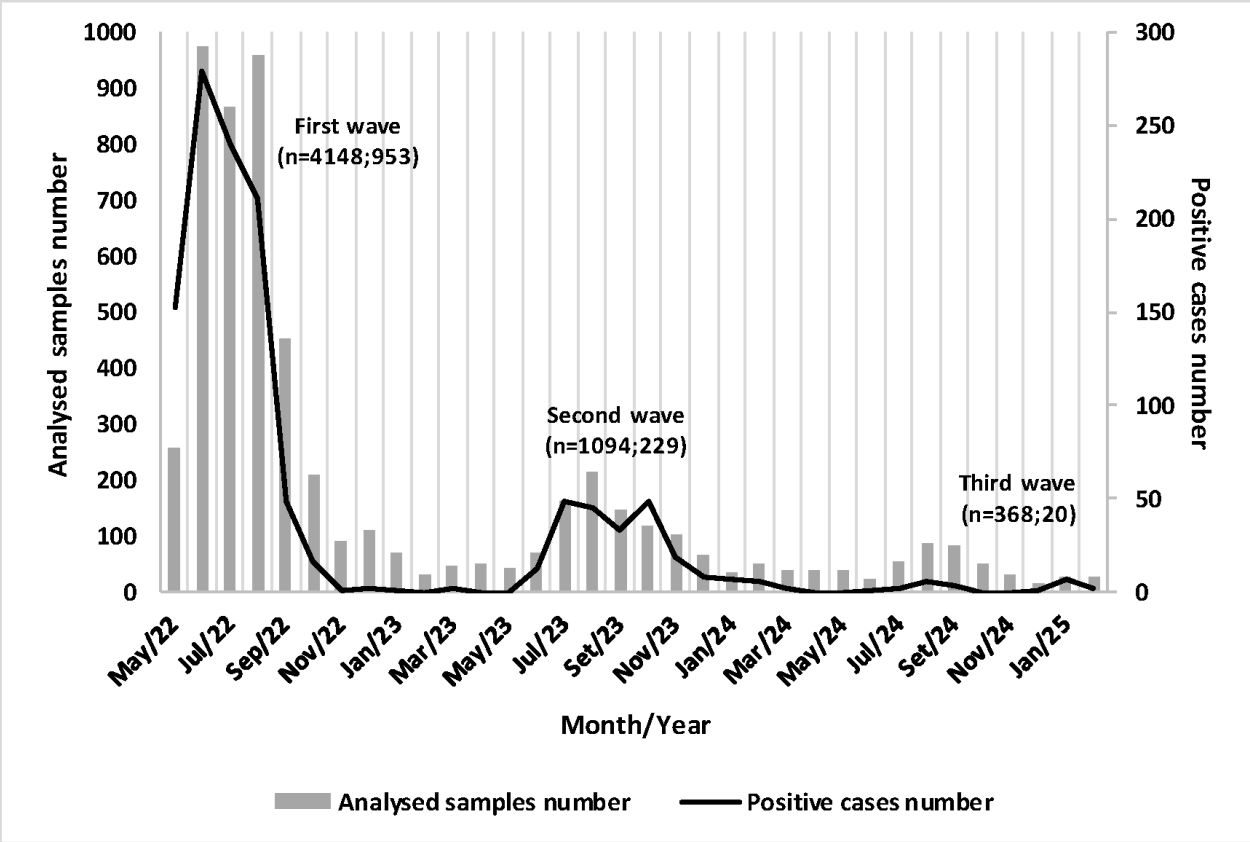
Mpox outbreak in Portugal

Epidemiological data

- **Positive cases** were detected in all regions of Portugal, but the highest number was reported in the **Lisbon Metropolitan Area** (n = 908; 75.5%), followed by the **North** (n = 234; 19.5%) and **Centre** (n = 29; 2.4%) **regions**.
- Notably, unlike the previous waves, which began in the Lisbon Metropolitan Area, the **third outbreak** started in the **Northern region**.



