

# Joint ECDC-WHO Regional Office for Europe Mpox Surveillance Bulletin

# 15 August 2024

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## **SURVEILLANCE SUMMARY**

A total of 27,529 cases of mpox (formerly named monkeypox) have been identified through IHR mechanisms, official public sources and The European Surveillance System (TESSy) up to 05 July 2024, 14:00, from 46 countries and areas throughout the European Region. Since the last report, in the last three months, 349 cases have been reported from 18 countries and areas. Over the past 4 weeks, 100 cases of mpox have been identified from 10 countries and areas.

Case-based data were reported for 27,424 cases from 42 countries and areas to ECDC and the WHO Regional Office for Europe through TESSy, up to 05 July 2024, 10:00.

Of the 27,424 cases reported in TESSy, 27,239 were laboratory confirmed. Furthermore, where sequencing was available, 500 were confirmed to belong to Clade II, formerly known as the West African clade. No cases of Clade I have been reported in the Region. The earliest known case has a specimen date of 07 March 2022 and was identified through retrospective testing of a residual sample. The earliest date of symptom onset was reported as 17 April 2022.

The majority of cases were male (26,906/27,354 - 98%) with the most affected age group being 31–40 years-old (10,793/27,389 - 39%). Of the 12,527 male cases with known sexual orientation, 97% self-identified as men who have sex with men. Among cases with known HIV status, 38% (4,349/11,522) were HIV-positive. The majority of cases presented with a rash (16,042/17,277 - 93%) and systemic symptoms such as fever, fatigue, muscle pain, chills, or headache (11,976/17,277 - 69%). There were 885 cases hospitalised (7%), of which 301 cases required clinical care. Eight cases were admitted to ICU, and 10 cases of mpox were reported to have died.

An overview of the global situation can be found here: https://worldhealthorg.shinyapps.io/mpx\_global/.

## INTRODUCTION

### **PURPOSE AND SCOPE**

This report provides an overview of the total number of cases of mpox (formerly named monkeypox) identified by ECDC and the WHO Regional Office for Europe through IHR mechanisms and official public sources and case-based data through The European Surveillance System (TESSy) up to 05 July 2024.

The first summary table and maps (first two tabs) describe the number of cases identified through the different platforms. The following figures and tables describe national case-based data for surveillance of mpox reported in TESSy from all the countries and areas of the WHO European Region, including the 27 countries of the European Union (EU) and the additional three countries of the European Economic Area (EEA).

Case Report Form Data are submitted through the case-based record type mpox (MPX) to The European Surveillance System (TESSy) database hosted at ECDC.

# **CASE DEFINITION (WHO and ECDC)**

As of 22 December 2022

Cases of mpox should be reported to TESSy if they meet any of the WHO, ECDC or national case definitions.

#### **Confirmed case**

• A person with laboratory confirmed MPXV infection by detection of unique sequences of viral DNA by real-time polymerase chain reaction (PCR)<sup>1</sup> and/or sequencing.

#### Probable case:

• A person presenting with an unexplained acute skin rash, mucosal lesions or lymphadenopathy (swollen lymph nodes). The skin rash may include single or multiple lesions in the ano-genital region or elsewhere on the body. Mucosal lesions may include single or multiple oral, conjunctival, urethral, penile, vaginal, or ano-rectal lesions. Ano-rectal lesions can also manifest as ano-rectal inflammation (proctitis), pain and/or bleeding.

## *AND One or more of the following:*

- has an epidemiological link<sup>2</sup> to a probable or confirmed case of mpox in the 21 days before symptom onset;
- identifies as gay, bisexual or other cis or trans man who has sex with men;
- has had multiple and/or casual sexual partners in the 21 days before symptom onset;
- has detectable levels of anti-orthopoxvirus (OPXV) IgM antibody<sup>3</sup> (during the period of 4 to 56 days after rash onset); or a four-fold rise in IgG antibody titer based on acute (up to day 5-7) and convalescent (day 21 onwards) samples; in the absence of a recent smallpox/mpox vaccination or other known exposure to OPXV;
- has a positive test result for orthopoxviral infection (e.g., OPXV-specific PCR without MPXV-specific PCR or sequencing)<sup>1</sup>.

#### **Suspected case**

• A person who is a contact of a probable or confirmed mpox case in the 21 days before the onset of signs or symptoms, and who presents with any of the following: acute onset of fever (>38.5°C), headache, myalgia (muscle pain/body aches), back pain, profound weakness or fatigue.

• A person presenting since 01 January 2022 with an unexplained acute skin rash, mucosal lesions or lymphadenopathy (swollen lymph nodes). The skin rash may include single or multiple lesions in the ano-genital region or elsewhere on the body. Mucosal lesions may include single or multiple oral, conjunctival, urethral, penile, vaginal, or ano-rectal lesions. Ano-rectal lesions can also manifest as ano-rectal inflammation (proctitis), pain and/or bleeding.

AND for which the following common causes of acute rash or skin lesions do not fully explain the clinical picture:

• varicella zoster, herpes zoster, measles, herpes simplex, bacterial skin infections, disseminated gonococcus infection, primary or secondary syphilis, chancroid, lymphogranuloma venereum, granuloma inguinale, molluscum contagiosum, allergic reaction (e.g., to plants); and any other locally relevant common causes of papular or vesicular rash.

