RAPID RISK ASSESSMENT

Risk assessment of the mpox epidemic caused by monkeypox virus clade I in affected African countries for the EU/EEA

16 August 2024

Summary

Epidemiological situation

The monkeypox virus (MPXV) epidemic of clade I infections that has been affecting the Democratic Republic of the Congo (DRC) since November 2023 has recently spread to several other African countries, including Burundi, Rwanda, Uganda and Kenya. Some of these countries could be experiencing larger epidemics than is currently being reported due to under-ascertainment and under-reporting.

Human-to-human transmission through close physical contact has been documented including sexual and non-sexual transmission. Although all age groups are represented among cases infected with MPXV clade I, preliminary data show that infections by clade Ib virus concern mostly the adult population, whereas infections by clade Ia concern mostly children. Human-to-human transmission, and sexual and non-sexual transmission have been documented in countries reporting clade I cases. To date, there are still significant uncertainties regarding the main transmission routes, transmissibility, severity, and natural disease history, and whether these differ between the two circulating variants of clade I MPXV.

Although no cases of MPXV clade I have been reported in the EU/EEA so far, it is likely that imported mpox clade I cases will occur in the EU/EEA. It is therefore important to be prepared to deal with such imported cases and prevent secondary transmissions.

Mpox symptoms usually appear 6–13 days (up to 21 days) after infection. The clinical manifestation of the disease includes general febrile symptoms, a distinct rash (papules) on the skin and sores on the mucosa, back pain and muscle aches. The rash may spread quickly throughout the body within three days of experiencing the initial symptoms. Most people experience mild to moderate symptoms that usually last two to four weeks, followed by a full recovery.

Suggested citation: European Centre for Disease Prevention and Control. Risk assessment of the mpox epidemic caused by monkeypox virus clade I in affected African countries for the EU/EEA – 15 August 2024. ECDC: Stockholm; 2024.

Risk assessment

In the affected areas in the African continent:

The likelihood of infection with MPXV clade I for EU/EEA citizens travelling to affected areas and having close contacts with affected communities is high. However, the severity of the disease is expected to be low. The same applies to EU/EEA citizens permanently living in the affected areas.

In the EU/EEA:

The overall risk for the EU/EEA general population is currently assessed as **low**.

The likelihood of infection with MPXV clade I for close contacts of possible or confirmed imported cases is **high**, yet the severity of the disease is expected to be **low**. However, in this same group, the severity of the disease is considered **moderate** amongst those with underlying conditions, particularly individuals who are immunocompromised.

The likelihood of infection for people with multiple sexual partners who were not previously infected with MPXV clade IIb or were not vaccinated in the 2022 outbreak is considered **moderate.** This assessment is based on the difficulty of controlling the spread of infection during the clade II outbreak in 2022/23 in this risk group. Although the severity of the disease would in most instances be low, people with underlying immunocompromising conditions and those with an untreated HIV infection could experience **moderate** clinical severity**.**

The overall likelihood of infection and severity of disease for the broader population are considered **very low** and **low** respectively**.** More detailed information can be found in the report below.

Recommendations

To contain any possible outbreak in the EU/EEA, detecting cases and preventing secondary transmission is vital. This can be achieved through:

- Raising awareness among clinicians and other health professionals about possible travel-associated mpox cases caused by MPXV clade I, including the possibility of different clinical presentations, transmission through sexual and non-sexual routes and different groups affected than in previous outbreaks.
- Ensuring effective surveillance, laboratory testing (including molecular clade identification), epidemiological investigation and contact tracing capacities. Importation of MPXV clade I infections, or notable mpox events (outbreaks related to mass gathering events or other specific settings, re-infections among cases, rise in cases among women, children or other risk groups) should be promptly reported via EpiPulse and/or EWRS. All mpox cases should be reported to TESSy.
- In the event of a MPXV clade I outbreak in the EU/EEA, identifying previously eligible unvaccinated high-risk individuals. If feasible, post-exposure vaccination of cases with the available third-generation smallpox vaccine can be offered as one of the response options. This can be complemented by vaccination programmes (pre-exposure vaccination for at-risk groups) that were put in place in the EU/EEA during the MPXV clade II outbreak in 2022.
- Rapidly isolating any suspected cases until proven negative and, if positive, until symptom resolution.
- Implementing contact tracing and testing of close contacts of confirmed cases following ECDC testing protocols.
- Providing travel advice to people visiting or returning from countries with confirmed MPXV clade I outbreaks.
- Continuing to implement risk communication activities and working with civil society organisations to engage population groups at higher risk of infection.

Epidemiological situation

Mpox (formerly monkeypox) is a viral disease caused by the monkeypox virus (MPXV), which is present in the wildlife in several central- and west-African countries. In 2022, an outbreak occurred in Europe and globally, in which the infection was transmitted between humans, mainly through sexual contact.

There are two genetically distinct clades described for MPXV: clade I, with sub-clades Ia and Ib [1], and clade II, with sub-clades IIa and IIb [2]. Note that sub-clade Ia is often referred to simply as clade I [3].

MPXV clade I has been reported in the past being associated with severe clinical symptoms and higher mortality compared to clade II [4,5] until the 2022 global outbreak, which was instead driven by MPXV clade IIb [6]. Clade IIb is characterised by a less severe illness and lower.

Since the end of 2023, a large outbreak of mpox has been affecting the Democratic Republic of the Congo (DRC), with recent geographical expansion to other African countries. Although both MPXV clades I and II are circulating

in different countries in the African continent. The rapid rise and spread of MPXV clade Ia and Ib has raised concerns at global level.

Since the beginning of the global mpox outbreak in 2022 and until end of July 2024, 99 176 confirmed cases of mpox, including 208 deaths, had been reported by 116 countries [7]. In 2024, 14 719 suspected and 2 822 confirmed mpox cases (total 17 541) have been reported in the African continent, including 517 deaths (case fatality, CF 3%), according to the Africa Centres for Disease Control and Prevention (Africa CDC) [8]. The 13 African Union Member States with reported cases in 2024 are Burundi, Cameroon, Central African Republic, Republic of the Congo (hereafter referred to as Congo), Côte d'Ivoire, Democratic Republic of the Congo (DRC), Ghana, Liberia, Kenya, Nigeria, Rwanda, South Africa and Uganda [8]. Both monkeypox virus (MPXV) genetic clade I and clade II are circulating in the continent [9].