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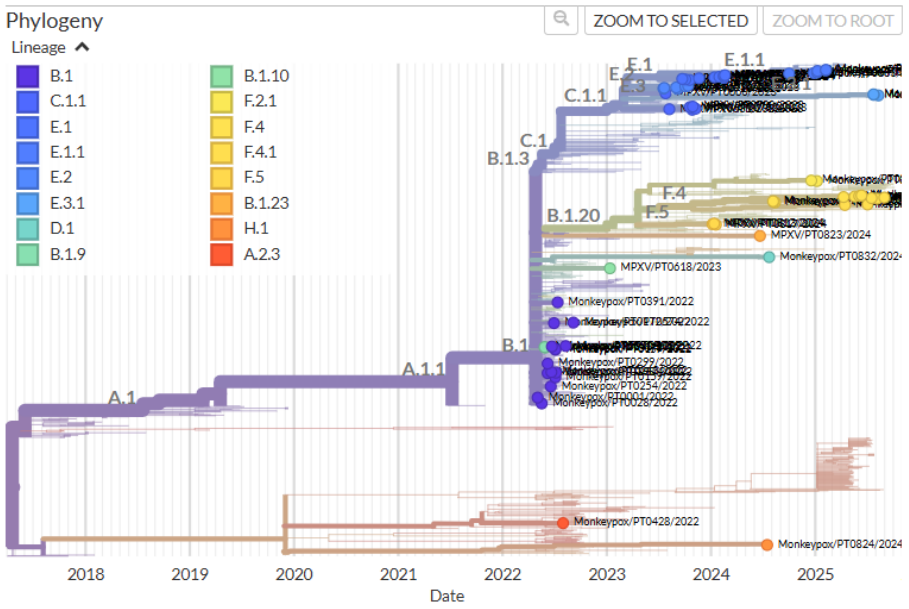
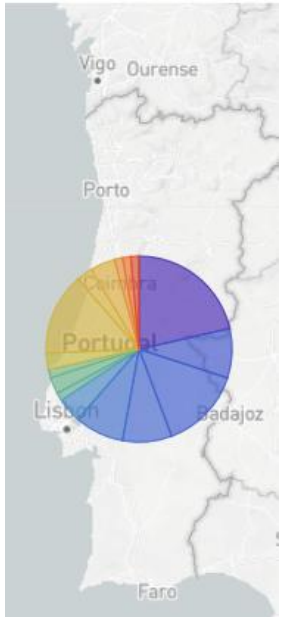
Mpox outbreak in Portugal

MPXV genomic characterization

- **Genomic surveillance** consistently identified **clade IIb** (B.1 lineages) throughout all three waves, with only one detection, recently, of **clade Ib**.





- A total of **790 MPXV samples** were sequenced, of which 576 high-quality consensus sequences were suitable for public release.
- **576 viral genome sequences** are currently available in public databases (GenBank and Pathoplexus), representing one of the largest MPXV genomic datasets from a single country.

https://nextstrain.org/pathogens?filter=mpox
Isidro, J et al. Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus.
Nat. Med. **2022** *28, 1569–1572*; **https://doi.org/10.1038/s41591-022-01907-y**
Borges V, et al. Viral genetic clustering and transmission dynamics of the 2022 mpox outbreak in Portugal.
Nat Med. **2023 Oct;29(10):2509-2517. doi: 10.1038/s41591-023-02542-x. Epub 2023 Sep**

Mpox outbreak in Portugal

Case Notification (SINAVE - National Epidemiological Surveillance System)

Case identification

A suspected or confirmed case of mpox is detected in a healthcare setting (hospital, emergency department, primary care unit, or private clinic)

Data entry by the Healthcare Professional

The clinician logs into SINAVE Médico and completes the electronic notification form, including:

- Patient identification
- Clinical signs and symptoms
- Epidemiological links
- Laboratory results (if available)
- Risk factors and exposure history

Automatic transmission to Public Health Authorities

SINAVE automatically sends the notification to the:

- Local Public Health Unit (USP)
- Regional Health Administration (ARS)
- National Health Directorate (DGS)

Validation and follow-up by the USP

The Public Health Unit:

- Verifies case information
- Initiates epidemiological investigation
- Identifies and manages contacts
- Updates case status (suspected → confirmed / ruled out)

Laboratory integration

Laboratory results (PCR, sequencing) are:

- Entered into SINAVE Lab or linked through electronic reporting
- Automatically associated with the case record

Central Data Consolidation (DGS / INSA)

National authorities compile:

- Epidemiological curves
- Geographic distribution
- Surveillance indicators
- Trends and risk assessments

Reporting and international communication

DGS communicates aggregated data to:

- ECDC (TESSy platform)
- WHO

Ensures compliance with International Health Regulations (IHR).

https://www.dgs.pt/paginas-de-sistema/saude-de-a-a-z/sinave/laboratorios.aspx

Mpox outbreak in Portugal

Case Notification (SINAVE - National Epidemiological Surveillance System)

- All **mpox cases**, both positive and negative, have been notified in **SINAVE**, since the beginning of the first outbreak.
- **Clade** and **lineage information** is also included, although this feature has only been available since **March 2025**.