N.B. It is not necessary to obtain negative laboratory results for listed common causes of rash illness in order to classify a case as suspected. Further, if suspicion of mpox or MPXV infection is high due to either history and/or clinical presentation or possible exposure to a case, the identification of an alternate pathogen which causes rash illness should not preclude testing for MPXV, as co-infections have been identified.

#### **Discarded case**

- A suspected or probable case for which laboratory testing of lesion fluid, skin specimens or crusts by PCR and/or sequencing is negative for MPXV<sup>1</sup>.
- Conversely, a retrospectively detected probable case for which lesion testing can no longer be adequately performed (i.e., after the crusts fall off) and no other specimen is found PCR-positive, would remain classified as a probable case.
- A suspected or probable case should not be discarded based on a negative result from an oropharyngeal, anal or rectal swab or from a blood test alone.

The previous who and ecoc case definitions can be found in the Affile	ex.

The provious WILO and ECDC case definitions can be found in the Annex

1. PCR on a blood specimen may be unreliable and should also not be used alone as a first line diagnostic test. If blood PCR is negative and was the only test done, this is not sufficient to discard a case that otherwise meets the definition of a suspected for probable case. This applies regardless of whether the blood PCR was for OPXV or MPXV specific.

- 2. The person has been exposed to a probable or confirmed monkeypox case.
- 3. Serology can be used for retrospective case classification for a probable case in specific circumstances such as when diagnostic testing through PCR of skin lesion specimens has not been possible, or in the context of research with standardized data collection. The primary diagnostic test for monkeypox diagnosis is PCR of skin lesion material or other specimen such as an oral or nasopharygeal swab as appropriate. Serology should not be used as a first line diagnostic test.

# **KEY INDICATORS**

## **IHR SUMMARY**

Table 1: Summary of number of cases of mpox identified through IHR mechanisms and official public sources and reported to TESSy, European Region, 2022–2024

Countries and areas reporting new cases in the past 4 ISO weeks are highlighted in blue

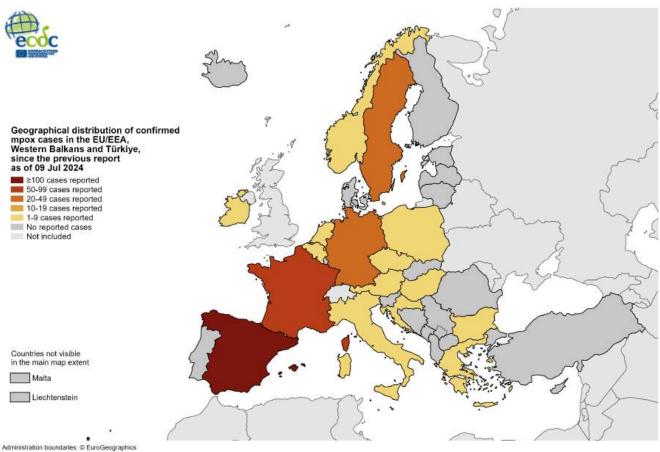
Country/Area	Number of new cases identified through IHR, official public sources and TESSy in the past 4 ISO weeks	Number of new cases identified through IHR, official public sources and TESSy in previous 3 months	Cumulative number of cases identified through IHR, official public sources and TESSy	Cumulative number of cases reported through TESSy
Spain	54	124	8084	8084
France	23	66	4272	4272
United Kingdom	0	44	3952	3866
Germany	10	27	3857	3850
Netherlands (Kingdom of the)	2	5	1304	1304
Portugal	0	0	1193	1193
Italy	2	7	1049	1049
Belgium	1	4	810	810
Switzerland	0	0	579	579
Austria	0	3	348	348
Israel	2	20	314	314
Sweden	2	27	299	299
Ireland	2	4	249	249
Poland	0	2	223	223
Denmark	0	0	198	198
Norway	0	1	106	106
Greece	0	7	99	99
Hungary	2	2	85	85
Czechia	0	4	82	82
Luxembourg	0	0	61	61
Slovenia	0	0	47	47
Romania	0	0	47	47
Finland	0	0	43	43
Serbia	0	0	40	40
Malta	0	0	35	35
Croatia	0	1	34	34
Iceland	0	0	17	17
Slovakia	0	0	16	16
Türkiye	0	0	12	12
Estonia	0	0	11	11
Bosnia and Herzegovina	0	0	9	9

Bulgaria	0	1	7	7
Gibraltar	0	0	6	5
Latvia	0	0	6	6
Cyprus	0	0	5	5
Lithuania	0	0	5	5
Ukraine	0	0	5	5
Andorra	0	0	4	4
Russian Federation	0	0	4	0
Monaco	0	0	3	0
Georgia	0	0	2	2
Montenegro	0	0	2	0
Republic of Moldova	0	0	2	2
Greenland	0	0	2	0
San Marino	0	0	1	1
Liechtenstein	0	0	0	0
Total	100	349	27529	27424