During 2024, **DRC** has reported 16 789 cases (14 151 suspected and 2 638 confirmed) including 511 deaths (case fatality (CF) 3%) from 25 of the 26 country's provinces [8] representing the highest number of cases due to clade I in Africa [9].

Confirmed mpox cases have also been reported in five of the eight neighbouring countries to DRC in 2024, i.e., **Burundi** (61 confirmed, 165 suspected), **Central African Republic** (35 confirmed, 223 suspected), **Congo** (19 confirmed, 150 suspected)**, Rwanda** (4 confirmed), and **Uganda** (2 confirmed) [8,10]. Additionally, suspected cases were investigated in South Sudan, according to media [11]. Out of the eight neighbouring countries to DRC, only the Central African Republic and Congo reported cases in 2023 [8]. Burundi, Uganda and Rwanda reported their first mpox cases end of July 2024 with Burundi reporting most cases indicating community transmission in the country [10]. Besides the neighbouring countries to DRC, **Kenya** reported its first confirmed mpox case at the end of July 2024 [12]. MPXV clade Ia has been isolated from cases in Central African Republic and Congo [9,13,14]. MPVX clade Ib, which was detected first in DRC and reported in April 2024, was also detected in confirmed cases in Burundi, Rwanda, Uganda and Kenya [10,13].

Although the degree of under ascertainment and underreporting of cases in affected countries is unknown, it is presumed to be substantial. Thus, the number of cases reported are likely an underestimation of the true number of infections. Furthermore, community transmission can be presumed in several African countries due to the widespread geographical distribution of reported cases and the wide age-groups ranges represented.

Multiple modes of transmission including human-to-human (e.g., sexual transmission, household transmission) and in some settings zoonotic have been documented in DRC and epidemiological links between confirmed cases in other countries and DRC have been documented [9,15] [10]. Sustained human-to-human transmission including through sexual contact has been shown to contribute to the spread of mpox clade Ib (e.g., in eastern DRC and neighbouring countries), as previously shown in the global outbreak of MPXV clade IIb [10,14]. An observational study conducted in Kamituga (South Kivu province) in April 2024 showed that among cases infected with sub-clade Ib, 29% reported involvement in sex work [1]. In another study conducted in the same area and published in May 2024, 88% of 371 hospitalised patients reported being involved in transactional sex [16]. Besides sexual contact, non-sexual contact, household and health care facility contacts have been reported by cases in DRC [17]. In areas where MPXV clade Ia circulates (endemic in DRC) multiple modes of transmission have been documented [10].

Overall, according to the World Health Organization External Situation Report published on 12 August 2024, in eastern areas of DRC and neighbouring countries where clade Ib circulates adults are the most affected. In areas where clade Ia circulates (e.g. endemic mpox in DRC, Congo, Central African Republic) children are mostly affected [10].

In DRC, most cases and deaths reported are among <15-year-olds, representing 66% of the total cases and 82% of the total deaths. Males account for 73% of the cases in DRC [8]. In Congo, based on information provided by Africa CDC, most confirmed cases (56%) were children <15-years-old and 58% were males; similarly, in the Central African Republic 43% of the confirmed cases were <15-year-olds and 62% males [9]. Moreover, within the Central African Republic, until 30 July 2024, cases were reported from 14 out of the 35 districts [9,18], including the capital city of Bangui [19]. In Burundi, where cases have been reported from 22 of 48 health districts (data published 9 August), 30% were in 0-5-year-olds and 52% of the confirmed cases were males [8].

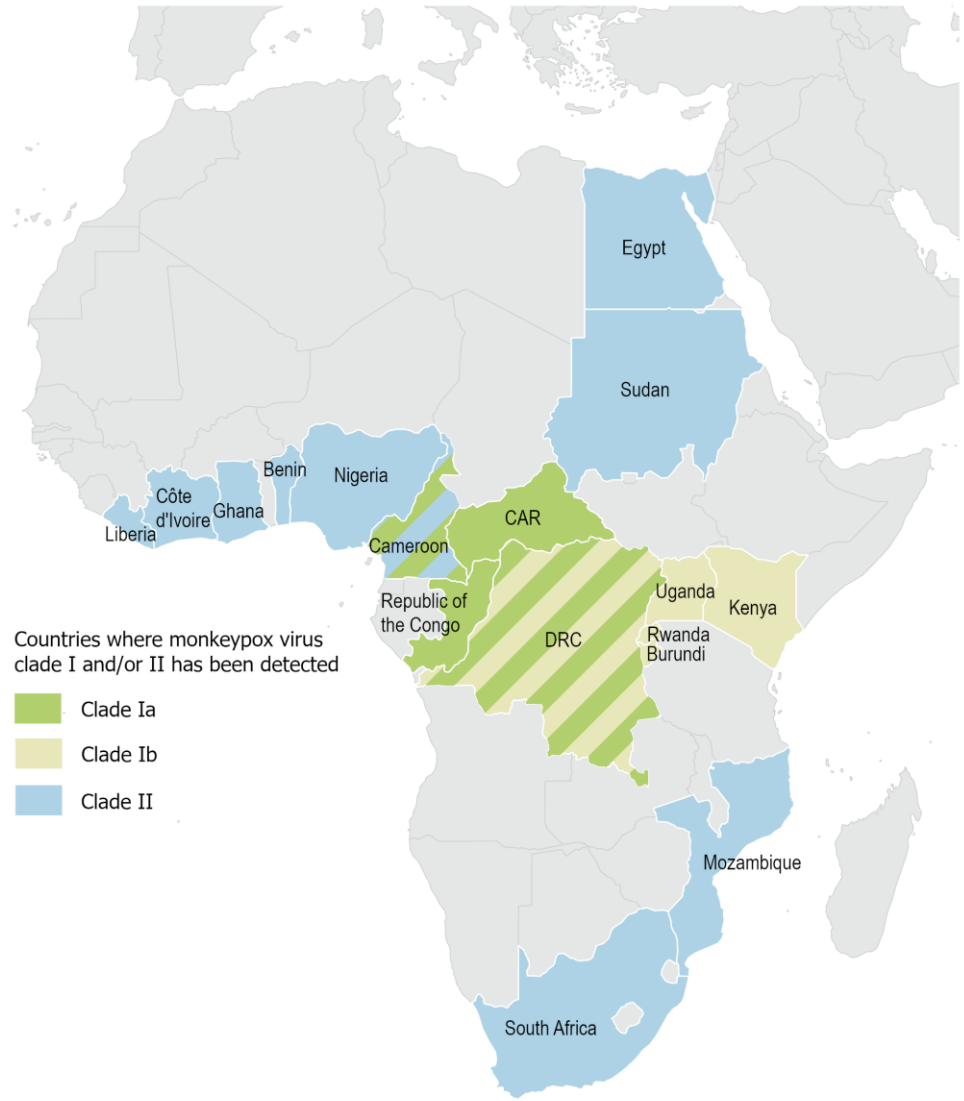
While information on clinical presentation of the cases reported by DRC and its neighbouring countries from surveillance is lacking [10], reports mention the presence of rash and in some cases fever and lymphadenopathy [1,16,17].