Laboratory integration

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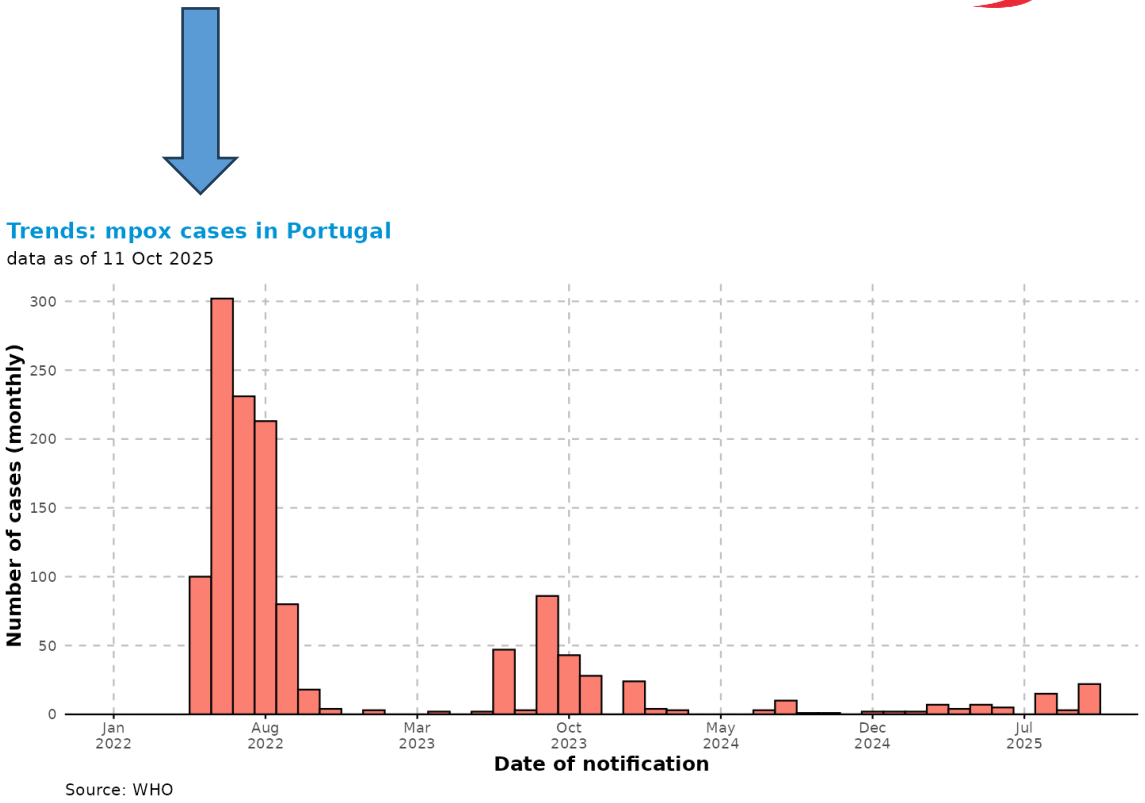
Mpox outbreak in Portugal

First wave

- To understand how **mpox first emerged** and **spread in Portugal**, we need to go back to the beginning, the first outbreak wave.



https://worldhealthorg.shinyapps.io/mpx_global/#sec-global

Cordeiro R, et al. An Overview of Monkeypox Virus Detection in Different Clinical Samples and Analysis of Temporal Viral Load Dynamics. *J Med Virol.* **2024** Dec;96(12):e70104. **https://doi.org/10.1002/jmv.70104**