## **MAPS**

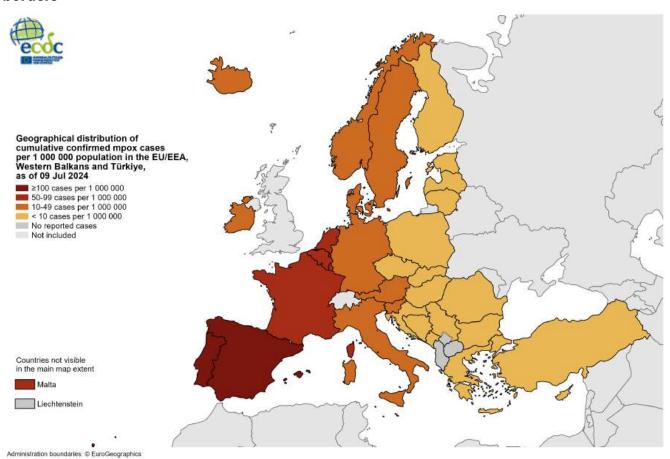
# **ECDC Map**

Map Figure 1a: Distribution of new cases of mpox reported in the past 4 ISO weeks, European Region, TESSy, 2022–2024, ECDC borders



The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. ECDC. Map produced on 10 Jul 2024

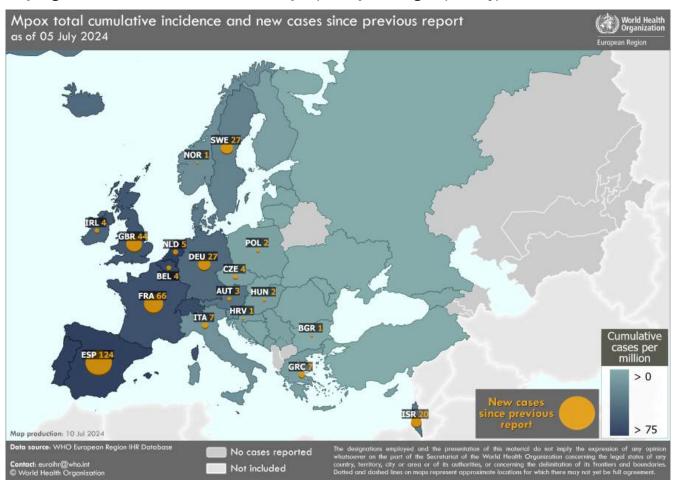
# Map Figure 1b: Distribution of all cases of mpox, European Region, TESSy, 2022-2024, ECDC borders



The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union, ECDC. Map produced on 10 Jul 2024

# **Map of WHO European Region**

# Map Figure 1c: Distribution of cases of mpox, European Region, TESSy, 2022-2024

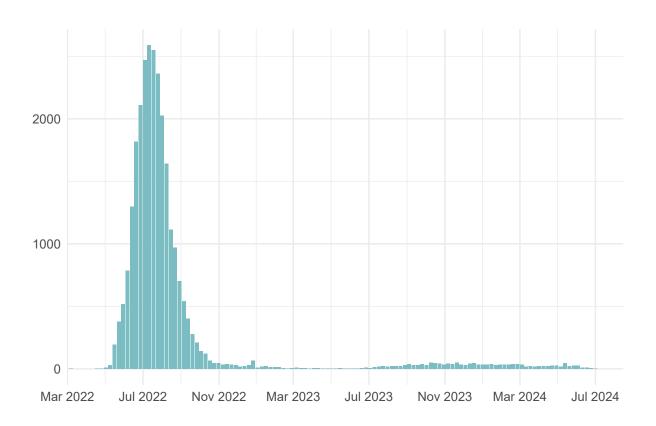


## **EPICURVES**

Date of notification is defined as the date when the case report is notified for the first time to the place of notification, date of diagnosis is defined as the first date of clinical or laboratory diagnosis, and date of onset as the date of onset of any symptoms.

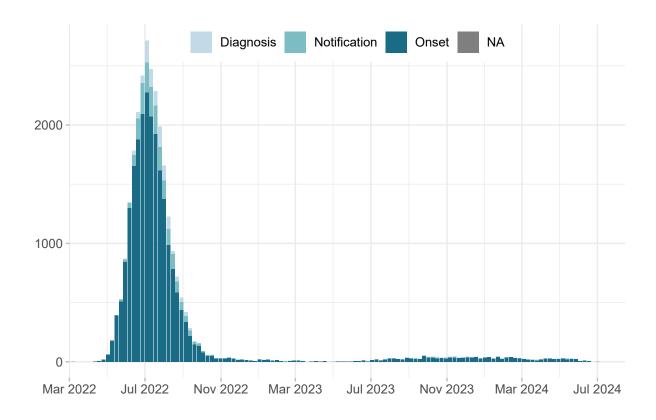
## Overall by date of notification

Figure 2: Overall number of cases of mpox, per date of notification, European Region, TESSy, 2022–2024