Further to the countries with reports of MPXV clade I circulation, additional African countries have reported cases of clade II including South Africa and Côte d'Ivoire [10]. As of 5 August 2024, **South Africa** has reported 24 mpox cases and three deaths. Twenty-two of the 24 cases were reported between 8 May and 6 July 2024 [20]. Cases reported by South Africa have a similar epidemiological profile to those reported in the global MPXV clade II outbreak i.e., most commonly in young males [21]. Six confirmed mpox cases have been reported in **Côte d'Ivoire** [22], with the first two confirmed cases reported in the Abidjan region [18].

On 13 August 2024, Africa CDC officially declared mpox a Public Health Emergency of Continental Security (PHECS), marking the first such declaration by the agency since its inception in 2017.The declaration will enable the mobilization of resources across affected countries, unlocking essential funding, strengthening risk

communication and community engagement, boosting surveillance and laboratory testing efforts, and enhancing human resource capacities to respond effectively to mpox [23]. On 14 August 2024, the Director General of the World Health Organization declared the outbreak a public health emergency of international concern (PHEIC) [24].

Figure 1. Countries where monkeypox virus clade I and/or clade II have been detected in Africa (CAR: Central African Republic; DRC: Democratic Republic of the Congo) [9,10]



Map produced on: 14 Aug 2024. Source: Africa CDC and WHO. Administrative boundaries: © EuroGeographics © UN–FAO © Turkstat.The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union.

EU/EEA

In EU/EEA countries, until 8 August 2024, 22 662 confirmed mpox cases had been reported by 29 countries via The European Surveillance System (TESSy). Most cases (93%) were reported during an intense period of circulation in 2022. In 2023, 860 cases were reported in 21 EU/EEA countries while so far in 2024, 685 cases have been reported by 20 EU/EEA countries. This indicates continued circulation of MPXV in the EU/EEA, but at very low levels. Information on the virus clade was reported for very few (2.1%) of all mpox cases reported into TESSy since 2022. Of these, all were from clade II, with no cases of clade I reported. From samples collected in 2024, as of 15 August, 29 genome sequences from the EU/EEA (from Austria, Germany, Netherlands, and Portugal) and 37 genome sequences from Africa (from DRC, Kenya, and Uganda) have been deposited in GISAID EpiPox [25],[26]. All of the sequences from the EU/EEA in GISAID belong to clade II, while all sequences from Africa belong to clade I.

Between 2022 and 2024, the profile and severity of mpox cases diagnosed in the EU/EEA has remained stable: 98% of mpox cases are males and 39% of cases are 31-40 years-old, while <0.1% of cases reported are in children <15 years of age. Of the 10 860 cases with data reported on sexual orientation, 95% self-identified as

men who have sex with men (MSM). Among cases with known HIV status, 38% (4 308/11 328) were HIV-positive. The cases reported to-date in the EU/EEA have mostly been mild, with 10 deaths (10/18 183, case fatality 0.1%) among all reported cases and a low proportion of hospitalised cases (867/12 924, 7%).

ECDC risk assessment

This rapid risk assessment has been developed based on the currently available data at the time of publication and follows the ECDC rapid risk assessment methodology, where the overall risk is determined by a combination of the probability of infection and its impact [27]. The probability of infection and the impact of the disease are assessed at the time of an emerging health threat, taking into consideration characteristics of place (country (-ies) where occurring) and person (prevalence of risk groups in EU/EEA population).

This assessment draws on historical data from MPXV clade I, the ongoing epidemic in DRC, and the recent global MPXV clade IIb outbreak. However, many aspects of the transmission and clinical outcomes, in particular the severity of the clinical presentation of MPXV clade Ib infection and the role of sexual transmission for this sub-clade remain uncertain.

Table 1. Summary of the risk due to MPXV clade I for the populations under assessment

	Likelihood of infection	Impact	Risk for the assessed population
In the affected countries			
EU/EEA citizens travelling to the affected countries and having close contact with affected communities (healthcare workers, household or other close contact and/or multiple sexual contacts) or living in the affected countries	High	Low	Moderate
EU/EEA citizens travelling to the affected countries, but not having close contacts with affected communities	Low	Low	Low
In the EU/EEA			
Close contacts of possible or confirmed imported cases	High	Low	Moderate
Close contacts of possible or confirmed imported cases with underlying immunocompromising conditions and those with an untreated HIV infection	High	Moderate	High
EU/EEA general population	Very low	Low	Low

What is the risk due to MPXV clade I circulation for EU/EEA citizens who are travelling to or living in the affected African countries?

Given the uncertainties on the extent of community transmission in the affected areas and the lack of conclusive evidence on the relative efficiency of different routes of transmission, EU/EEA citizens visiting affected countries and engaging in activities that involve close contacts with the local communities are considered at high risk of infection. The same apply to EU/EEA citizens living permanently in these countries. Preliminary data from the field show that close contacts are contributing to sustain the epidemic in Africa.

On the other hand, EU/EEA citizens travelling to the affected countries but being able to avoid close contacts with the affected communities have a much lower likelihood of infection.

While the morbidity and CF for clade I has been reported in the past to be higher than that for clade II [28], current preliminary data from Africa are not showing higher clinical severity in confirmed cases. Based on this assumption and considering the relatively little number of EU/EEA citizens potentially affected, the impact of mpox on EU/EEA citizens visiting or living in the areas affected by the current epidemic is considered **low**.

Based on these levels of likelihood and impact, the risk for EU/EEA citizens EU/EEA citizens travelling to the affected countries and having close contacts with affected communities (healthcare workers, household or other close contact and/or multiple sexual contacts) or living in the affected countries is assessed as **moderate**.