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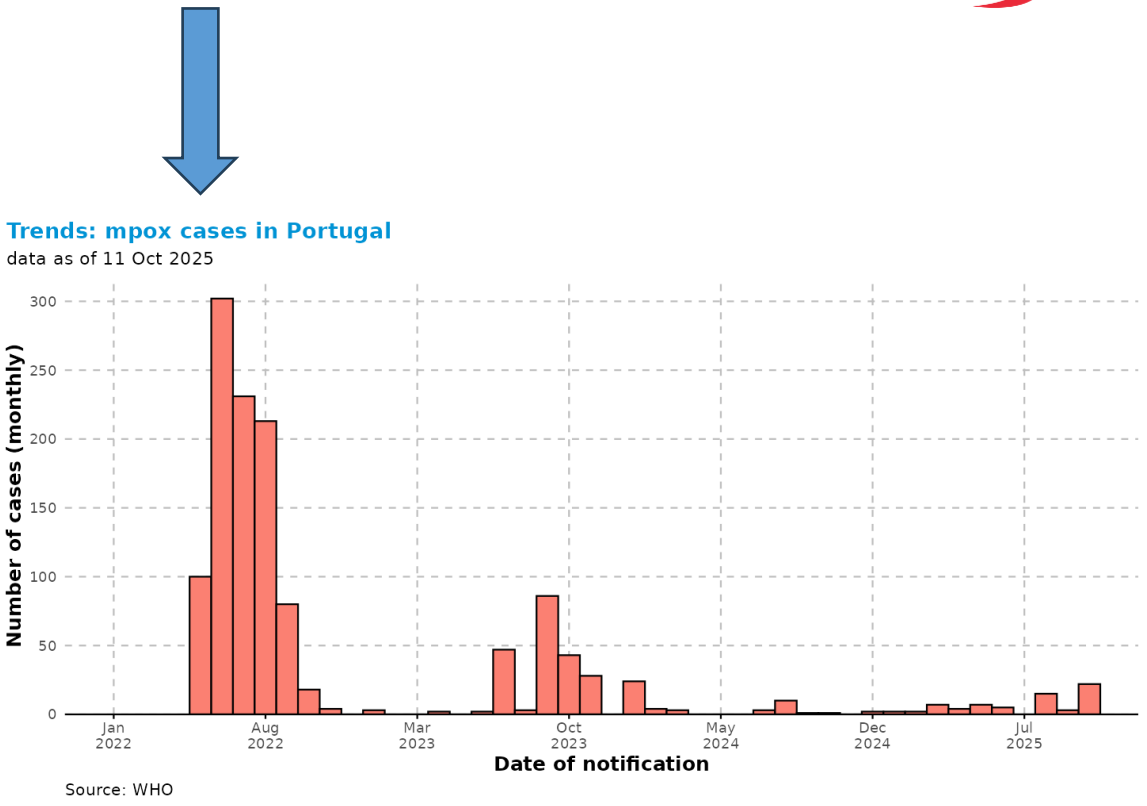
Mpox outbreak in Portugal

First wave

- **Retrospective data** suggest the **virus had been silently circulating** in Portugal before official notification, which may explain the **abrupt surge in early cases:**
  - *"Additionally, a retrospective study was carried out with **84 genital ulcer swabs from 81 patients**, collected in clinics located in the **Lisbon Metropolitan Area** and that had been sent to the reference laboratory for Sexually Transmitted Infections, **between January 3 and May 17, 2022**. **Two samples from April 2022 tested positive for MPXV**, indicating that the virus was already circulating in Portugal the first cases were notified."*



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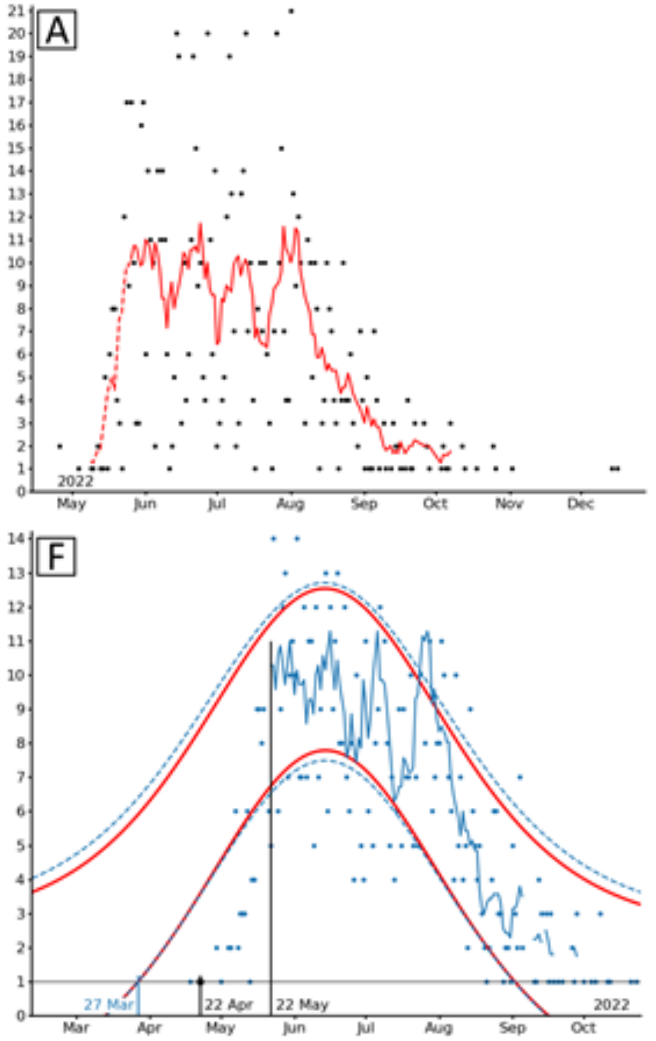
Mpox outbreak in Portugal

First wave

- By using a **mathematical model** combining a **negative binomial distribution** with **Richards' logistic curve**, we reconstructed the hidden phase of mpox transmission in Portugal.
- The analysis of **950 PCR positive** and **986 negative cases** suggested symptom onset between March 24 and April 2, 2022, with **March 27** being the **most probable date**.
- Thus, the present study offers robust evidence that **mpox was circulating in Portugal for nearly 50 days**, before the first official case detection.