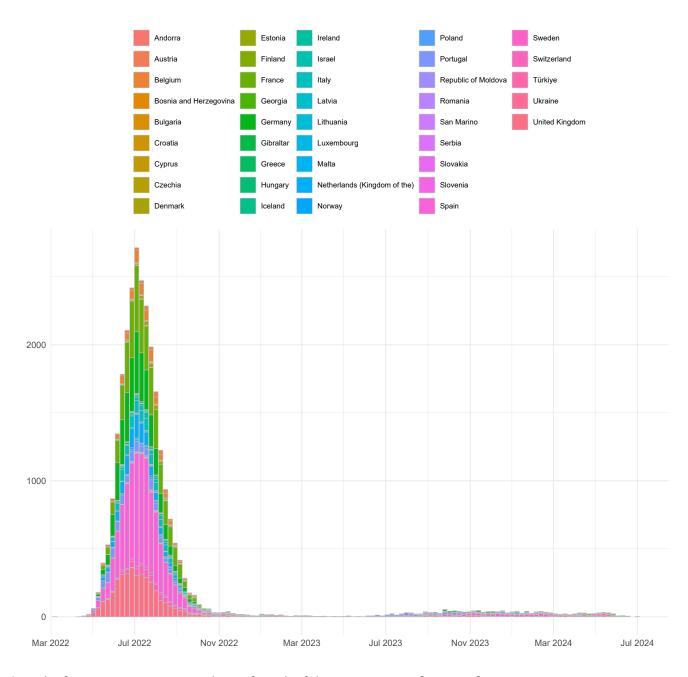
# Overall by date of symptom onset

Figure 3: Overall number of cases of mpox, Week of symptom onset (or earliest of week of diagnosis or notification if missing), European Region, TESSy, 2022–2024



# By date of onset and by country or area

Figure 4: Number of cases of mpox, per ISO week\* and per country/area of notification, European Region, TESSy, 2022–2024

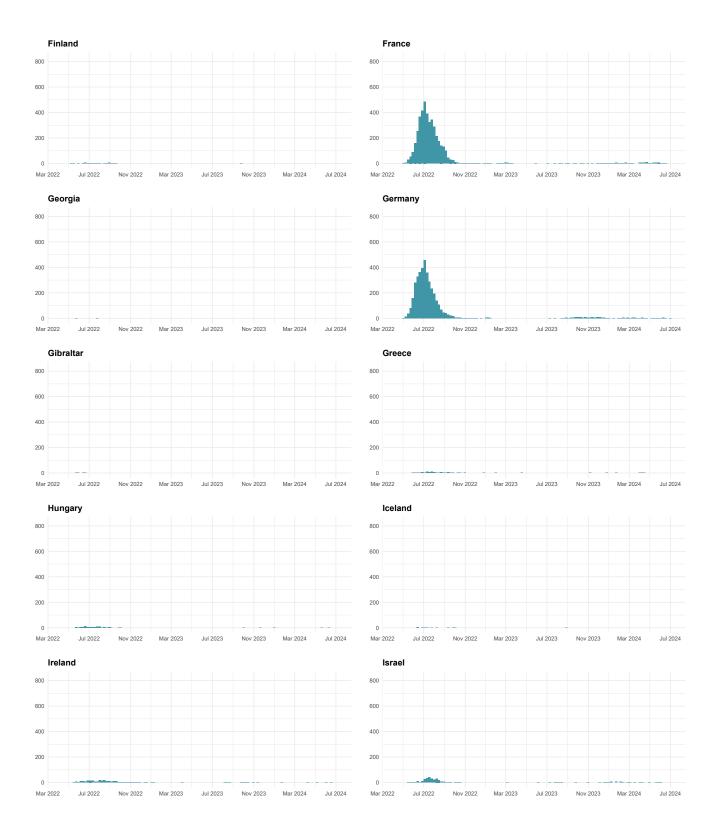


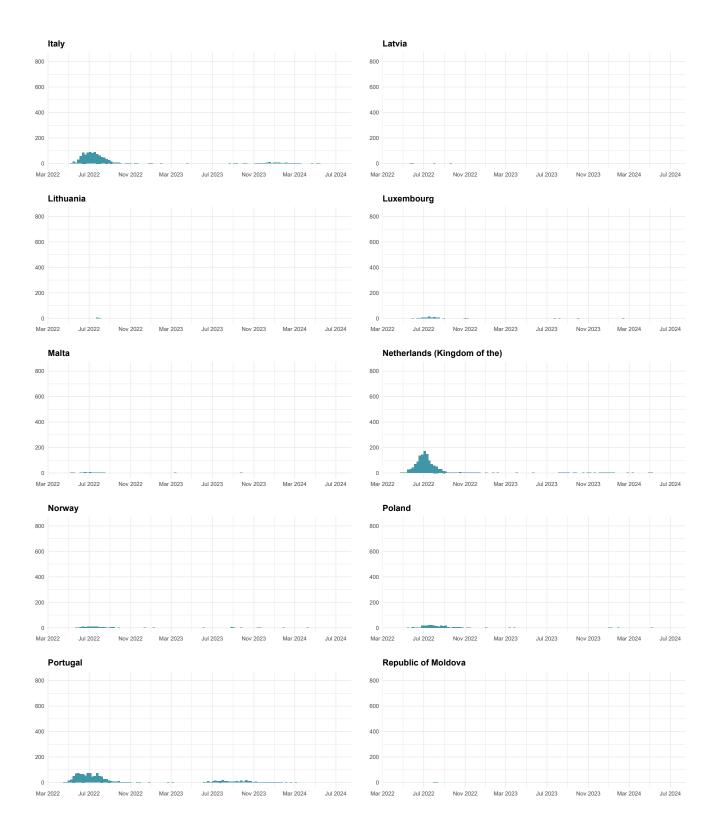
<sup>\*</sup>Week of symptom onset or earliest of week of diagnosis or notification if missing