Conversely, the risk for EU/EEA citizens travelling to the affected countries but being able to avoid close contacts with the local community is assessed as **low**.

What is the risk due to MPXV clade I in the EU/EEA?

The increase in number of mpox cases due to MPXV clade I and the geographical expansion in newly affected African countries implies an increased probability of sporadic case introductions into the EU/EEA, which is assessed as highly likely.

In the event of sporadic importations of the MPXV clade I in the EU/EEA, the likelihood of infection for close contacts of possible or confirmed imported cases in the EU/EEA is assessed as **high**. The likelihood of infection is much lower for contacts that have been vaccinated or have a history of previous infection with MPXV clade IIb.

The likelihood of infection in the general population in the EU/EEA is assessed as **very low**, provided that imported cases are timely diagnosed, and control measures implemented.

Severe disease is more likely for people with underlying immunocompromising conditions and those with an untreated HIV infection (as it was the case for clade IIb). Based on these elements, the impact of the disease is assessed as **moderate** for these people, and **low** for the general population.

Therefore, the level of **risk** is assessed as high for close contacts with underlying immunocompromising conditions and those with an untreated HIV infection, **moderate** for healthy close contacts, and **low** for the remaining general EU/EEA population.

If a sustained transmission of MPXV clade I will be established in the EU/EEA, people with multiple sexual partners are at higher likelihood of infection. Within this group, unvaccinated, immunocompromised individuals, and those that do not have a history of previous infections with MPXV clade IIb are at higher risk of a more severe illness.

After the outbreak of MPXV clade II in the EU in 2022, the European Commission and EU Member States took measures to acquire and make medical countermeasures (MCM: treatments and vaccines) accessible to patients. As a result, according to DG HERA, no issue in access to both MCM is expected in the EU, should MPXV clade I be introduced.

ECDC recommendations

ECDC issues the following recommendations targeted for specific stakeholders, which are summarised under the following bullet points and detailed in the next paragraphs.

For public health authorities

- Follow ECDC guidelines for case detection and investigation;
- Investigate every case and report any significant increases in case numbers or changes in epidemiology (increased severity, detections of MPXV clade I, outbreaks related to mass gathering events, re-infections among cases, rise in cases among women, children or other risk groups;
- Implement effective surveillance, ensuring that the system is very sensitive to ensure prompt response to possible cases;
- Rapidly isolate any suspect cases until proven negative and, if confirmed, until symptoms resolution.
- Implement contact tracing and testing of close contacts of confirmed cases following the ECDC testing indications.
- Develop information material for clinicians;
- Map laboratory capacity;
- ECDC is recommending EU/EEA countries to be able to identify previously eligible unvaccinated high-risk individuals, in the event of a MPXV clade I outbreak in the EU/EEA mainly transmitted sexually as in 2023. If feasible, post-exposure vaccination of cases with the available third generation smallpox vaccine can be offered as one of the response options. This can be complemented by the vaccination programmes (pre-exposure vaccination for at-risk groups) that have been put in place in the EU/EEA during the MPXV clade II outbreak in 2022.

For people planning to travel to the affected areas in the African continent

- Consult the ECDC outputs and epidemiological information;
- Refrain from sexual or other close contact with individuals with possible or known mpox infection and with those with visible lesions or other mpox compatible symptoms.
- Consult your healthcare provider regarding eligibility for vaccination against mpox
- Avoid contacts with wild animals.

For people living in the EU/EEA

- No special recommendations are issued at this stage for the general public.

Surveillance

National mpox surveillance

At national level, EU/EEA countries should maintain their mpox event-based and indicator-based surveillance and testing capacities to be able to timely identify cases and clusters, monitor their epidemiological characteristics, including affected population sub-groups, and rapidly detect changes in disease trends. In this regard, EU/EEA countries are also encouraged to define mpox as a nationally notifiable disease.

In order to meet these objectives, surveillance systems should be very sensitive and prompt a thorough investigation of each suspected case as recommended by ECDC. Furthermore, these are the ECDC interim indications for testing:

- Individuals returning from an affected area and reporting exposure to a possible or confirmed cases
  - test at first encounter and then weekly with the last test performed 21 days after return if still asymptomatic
- Individuals returning to an affected area and reporting any of the symptoms described above in this document
- Close contacts of confirmed cases in the EU/EEA (regardless of type of contact)
  - test at first encounter and then weekly with the last test performed 21 days after the contact if still asymptomatic.
- Individuals presenting with mpox compatible lesions or any other typical symptom, including isolated genital lesions.

EU/EEA mpox surveillance

EU/EEA level surveillance by ECDC is based on indicator-based data collection through TESSy, complemented by event-based surveillance with reporting through EpiPulse (and/or EWRS depending on the event).

National EU/EEA public health authorities should report all mpox cases on a monthly basis to TESSy. As much as possible, case details should include information about the clade. Information on clade can be updated in the TESSy system as it becomes available.

Any significant increases in case numbers or changes in epidemiology, such as increased severity, detections of MPXV clade I, outbreaks related to mass gathering events or other specific settings, re-infections among cases, rise in cases among women, children or other risk groups (sex workers, transgender people) should be reported through event-based surveillance as a new event on EpiPulse and/or EWRS.

According to a survey carried out by the European Commission Joint Research Centre (JRC) in August 2024, MPXV is not systematically included in the list of pathogens monitored in wastewater in EU Member States. Among the 16 EU MS responding, only 4 are monitoring MPXV in wastewater (2 in both community and airport wastewater, and 2 only in community wastewater). Several EU MS indicated that they are currently setting up the methods for MPXV monitoring in view of the upcoming GLOWACON's first synchronised airport sampling exercise, which will include MPXV. This exercise, supported by DG HERA in collaboration with the JRC, will take place in the week of 23 September 2024 and is dedicated to the synchronised collection and coordinated examination of wastewater samples originating from aircraft at a variety of global airports, including in Africa.

Genomic surveillance

Sequencing of MPXV contributes to understanding viral evolution, transmission chains and patterns of spread. Countries are encouraged to sequence a representative sample of mpox specimens and share sequences in publicly available sequence repositories, particularly when sudden clinical and/or epidemiological changes are observed. Such changes may include, but are not limited to, increase in virulence, or change in clinical disease presentation, change in performance of laboratory diagnostics, from cases associated with transmission in specific settings with unusually high transmission or outbreaks/cluster with unusual signature (e.g. behaviour or age-group).