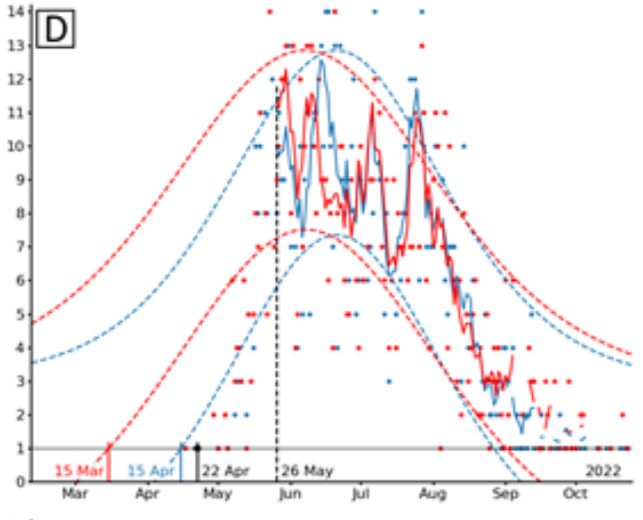
(A) Distribution of positive cases collection dates with MA in 2022 (red line). (F) Epidemic curve symptom onset dates based on MA starting May 22, showing the most probable onset date (March 27, 2022). Blue line: MA; dashed lines: prediction interval limits; red lines: average limits between simulations with the lower limit on March 27.

Cordeiro R, et al. Undetected Circulation of Monkeypox Virus in Portugal: Evidence for a 50-Day Gap Before First Detection. *Glob Epidemiol*. **2025** *(GEPI-D-25-00079R1 - Under review).*

Mpox outbreak in Portugal

First wave

- Despite the initial delay, the **public health response** was **rapid and effective**.
- Data indicate that **by 26 May 2022**, the epidemic curve had already stabilised, suggesting that transmission reached equilibrium, driven by **timely and appropriate control measures**.
- Although reference laboratory was prepared to perform diagnostic testing, the **atypical clinical presentation** and the **rarity of mpox outside endemic regions** limited early recognition by healthcare professionals and the affected community**.**



(D) Estimated symptom onset dates combining known data and simulated values, with MA starting on May 26 (solid lines); dashed lines indicate the 95% prediction confidence interval, marking earliest (Mar 15) and latest (Apr 15) onset estimates.

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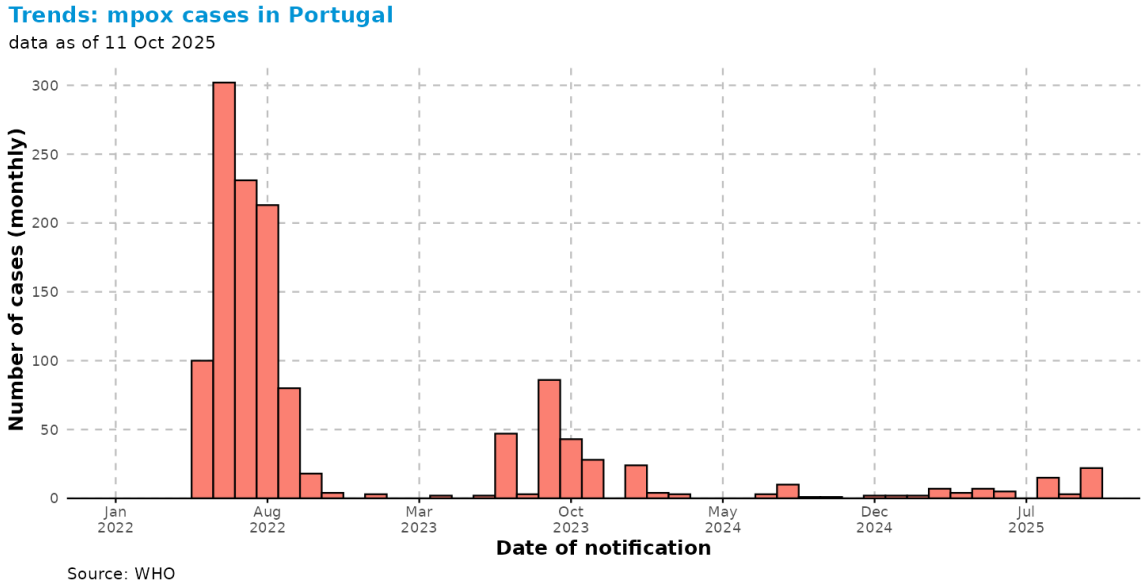
Mpox outbreak in Portugal

Second wave

- After controlling the first wave, cases resurged in mid-2023. This **second wave** provided a unique opportunity to explore transmission dynamics using mathematical modelling, particularly to understand the **role of sexual behaviour** and **vaccination**.