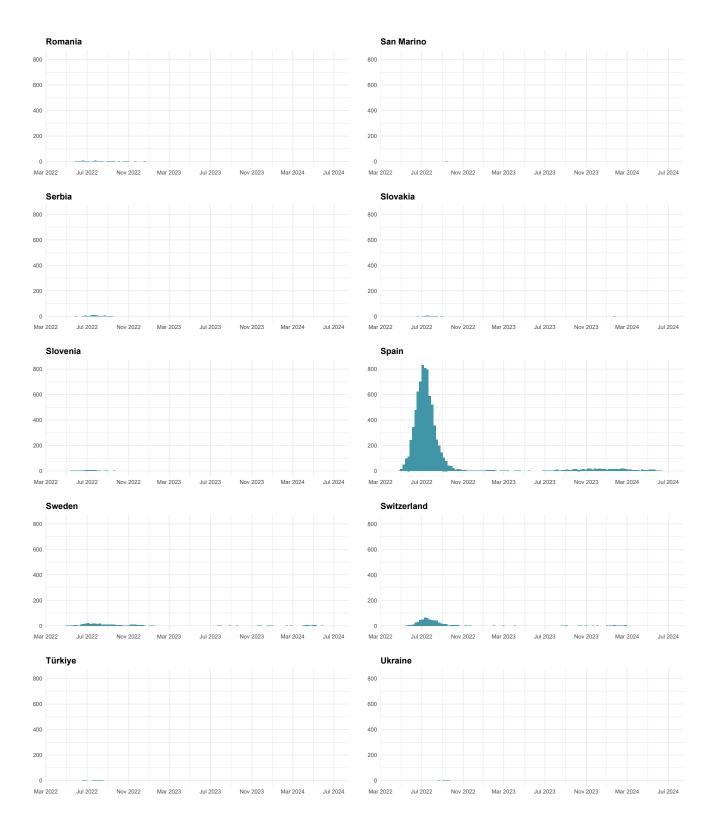
# By date of onset and by country or area - country/area level

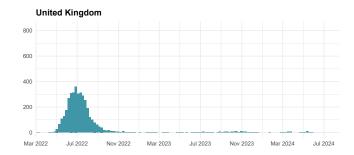
Figure 5: Number of cases of mpox, per ISO week\* and per country/area of notification, European Region, TESSy, 2022–2024











\*Week of symptom onset or earliest of week of diagnosis or notification if missing

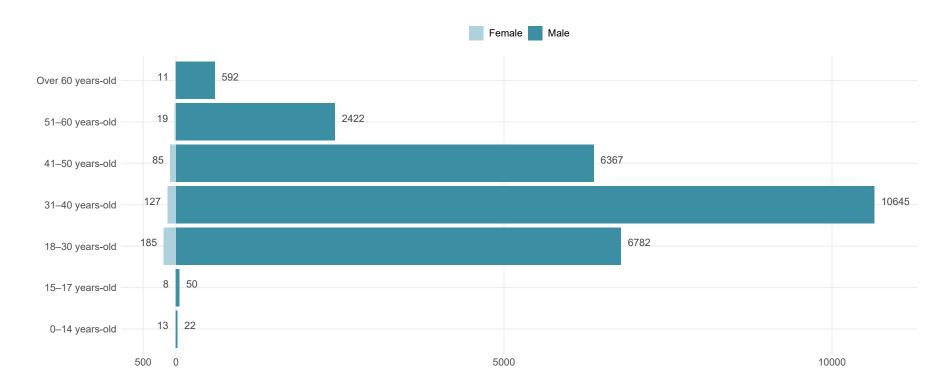
# **SUMMARY TABLE**

Table 2: Summary of number of probable and confirmed cases of mpox as well as deaths, by reporting country/area, European Region, TESSy, 2022–2024

Country	Confirmed cases	Probable cases	Total cases	Total deaths	
Andorra	4	0	4	0	
Austria	347	1	348	1	
Belgium	810	0	810	2	
Bosnia and Herzegovina	9	0	9	0	
Bulgaria	6	1	7	0	
Croatia	34	0	34	0	
Cyprus	5	0	5	0	
Czechia	82	0	82	1	
Denmark	198	0	198	0	
Estonia	11	0	11	0	
Finland	43	0	43	0	
France	4272	0	4272	0	
Georgia	2	0	2	0	
Germany	3850	0	3850	0	
Gibraltar	5	0	5	0	
Greece	99	0	99	0	
Hungary	85	0	85	0	
Iceland	17	0	17	0	
Ireland	245	4	249	0	
Israel	312	2	314	0	
Italy	1049	0	1049	0	
Latvia	6	0	6	0	
Lithuania	5	0	5	0	
Luxembourg	61	0	61	0	
Malta	35	0	35	0	
Netherlands (Kingdom of the)	1304	0	1304	0	
Norway	106	0	106	0	
Poland	195	28	223	0	
Portugal	1192	1	1193	3	
Republic of Moldova	2	0	2	0	
Romania	47	0	47	0	
San Marino	1	0	1	0	
Serbia	40	0	40	0	
Slovakia	16	0	16	0	
Slovenia	47	0	47	0	
Spain	8084	0	8084	3	
Sweden	299	0	299	0	
Switzerland	579	0	579	0	
Türkiye	12	0	12	0	
Ukraine	5	0	5	0	
United Kingdom	3718	148	3866	0	
Liechtenstein	0	0	0	0	
Total	27239	185	27424	10	

## **DEMOGRAPHICS**

Figure 7: Age and gender distribution of cases of mpox, European Region, TESSy, 2022-2024



Gender from 18 cases is reported as Other and these cases are not depicted on this graph. Information on gender is missing for 52 cases and information on age is missing for 35 cases.