Laboratory testing

The laboratory diagnosis of mpox is predominantly based on the direct demonstration of the *Orthopoxvirus monkeypox* (MPXV) in clinical specimen. Real-time polymerase chain reaction (real-time PCR) on skin lesion materials (e.g. swabs, exudate, or lesion crusts) are used most frequently. Several real-time PCR assays for the specific detection of MPXV, or for generic orthopoxvirus detection are available [29-34]. Over 80 MPXV laboratory tests are CE-validated, mostly based on PCR [29-34]. Mpox laboratory diagnostics are well established in several laboratories in Europe (see Emerging Viral Diseases-Expert Laboratory Network – EVD-LabNet [35]). Identification of the genetic clade of MPXV is mainly based on the determination and analysis of the partial genome sequences of the detected virus; however, clade-specific real-time PCR assays are also used for this purpose in some laboratories. Recent studies revealed that a novel clade I MPXV which was detected in the current mpox outbreak in the DRC has a deletion in and surrounding the OPG032 gene. This mutation may result in false negative test results for certain real-time PCR assays to discriminate between clade I and clade II MPXV strains [36,37]. However, validated assays are available for the detection of the new clade Ib variant [38]. Mpox diagnostic

laboratories in the EU/EEA have been alerted through the EVD-LabNet about this finding and were advised to use molecular assays which are able to detect this mutant strain. The timely detection of the potential emergence of clade I MPXV in the EU/EEA requires molecular identification of viruses detected in diagnostic specimens. Therefore, nucleotide sequencing and sharing sequence information through public databases (e.g., GISAID) remains an essential component for the monitoring of the mpox epidemiological situation in Europe and globally.

Raising awareness among clinicians and laboratories

Testing for MPXV should be easily accessible to those at risk of infection. Clinicians should be aware of symptoms and when to offer a test. People who suspect that they are infected should be aware of the need to test and where to access testing, and results should be shared with health authorities. People who have been previously infected with MPXV or who received one or two doses of vaccine should still be tested if infection is suspected.

Given that case numbers of mpox have declined substantially since the summer 2022, there might be a need to remind clinicians – especially those who do not work directly in STI clinics or with MSM – of the need to be aware of mpox symptoms and the possibility that cases may reappear. Testing should be made available to improve rapid access, in particular in clinical settings that serve gay, bisexual or other men or transgender people who have sex with men as this is where the populations at highest risk are likely to access services including sexual health clinics, HIV PreP clinics, HIV clinics and low threshold services. Testing for mpox can also be linked to testing for other STIs. Public health authorities, community partners and others should consider raising awareness among MSM of symptoms of mpox, the need for rapid testing and up-to-date information on where to access testing.

Clinicians and laboratories should be made aware of how to rapidly report cases of mpox to public health authorities as appropriate to ensure that a potential increase in transmission is rapidly detected. This will facilitate early reporting which is particularly important at the start of a possible resurgence in order to focus public health interventions appropriately. Similarly, rapid reporting to partner notification or contact tracing services can ensure that potential contacts are notified as quickly as possible.

Cases diagnosed with mpox should also be considered for testing for HIV and other sexually transmitted infections as cases with mpox have been shown to also have high prevalence of HIV and other STIs and people with untreated HIV are more likely to have complications of mpox.

Awareness should be maintained or raised among clinicians and other health professionals in EU/EEA countries of the ongoing possibility of introduction of clade I or increased circulation of clade II in new risk groups, and the recommendation to promptly test all suspected cases and inform public health authorities even before test results are available. This includes clinicians at sexual health clinics serving MSM and other populations with multiple sexual partners, but also clinicians serving the general population (dermatologists, paediatricians, primary care providers). Clinicians should also be made aware of the possibility of seeing more severe cases due to infection with MPXV clade I. Such patients, as has been observed in the outbreak of MPXV clade II, require prompt initiation of supportive and antiviral treatment and/or post exposure vaccination.

In case of emergence of MPXV clade I in Europe, public health authorities should be ready to perform comprehensive contact tracing with thorough interview of cases to collect essential epidemiological data, such as travel history, list of contacts and type of contact, behavioural risk factors, underlying conditions, vaccination status for previous mpox and/or smallpox vaccination and date of last vaccination.

Travellers to areas where MPXV clade I outbreaks are ongoing should receive pre- and post-travel advice. Hence, travel medicine clinics should be aware of the ongoing outbreaks and familiar with the available preventive and control methods.

Vaccination

Vaccination campaigns in the EU/EEA and other countries were implemented to control the outbreak of clade IIb MPXV in 2022, with a third-generation non-replicating smallpox vaccine that has been authorised by the European Medicines Agency (EMA) for protection against mpox in adults [39,40]. The vaccine effectiveness of two pre-exposure vaccine (PPV) doses is estimated as 82% (95% CI: 72-92), while even one PPV dose provides effectiveness of 76% (95% CI: 64-88) [41]. For post-exposure vaccination (PEPV) the vaccine effectiveness was estimated as 20% (95%CI: -24-65) [41]. In individuals who experienced infection after having been vaccinated, disease was less severe compared to unvaccinated individuals [42]. Clade-specific vaccine effectiveness evidence is currently lacking [43,44] but the third-generation smallpox vaccine is expected to have similar vaccine effectiveness against MPXV clade I, although real-world data is lacking.

Reaching the target population for vaccination also presents challenges, although in the first months of the multicountry mpox outbreak in 2022, the number of countries administering this vaccine, and the number of doses administered, increased rapidly. Pop-up vaccination clinics with extended working hours, as well as vaccination in the context of mass gathering events frequented by groups at high risk have provided good practice in this area [45,46].

A survey based on a convenience sample of more than 15 000 MSM at higher risk of HIV infection conducted in October 2023 to April 2024 in 20 countries in Europe found self-reported receipt of at least one dose of the mpox vaccine to be 39%, with wide variation between countries ranging from 51% of the sample in France to <10% of the sample in Poland and Greece [47]. In another exercise to estimate mpox vaccination coverage among MSM with multiple sexual partners using general population data, EMIS-2017 data, and mpox doses reported to ECDC by European countries (as of March 2023), receipt of two doses of the mpox vaccine was estimated to be much lower, ranging from <1% to 12% in EU/EEA countries [48].