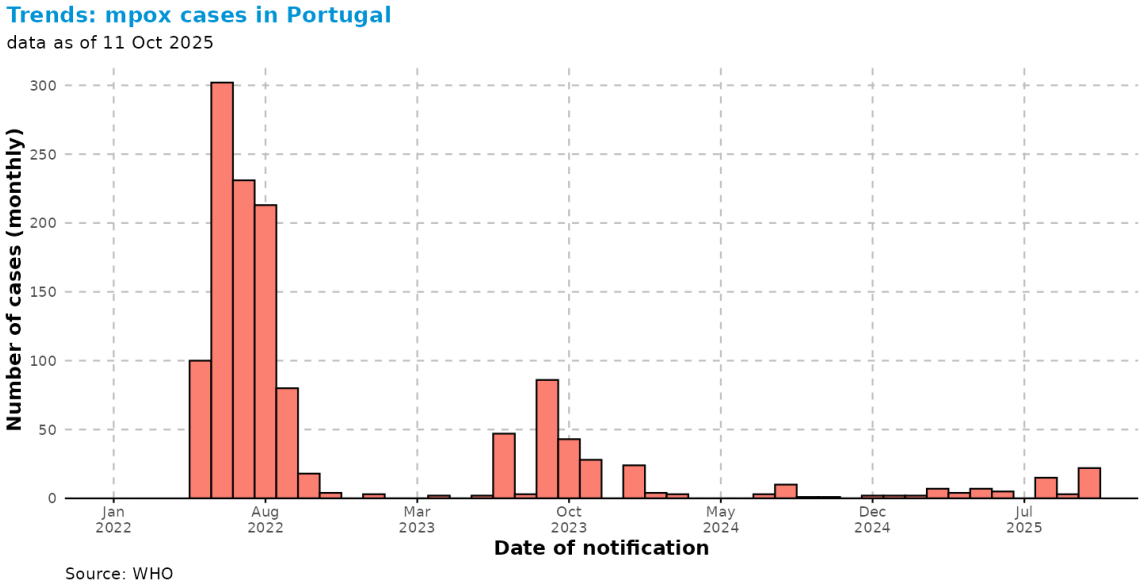


https://worldhealthorg.shinyapps.io/mpx_global/#sec-global

Mpox outbreak in Portugal

Second wave

- In 2023, Portugal had a **second epidemic wave of mpox**, resulting in a total of 240 confirmed cases.
- To understand how epidemiologically **relevant groups**, **vaccinated** vs. unvaccinated individuals and those with low vs. **high sexual activity**, **contributed to mpox transmission**, while also generating public health scenarios for **potential future epidemic waves**.
- A **SEIR** (**Susceptible–Exposed–Infectious–Recovered**) **mathematical model** was developed to describe the **transmission dynamics of mpox** during the second epidemic wave.



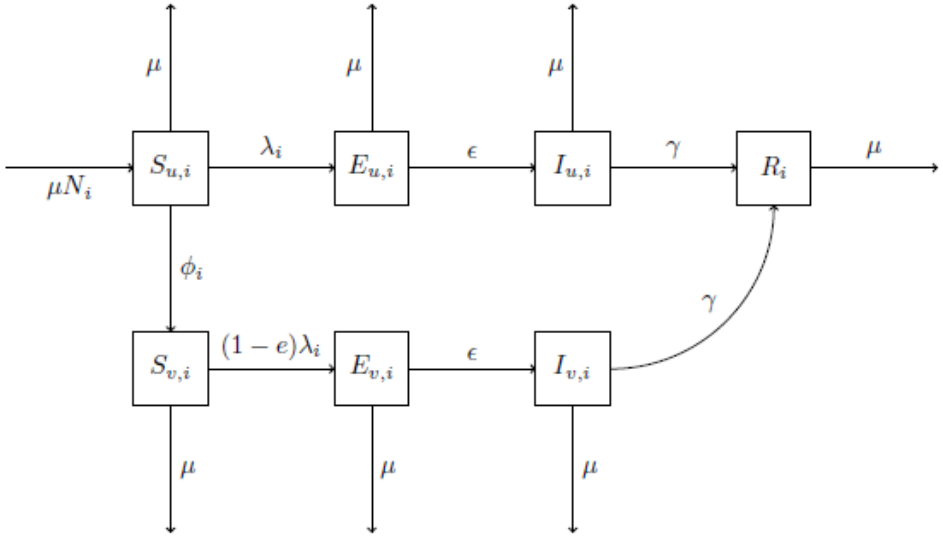
https://worldhealthorg.shinyapps.io/mpx_global/#sec-global