Data on gender is collected as Female, Male, Other (e.g., transgender man, transgender woman and collected as free text), or Unknown.

## **CLINICAL DESCRIPTION**

The median time between symptom onset and diagnosis was 7 days.

Figure 8: Distribution of symptoms among those reporting at least one type of symptom (N=17277), European Region, TESSy, 2022–2024

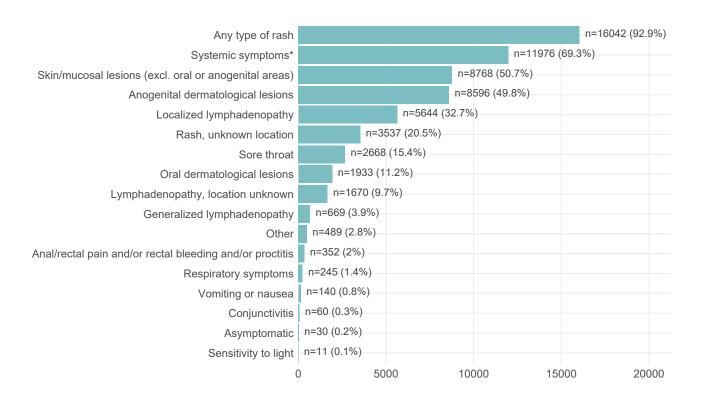


Table 3: Distribution of rash and systemic symptoms among those reporting at least one type of symptom (N=17277), European Region, TESSy, 2022–2024

Any type of rash	Systemic Symptoms*	Count (%)
Absent	Absent	177 (1.0%)
Absent	Present	1,058 (6.1%)
Present	Absent	5,124 (29.7%)
Present	Present	10,918 (63.2%)
Total	-	17,277 (100%)

<sup>\*</sup>Fever, fatigue, muscle pain, chills, headache

Detection of asymptomatic cases is dependent on testing guidelines which currently do not recommend testing asymptomatic persons

# **OUTCOME, HIV STATUS**

Table 4: Summary of outcome and HIV status of cases, European Region, TESSy, 2022–2024

	Yes	No	Total
Admitted to ICU	8 (0.1%)	7,708 (99.9%)	7,716 (100%)
Hospitalized*	885 (6.8%)	12,188 (93.2%)	13,073 (100%)
Died	10 (0.1%)	19,237 (99.9%)	19,247 (100%)
HIV-Positive	4,349 (37.7%)	7,173 (62.3%)	11,522 (100%)

<sup>\*</sup>Includes cases hospitalized for isolation or treatment (196 cases were hospitalized for isolation purposes, 301 required clinical care and 388 were hospitalized for unknown reasons).

## **SEXUAL ORIENTATION**

Sexual orientation in TESSy is defined according to the following non-mutually exclusive categories:

- Heterosexual
- MSM = MSM/homo or bisexual male
- Women who have sex with women
- Bisexual
- Other
- Unknown or undetermined

Sexual orientation is not necessarily representative of the gender of the person the case had sex with in the past 21 days nor does it imply sexual contact and sexual transmission.

We summarize here the sexual orientation that male cases identified with.

Table 5: Summary of reported sexual orientations among male cases of mpox, European Region, TESSy, 2022–2024

Sexual Orientation	Count (%)	
MSM	12,110 (45.0%)	
Bisexual	51 (0.2%)	
Heterosexual	366 (1.4%)	
Unknown or undetermined	3,017 (11.2%)	
Not reported	11,362 (42.2%)	
Total	26,906 (100%)	

# **MICROBIOLOGICAL ANALYSES**

# **SPECIMEN TYPES**

Table 6: Summary of specimen types with positive test result used for diagnosis of mpox, European Region, TESSy, 2022–2024

Specimen type	Count	
Lesion swab	5,824 (59.2%)	
Lesion crust	3,018 (30.7%)	
Oropharyngeal swab	615 (6.2%)	
Rectal swab	237 (2.4%)	
Genital swab	112 (1.1%)	
Urine	22 (0.2%)	
Serum	15 (0.2%)	
Semen	0 (0.0%)	
Total	9,843 (100%)	

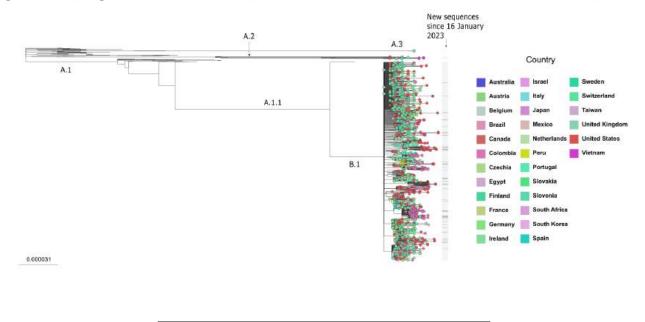
#### **PHYLOGENETICS**

## Phylogenetics of mpox virus

Phylogeny of human monkeypox virus was performed using Nextstrain. Briefly, genome sequences were extracted from Nextstrain repository comprising the curated NCBI GenBank sequences and metadata that were quality assessed using Nextclade<sup>1</sup>. The sequences were filtered for the Nextstrain curated exclusions, minimum length of 10000 bp, collected from 2017 and subsampling of 40 samples per country during the same sampling month and year. The phylogenetic analysis was performed using Nextalign (masking specific sites), IQTREE to construct the tree and TreeTime to refine the tree and visualized using Microreact<sup>2</sup>.