Tailored interventions are needed to increase confidence in the vaccine, maximize uptake, and increase vaccine access especially among key populations residing in regions with low rates of acceptance and uptake [49].

ECDC is recommending EU/EEA countries to be able to identify previously eligible unvaccinated high-risk individuals, in the event of a MPXV clade I outbreak in the EU/EEA. If feasible, post-exposure vaccination of cases with the available third generation smallpox vaccine cane be offered as one of the response options. This can be complemented by the vaccination programmes (pre-exposure vaccination for at-risk groups) that have been put in place in the EU/EEA during the MPXV clade II outbreak in 2022.

ECDC recommends travellers to epidemic areas to consult their healthcare provider or travel health clinic regarding eligibility for vaccination against mpox. The US CDC has issued recommendations for vaccination which may be useful for Member States to consider [50].

Risk communication and community engagement

Close collaboration with community-based organisations that work with MSM or other groups at high risk is essential to reach target groups. Public health authorities can use guidance and good examples of risk communication and community engagement developed during the 2022-23 mpox outbreak and available in the ECDC mpox webpage [51]. Key messages include awareness of symptoms, seeking testing and avoiding sex and close contacts until symptoms resolve and to seek vaccination if available. Risk communication with the general population in cases of increased community circulation in the EU/EEA, should include the risk of exposure to mpox through sex. Anyone presenting with symptoms compatible with mpox should be advised to seek medical care and abstain from sex and close contacts until a diagnosis is made or until symptoms resolve if infected.

Global efforts to control the outbreak in the affected African countries could reduce geographical spread

The control of the ongoing outbreak in DRC and other affected countries on the African continent would, apart from the direct benefit for the affected population, also reduce the likelihood of geographical spread of MPXV clade I on the continent, to the EU/EEA and globally. Building capacity for contact tracing, diagnosis and sequencing, and the provision of vaccines to affected communities are priorities in affected countries to support public health authorities' control efforts. In this regards, DG HERA, Africa CDC and Bavarian Nordic (BN) have signed on 14th August 2024 a tripartite agreement to secure 215 000 doses of mpox vaccines to the most affected African countries where the BN vaccine is authorized at national level, for initial doses delivery in September 2024 [52].

ECDC is supporting the GOARN efforts in response to the mpox outbreak is DRC by expert deployment. The deployment is operationalised by the EU Health Task Force (EUHTF) and funded by DG INTPA of the European Commission through the 'ECDC for Africa CDC' project. The EUHTF is planning to continue supporting the response with a series of deployments, as needed.

Limitations

This assessment is based on historical data on MPXV clade I, on data from the ongoing epidemic in DRC, and on data from the recent MPXV clade IIb outbreak. Many elements on which this assessment is based contain a significant level of uncertainty.

The number of reported outbreaks of mpox and the number of cases in Africa within the past one year are unprecedented and the ecological and epidemiological drivers are poorly identified. The sustained transmission chains in the communities and household transmissions may indicate changes in mpox epidemiology, but detailed data on secondary attack rates, basic reproduction numbers and transmission routes, particularly when stratified by clade Ia, Ib and II are not available. Altered transmission modes (e.g., through direct vs. indirect contact) may influence the probability of infection of EU/EEA travellers to affected areas in Africa.

So far, mpox outbreaks reported outside of Africa have been caused by MPXV clade IIb exclusively. To-date these outbreaks have predominantly affected MSM in the EU/EEA, with transmission mainly attributed to sexual contact, and resulting symptoms in those infected typically mild. In case of the emergence of MPXV clade I in the EU/EEA, it is unknown whether the same risk groups will be affected, and whether the severity of the disease will be similar to or higher than observed in mpox cases caused by MPXV clade IIb.

Although vaccines and antivirals used against MPXV clade II should work for MPXV clade I too, there is limited scientific data from real-world settings to confirm this.

Relevant new information about transmission modes, disease severity and the effectiveness of preventive and treatment methods might justify an update of this risk assessment.

ECDC contributors (in alphabetical order)

Mohammed Afzal, Luis Alves de Sousa, Erik Alm, Angela Ancona, Leonidas Alexakis, Xanthi Andrianou, Tamás Bakonyi, Jon Bilbatua, Olivier Cecchi, Orlando Cenciarelli, Silvia Funke, Céline Gossner, Konstantinos Koutentakis, Anastasia Pharris, Maryoli Veloso Fraigola.

External reviewers

Emerging Viral Diseases-Expert Laboratory Network (EVD-LabNet): Chantal Reusken, Harry Vennema (National Institute for Public Health and the Environment, the Netherlands), Klara Sondén (The Public Health Agency of Sweden).

Public Health Agency, Sweden: Erik Sturegård.

DG HERA: Experts from DG HERA were consulted and provided comments to this document.

WHO Regional Office for Europe: Kareena Hundal, Ioannis Karagiannis, Tran Minh Nhu Nguyen, Marc-Alain Widdowson.

Africa CDC: Kyeng Mercy.

All experts have submitted declarations of interest. A review of these declarations did not reveal any conflict of interest except for two reviewers for which mitigations measures were put in place, i.e. disregarding comments related to a specific product and/or area of interest.

Disclaimer

ECDC issues this risk assessment document based on an internal decision and in accordance with Article 10 of Decision No 1082/13/EC and Article 7(1) of Regulation (EC) No 851/2004 establishing a European centre for disease prevention and control (ECDC). In the framework of ECDC's mandate, the specific purpose of an ECDC risk assessment is to present different options on a certain matter. The responsibility on the choice of which option to pursue and which actions to take, including the adoption of mandatory rules or guidelines, lies exclusively with the EU/EEA Member States. In its activities, ECDC strives to ensure its independence, high scientific quality, transparency and efficiency.

This report was written with the coordination and assistance of an internal response team at the European Centre for Disease Prevention and Control. All data published in this risk assessment are correct to the best of our knowledge at the time of publication. Maps and figures published do not represent a statement on the part of ECDC or its partners on the legal or border status of the countries and territories shown.