Mpox outbreak in Portugal

Second wave

Forecasting public health scenarios for a future epidemic wave

- In the **SEIR mathematical model**, **MSM individuals** were classified into two categories:
  - **Vaccinated** or **unvaccinated**
  - **Low** or **high sexual activity**, with **high activity** defined as reporting **more than 30 non-steady partners in the previous 12 months:**
    - Both **steady and non-steady sexual contacts** were incorporated into the model.
    - Data on sexual behaviour and steady partnerships were obtained from **EMIS – European Men Who Have Sex With Men Internet Survey**, conducted in 2017.



SEIR model diagram

Mpox outbreak in Portugal

Second wave

Forecasting public health scenarios for a future epidemic wave

- The period was projected between **22 May 2024 and 9 October 2024 (third wave)**;
- **Three possible scenarios** were developed for the weekly number of mpox cases after week 20 of 2024 (18 May 2024):
  - **Scenario 1**: **five latent mpox imports** with **high sexual activity** are introduced in the population;
  - **Scenario 2**: **five latent mpox imports** with **high sexual activity +1% of the unvaccinated** and **low sexual activity MSM population** change to **unvaccinated with high sexual activity**;
  - **Scenario 3**: **five latent mpox imports** with **high sexual activity +2% of the unvaccinated** and **low sexual activity MSM population** change to **unvaccinated with high sexual activity**.

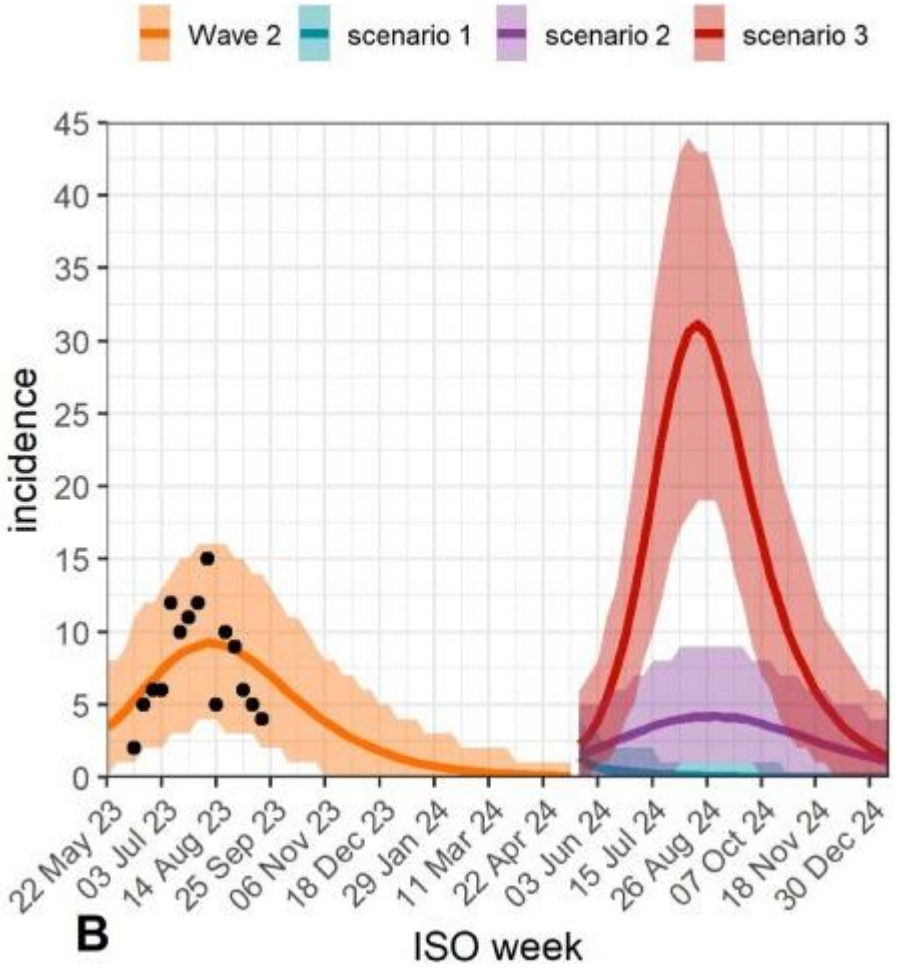
Mpox outbreak in Portugal

Second wave

Forecasting public health scenarios for a future epidemic wave

- The **SEIR mathematical model** showed that **mpox transmission** is strongly influenced by **sexual behaviour**, particularly among **MSM with high sexual activity**, who contributed approximately **120 times more to viral transmission** than those with low sexual activity.