There are two genetically distinct clades described for monkeypox virus: Clade I and Clade II with sub-clades IIa and IIb<sup>3,4</sup>. The current outbreak falls within Clade IIb and following the nomenclature used in Nextstrain, a majority of the 2022 sequences belong to lineage B.1<sup>4,5</sup>. A few sequences do not cluster with the outbreak sequences but fall into lineages A.2 and A.3<sup>6-8</sup>. Figure A shows a phylogeny based on sequences from Clade IIb. The phylogeny is also visualized in Microreact along with the sequence metadata. Sequences from 2022 and 2023 are indicated with coloured circles and the binary heatmap shows sequences submitted after 16 January 2023.





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# **ACKNOWLEDGMENTS**

We gratefully acknowledge the Nextstrain team, the authors, originating and submitting laboratories of the genetic sequences and metadata (NCBI Genbank) for sharing their work.

#### **ANNEX**

## WHO and ECDC case definition prior to 22/12/2022

Cases of monkeypox should be reported to TESSy if they meet any of the WHO, ECDC or national case definitions.

#### **Confirmed case**

• Laboratory confirmed monkeypox virus infection by detection of unique sequences of viral DNA by real-time polymerase chain reaction (PCR)<sup>1</sup> and/or sequencing.

#### Probable case

• A person presenting with an unexplained acute skin rash, mucosal lesions or lymphadenopathy (swollen lymph nodes). The skin rash may include single or multiple lesions in the ano-genital region or elsewhere on the body. Mucosal lesions may include single or multiple oral, conjunctival, urethral, penile, vaginal, or ano-rectal lesions. Anorectal lesions can also manifest as ano-rectal inflammation (proctitis), pain and/or bleeding.

## AND One or more of the following:

- has an epidemiological link<sup>2</sup> to a probable or confirmed case of monkeypox in the 21 days before symptom onset;
- identifies as gay, bisexual or other man who has sex with men;
- has had multiple or anonymous sexual partners in the 21 days before symptom onset;
- has detectable levels of anti-orthopoxvirus (OPXV) IgM antibody<sup>3</sup> (during the period of 4 to 56 days after rash onset); or a four-fold rise in IgG antibody titre based on acute (up to day 5-7) and convalescent (day 21 onwards) samples; in the absence of a recent smallpox/monkeypox vaccination or other known exposure to OPXV; \*has a positive test result for orthopoxviral infection (e.g. OPXV-specific PCR without MPXV-specific PCR or sequencing)<sup>1</sup>.

## **Suspected case**

A person who is a contact of a probable or confirmed monkeypox case in the 21 days before
the onset of signs or symptoms, and who presents with any of the following: acute onset of
fever (>38.5°C), headache, myalgia (muscle pain/body aches), back pain, profound weakness or
fatigue.

• A person presenting since 01 January 2022 with an unexplained acute skin rash, mucosal lesions or lymphadenopathy (swollen lymph nodes). The skin rash may include single or multiple lesions in the ano-genital region or elsewhere on the body. Mucosal lesions may include single or multiple oral, conjunctival, urethral, penile, vaginal, or ano-rectal lesions. Ano-rectal lesions can also manifest as ano-rectal inflammation (proctitis), pain and/or bleeding.

AND for which the following common causes of acute rash or skin lesions do not fully explain the clinical picture:

• varicella zoster, herpes zoster, measles, herpes simplex, bacterial skin infections, disseminated gonococcus infection, primary or secondary syphilis, chancroid, lymphogranuloma venereum, granuloma inguinale, molluscum contagiosum, allergic reaction (e.g., to plants); and any other locally relevant common causes of papular or vesicular rash.

N.B. It is not necessary to obtain negative laboratory results for listed common causes of rash illness in order to classify a case as suspected. Further, if suspicion of monkeypox infection is high due to either history and/or clinical presentation or possible exposure to a case, the identification of an alternate pathogen which causes rash illness should not preclude testing for MPXV, as coinfections have been identified.

#### **Discarded case**

- A suspected or probable case for which laboratory testing of lesion fluid, skin specimens or crusts by PCR and/or sequencing is negative for MPXV<sup>1</sup>.
- Conversely, a retrospectively detected probable case for which lesion testing can no longer be adequately performed (i.e., after the crusts fall off) and no other specimen is found PCR-positive, would remain classified as a probable case.
- A suspected or probable case should not be discarded based on a negative result from an oropharyngeal, anal or rectal swab.

Both the previous W	/HO and ECDC	case definitions	s can be	found in	i the A	ınnex

1. PCR on a blood specimen may be unreliable and should also not be used alone as a first line diagnostic test. If blood PCR is negative and was the only test done, this is not sufficient to discard a case that otherwise meets the definition of a suspected for probable case. This applies regardless of whether the blood PCR was for OPXV or MPXV specific.

- 2. The person has been exposed to a probable or confirmed monkeypox case. Please see below definition of a contact.
- 3. Serology can be used for retrospective case classification for a probable case in specific circumstances such as when diagnostic testing through PCR of skin lesion specimens has not been possible, or in the context of research with standardized data collection. The primary diagnostic test for monkeypox diagnosis is PCR of skin lesion material or other specimen such as an oral or nasopharyngeal swab as appropriate. Serology should not be used as a first line diagnostic test.