References

1. Vakaniaki EH, Kacita C, Kinganda-Lusamaki E, O'Toole Á, Wawina-Bokalanga T, Mukadi-Bamuleka D, et al. Sustained Human Outbreak of a New MPXV Clade I Lineage in the Eastern Democratic Republic of the Congo. Nature Medicine. 2024:1-11. Available at: https://www.nature.com/articles/s41591-024-03130-3
2. Likos AM, Sammons SA, Olson VA, Frace AM, Li Y, Olsen-Rasmussen M, et al. A tale of two clades: monkeypox viruses. Journal of General Virology. 2005;86(10):2661-72. Available at: https://www.microbiologyresearch.org/content/journal/jgv/10.1099/vir.0.81215-0
3. Nextstrain.org. Genomic epidemiology of mpox viruses across clades. 2024. Available at: https://nextstrain.org/mpox/all-clades
4. Van Dijck C, Hoff NA, Mbala-Kingebeni P, Low N, Cevik M, Rimoin AW, et al. Emergence of mpox in the post-smallpox era-a narrative review on mpox epidemiology. Clinical Microbiology and Infection. 2023;29(12):1487-92. Available at: https://www.sciencedirect.com/science/article/pii/S1198743X23003890
5. Bunge EM, Hoet B, Chen L, Lienert F, Weidenthaler H, Baer LR, et al. The changing epidemiology of human monkeypox—A potential threat? A systematic review. PLoS Neglected Tropical Diseases. 2022;16(2):e0010141. Available at: https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0010141
6. World Health Organization (WHO). Mpox (monkeypox) - Democratic Republic of the Congo. Geneva: WHO; 2023. Available at: https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON493
7. World Health Organization (WHO). 2022-24 Mpox (Monkeypox) Outbreak: Global Trends. Geneva: WHO; 2024. Available at: https://worldhealthorg.shinyapps.io/mpx_global/
8. Africa Centres for Disease Control and Prevention (AfricaCDC). Africa CDC Epidemic Intelligence Weekly Report, 9 August 2024. Addis Ababa: AfricaCDC; 2024. Available at: https://africacdc.org/download/africa-cdc-weekly-event-based-surveillance-report-august-2024/
9. Africa Centres for Disease Control and Prevention (AfricaCDC). Mpox Situation in Africa. Addis Ababa: AfricaCDC; 2024. Available at: https://africacdc.org/disease-outbreak/mpox-situation-in-africa/
10. World Health Organization (WHO). Multi-country outbreak of mpox, External situation report#35- 12 August 2024. Geneva: WHO; 2024. Available at: https://www.who.int/publications/m/item/multi-country-outbreak-of-mpox--external-situation-report-35--12-august-2024
11. Radio Tamazuj. South Sudan detects two suspected monkeypox cases in Aweil. 2024. Available at: https://www.radiotamazuj.org/en/news/article/south-sudan-detects-two-suspected-monkeypox-cases-in-aweil
12. The Ministry of Health - Kenya. Ministry of Health Confirms Mpox Outbreak at Taita-Taveta Border Point. Facebook. 31 July 2024, 05:21. Available at: https://www.facebook.com/MinstryofHealthKE/posts/pfbid023nGb8hu34UHAoyzRhNfzZcRd33Be2TSFF8ee9MUmmwhEKMCj3cxZxgw99p4q8P3Ml
13. World Health Organization (WHO). WHO Director-General's opening remarks at the media briefing – 7 August 2024. Geneva: WHO; 2024. Available at: https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing---7-august-2024
14. World Health Organization (WHO). African region faces an unprecedent surge in mpox cases. Geneva: WHO; 2024. Available at: https://www.afro.who.int/news/african-region-faces-unprecedent-surge-mpox-cases
15. Uganda Medical Association Central Branch. Uganda reports an outbreak of the Mpox virus. Let's act swiftly to contain its spread! X. 5 August 2024, 13.36. Available at: https://x.com/UMACentralb_Off/status/1820423714338488477
16. Masirika LM, Nieuwenhuijse DF, Ndishimye P, Udahemuka JC, Steeven BK, Gisèle NB, et al. Mapping the distribution and describing the first cases from an ongoing outbreak of a New Strain of mpox in South Kivu, Eastern Democratic Republic of Congo between September 2023 to April 2024. medRxiv [Preprint]. 2024. DOI: 10.1101/2024.05.10.24307057. Available at: https://www.medrxiv.org/content/10.1101/2024.05.10.24307057v1
17. World Health Organization (WHO). Mpox - Democratic Republic of the Congo. Geneva: WHO; 2024. Available at: https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON522
18. Africa Centres for Disease Control and Prevention (AfricaCDC). Africa CDC Epidemic Intelligence Weekly Report, 2 August 2024. Addis Ababa: AfricaCDC; 2024. Available at: https://africacdc.org/download/africa-cdc-weekly-event-based-surveillance-report-august-2024/
19. Ministère de la Santé et de la Population - RCA. Épidémie de Monkeypox à Bangui!!! Facebook. 29 July 2024, 04:32. Available at:

https://www.facebook.com/RCAMSP/posts/pfbid02J8Z9hehMvvQMz89YFAwYv7JQ17YDLVpbwF7XG4wceQWAiWzhMKXRZUgkNoqnLazRl