- These findings indicate that **increases in sexual activity** within certain groups may **trigger new epidemic waves**.



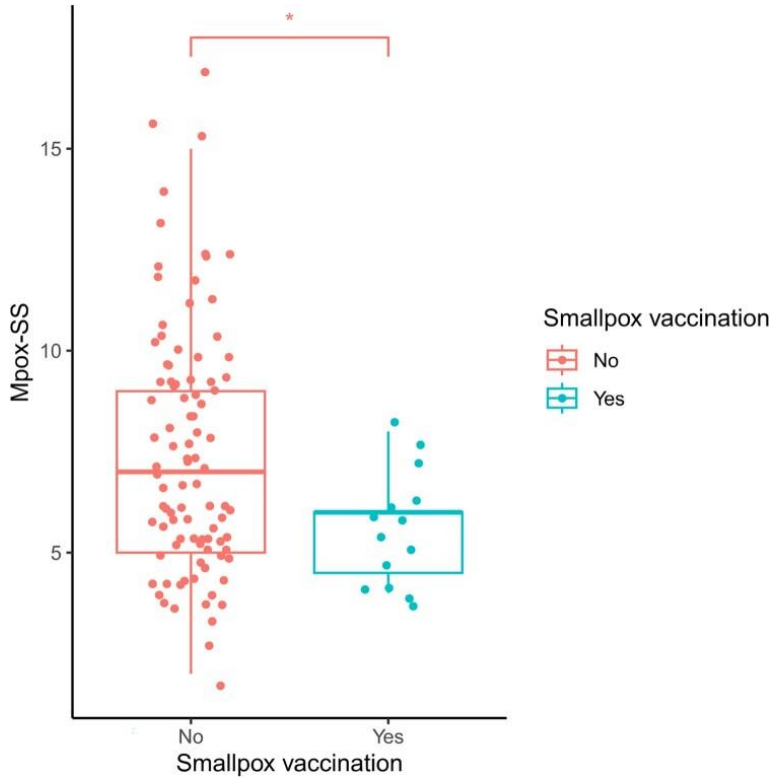
Transmission modelling of the second mpox wave in Portugal and forecasting of public health scenarios were carried out using a compartmental SEIR model, fitted with Bayesian techniques. Shows the modelled weekly incidence for the second wave, along with the projected trajectories for the potential epidemic scenarios for the summer of 2024.

Mpox outbreak in Portugal

Second wave

Impact of vaccination status

- **Vaccination** has shown **significant effectiveness** in reducing both **transmission** and **disease severity**.
- Among individuals with **high sexual activity**, those who were **vaccinated** contributed approximately **8 times less to the Rt** (transmissibility index) compared with unvaccinated individuals, **helping to contain the second epidemic wave**.
- In addition, **vaccinated individuals** presented with **less severe symptoms**.



Vaccinated individuals present lower MPox Severity Score (Mpox-SS) values than unvaccinated individuals. MpoxSS evaluation between vaccinated and unvaccinated patients using the Wilcoxon rank-sum test.

Mpox outbreak in Portugal

IgG antibody anti-OPXV titres

- To complement the epidemiological and modelling findings, we also analysed the **humoral immune response** through **IgG serology**, aiming to better interpret **immunity patterns** across PCR-positive and PCR-negative individuals.

Preliminary results – not published

Mpox outbreak in Portugal

Key findings

- Surveillance identified **three distinct outbreak waves**, each with a **progressive decline in transmission intensity**.

- The Portuguese reference laboratory maintains **active mpox surveillance**, including **genomic characterization of all confirmed cases**.

  Recent detection of the **first clade Ib case** demonstrates strong operational capacity and highlights the importance of **continuous genomic monitoring** for rapid detection of new introductions.

- These efforts support **timely, evidence-based public health responses**, contributing to effective outbreak control.

Mpox outbreak in Portugal

Lessons learned

- The decline across waves reflects the impact of **early diagnosis**, **targeted public health** messaging, and proactive pre-exposure **vaccination**, which distinguished Portugal's response from most other countries.
- Reduced case numbers likely also resulted from **increasing immunity** (vaccination or prior infection) and **behavioural changes** within MSM communities following **public health interventions**.
- Ongoing **MPXV circulation** in high-risk groups reinforces the need for **diagnostic readiness**, strengthened **surveillance**, and **risk-adapted** interventions.
- Integrating **clinical**, **behavioural**, **genomic** and **immunological** datasets will be essential for anticipating and **mitigating potential** re-emergence events.
- Portugal's experience, **early detection**, **continuous genomic surveillance**, and proactive **vaccination**, provides valuable guidance for improving **mpox preparedness** in non-endemic regions.

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