## ECDC case definition for monkeypox prior to 08/09/2022:

#### **Confirmed case**

 A person with a laboratory-confirmed monkeypox infection (1) monkeypox virus specific PCR assay positive result or (2) orthopoxvirus-specific PCR assay positive result which is then confirmed by nucleotide sequence determination of the detected virus as MPXV) with symptom onset since 1 March 2022.

#### Probable case

(1) A person with an unexplained rash<sup>1</sup> on any part of their body AND one or more other symptom(s) of monkeypox infection<sup>2</sup> with symptom onset since 1 March 2022

## AND one of the following:

- has a positive laboratory test result on orthopoxviral infection (e.g., orthopoxvirus-specific positive PCR without sequencing, electron microscopy, serology);
- has an epidemiological link to a confirmed or probable case of monkeypox in the 21 days before symptom onset;
- reports travel to MPX endemic countries in the 21 days before symptom onset;
- is a person (of any sexual orientation) who had multiple or anonymous sexual partners in the 21 days before symptom onset;
- is a man who has sex with men.

OR

(2) A person with an unexplained generalized or localized maculopapular or vesiculopustular rash with centrifugal spread, with lesions showing umbilication or scabbing, lymphadenopathy and one or more other MPX-compatible symptoms<sup>2</sup>.

- Since EU/EEA countries are just starting to identify cases and if testing capacity is sufficient, the
  above more sensitive case definition can be used. In countries with limited testing capacity for
  orthopoxviruses, the following description can be added to characterize the rash: 'unexplained
  localized or generalized maculopapular or vesiculopustular rash potentially with umbilication
  or scabbing'.
- 2. Fever (usually higher >38.5°C), headache, back ache, fatigue, lymphadenopathy (localized or generalized).

## WHO case definition for monkeypox prior to 25/08/2022:

#### **Confirmed case**

• Laboratory confirmed monkeypox virus by detection of unique sequences of viral DNA by real-time polymerase chain reaction (PCR)<sup>1</sup> and/or sequencing.

#### Probable case

A person meeting the case definition for a suspected case

#### AND One or more of the following:

- has an epidemiological link [prolonged<sup>2</sup> face-to-face exposure in close proximity, including health workers without appropriate PPE (gloves, gown, eye protection and respirator); direct physical contact with skin or skin lesions, including sexual contact; or contact with contaminated materials such as clothing, bedding or utensils] to a probable or confirmed case of monkeypox in the 21 days before symptom onset;
- has had multiple or anonymous sexual partners in the 21 days before symptom onset;
- has detectable levels of anti-orthopoxvirus (OPXV) IgM antibody<sup>3</sup> (during the period of 4 to 56 days after rash onset); or a four-fold rise in IgG antibody titre based on acute (up to day 5-7) and convalescent (day 21 onwards) samples; in the absence of a recent smallpox/monkeypox vaccination or other known exposure to OPXV;
- has a positive test result for orthopoxviral infection (e.g. OPXV-specific PCR without MPXV-specific PCR or sequencing) <sup>1</sup>.

## **Suspected case**

• A person of any age presenting since 01 January 2022 with an unexplained acute rash or one or more acute skin lesions

AND one or more of the following signs or symptoms:

• headache, acute onset of fever (>38.5°C), lymphadenopathy (swollen lymph nodes), myalgia (muscle pain/body aches), back pain, asthenia (profound weakness)

AND for which the following common causes of acute rash or skin lesions do not fully explain the clinical picture:

• varicella zoster, herpes zoster, measles, herpes simplex, bacterial skin infections, disseminated gonococcus infection, primary or secondary syphilis, chancroid, lymphogranuloma venereum, granuloma inguinale, molluscum contagiosum, allergic reaction (e.g., to plants); and any other locally relevant common causes of papular or vesicular rash.

N.B. It is not necessary to obtain negative laboratory results for listed common causes of rash illness in order to classify a case as suspected. Further, if suspicion of monkeypox infection is high due to either history and/or clinical presentation or possible exposure to a case, the identification of an alternate pathogen which causes rash illness should not preclude testing for MPXV, as coinfections have been identified.

#### **Discarded case**

- A suspected or probable case for which laboratory testing of lesion fluid, skin specimens or crusts by PCR and/or sequencing is negative for MPXV<sup>1</sup>.
- Conversely, a retrospectively detected probable case for which lesion testing can no longer be adequately performed (i.e., after the crusts fall off) and no other specimen is found PCR-positive, would remain classified as a probable case.

1. PCR on a blood specimen may be unreliable and should also not be used alone as a first line diagnostic test. If blood PCR is negative and was the only test done, this is not sufficient to discard a case that otherwise meets the definition of a suspected for probable case. This applies regardless of whether the blood PCR was for OPXV or MPXV specific.

- 2. Evidence is currently lacking as to the duration of exposure necessary for infection by the respiratory route, including how it relates to the severity of the index case's disease. Characterization of this parameter is one of the goals of the case investigation form described below
- 3. Serology can be used for retrospective case classification for a probable case in specific circumstances such as when diagnostic testing through PCR of skin lesion specimens has not been possible, or in the context of research with standardized data collection. The primary diagnostic test for monkeypox diagnosis is PCR of skin lesion material or other specimen such as an oral or nasopharyngeal swab as appropriate. Serology should not be used as a first line diagnostic test.