20. National Department of Health - South Africa. Health Department calls for vigilance as mpox cases re-emerge. Cape Town: National Department of Health; 2024. Available at: https://www.nicd.ac.za/wp-content/uploads/2024/08/Health-Department-calls-for-vigilance-as-mpox-cases-re-emerge.pdf
21. National Department of Health - South Africa. Update on mpox outbreak and response efforts. Cape Town: National Department of Health; 2024. Available at: https://www.nicd.ac.za/wp-content/uploads/2024/06/Update-on-mpox-outbreak-and-response-efforts.pdf
22. Ministère de la Santé et de l'Hygiène Publique. Variole du Singe/ 6 cas détectés en Côte d'Ivoire. Facebook. 1 August 2024, 12:38. Available at: https://www.facebook.com/mshpcmu/posts/pfbid0Yq498V6NTA6Lw8j9kchhY9v2opSvpEiK9UDuZmLvGSa59o84Ekih99eHTnmPs9Bml
23. Africa Centres for Disease Control and Prevention (AfricaCDC). Africa CDC Declares Mpox A Public Health Emergency of Continental Security, Mobilizing Resources Across the Continent. Addis Ababa: AfricaCDC; 2024. Available at: https://africacdc.org/news-item/africa-cdc-declares-mpox-a-public-health-emergency-of-continental-security-mobilizing-resources-across-the-continent/
24. World Health Organization (WHO). WHO Director-General declares mpox outbreak a public health emergency of international concern. Geneva: WHO; 2024. Available at: https://www.who.int/news/item/14-08-2024-who-director-general-declares-mpox-outbreak-a-public-health-emergency-of-international-concern
25. Global Initiative on Sharing All Influenza Data (GISAID). EpiPox. Munich: Freunde von GISAID e.V.; 2024. Available at: https://gisaid.org/
26. National Library of Medicine. GenBank Overview. Bethesda: National Institutes of Health (NIH); 2024. Available at: https://www.ncbi.nlm.nih.gov/genbank/
27. European Centre for Disease Prevention and Control (ECDC). Operational tool on rapid risk assessment methodology - ECDC 2019. Stockholm: ECDC; 2019. Available at: https://www.ecdc.europa.eu/en/publications-data/operational-tool-rapid-risk-assessment-methodology-ecdc-2019
28. European Centre for Disease Prevention and Control (ECDC). Factsheet for health professionals on mpox (monkeypox). Stockholm: ECDC; 2023. Available at: https://www.ecdc.europa.eu/en/all-topics-z/monkeypox/factsheet-health-professionals
29. Maksyutov RA, Gavrilova EV, Shchelkunov SN. Species-specific differentiation of variola, monkeypox, and varicella-zoster viruses by multiplex real-time PCR assay. Journal of Virological Methods. 2016;236:215-20. Available at: https://www.sciencedirect.com/science/article/pii/S0166093416300672
30. Li Y, Zhao H, Wilkins K, Hughes C, Damon IK. Real-time PCR assays for the specific detection of monkeypox virus West African and Congo Basin strain DNA. Journal of Virological Methods. 2010;169(1):223-7. Available at: https://www.sciencedirect.com/science/article/pii/S0166093410002545
31. Li Y, Olson VA, Laue T, Laker MT, Damon IK. Detection of monkeypox virus with real-time PCR assays. Journal of Clinical Virology. 2006;36(3):194-203. Available at: https://www.sciencedirect.com/science/article/pii/S1386653206001223
32. Schroeder K, Nitsche A. Multicolour, multiplex real-time PCR assay for the detection of human-pathogenic poxviruses. Molecular and Cellular Probes. 2010;24(2):110-3. Available at: https://www.sciencedirect.com/science/article/pii/S0890850809000772
33. Luciani L, Inchauste L, Ferraris O, Charrel R, Nougairède A, Piorkowski G, et al. A novel and sensitive real-time PCR system for universal detection of poxviruses. Scientific Reports. 2021;11(1):1798. Available at: https://www.nature.com/articles/s41598-021-81376-4
34. Li D, Wilkins K, McCollum AM, Osadebe L, Kabamba J, Nguete B, et al. Evaluation of the GeneXpert for human monkeypox diagnosis. The American Journal of Tropical Medicine and Hygiene. 2017;96(2):405. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5303045/
35. European Centre for Disease Prevention and Control (ECDC). Directory of EVD-LabNet. Stockholm: ECDC; 2024. Available at: https://qap.ecdc.europa.eu/public/extensions/EVD_LabNet/EVD_LabNet.html#main-tab
36. Masirika LM, Udahemuka JC, Schuele L, Ndishimye P, Otani S, Mbiribindi JB, et al. Ongoing mpox outbreak in Kamituga, South Kivu province, associated with monkeypox virus of a novel Clade I sub-lineage, Democratic Republic of the Congo, 2024. Euro Surveill. 2024;29(11):2400106. Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2024.29.11.2400106
37. Masirika LM, Udaheuka J, Schuele L, Ndishimye P, Otani S, Mbiribindi JB, et al. Novel Clade I genome sequences from the ongoing mpox virus outbreak of Kamituga in South Kivu province, Democratic Republic of Congo.

Virological [Preprint]. 2024. Available at: https://virological.org/t/novel-clade-i-genome-sequences-from-the-ongoing-mpox-virus-outbreak-of-kamituga-in-south-kivu-province-democratic-republic-of-congo/956

38. Schuele L, Masirika LM, Udahemuka JC, Siangoli FB, Mbiribindi JB, Ndishimye P, et al. Real-time PCR assay to detect the novel Clade Ib monkeypox virus, September 2023 to May 2024. Euro Surveill. 2024;29(32):2400486. Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2024.29.32.2400486

39. European Medicines Agency (EMA). Imvanex -Smallpox vaccine (Live Modified Vaccinia Virus Ankara). Amsterdam: EMA; 2022. Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/imvanex

40. European Medicines Agency (EMA). EMA recommends approval of Imvanex for the prevention of monkeypox disease. Amsterdam: EMA; 2022. Available at: https://www.ema.europa.eu/en/news/ema-recommends-approval-imvanex-prevention-monkeypox-disease

41. Pischel L, Martini BA, Yu N, Cacesse D, Tracy M, Kharbanda K, et al. Vaccine effectiveness of 3rd generation mpox vaccines against mpox and disease severity: A systematic review and meta-analysis. Vaccine [Preprint]. 2024. DOI: 10.1016/j.vaccine.2024.06.021. Available at: https://www.sciencedirect.com/science/article/pii/S0264410X24006947

42. Guagliardo SAJ, Kracalik I, Carter RJ, Braden C, Free R, Hamal M, et al. Monkeypox Virus Infections After 2 Preexposure Doses of JYNNEOS Vaccine - United States, May 2022 - May 2024. Morbidity and Mortality Weekly Report. 2024;73(20):460-6. Available at: https://www.cdc.gov/mmwr/volumes/73/wr/mm7320a3.htm

43. Palich R, Jedrzejewski T, Schneider L, Qatib N, Orriere T, Gosset D, et al. High uptake of vaccination against mpox in men who have sex with men (MSM) on HIV pre-exposure prophylaxis (PrEP) in Paris, France. Sexually Transmitted Infections. 2023;99(8):552-3. Available at: https://sti.bmj.com/content/99/8/552

44. Svartstein AW, Knudsen AD, Heidari SL, Heftdal LD, Gelpi M, Benfield T, et al. Mpox Incidence and Vaccine Uptake in Men Who Have Sex with Men and Are Living with HIV in Denmark. Vaccines (Basel). 2023;11(7):1167. Available at: https://www.mdpi.com/2076-393X/11/7/1167

45. Dukers-Muijrers NH, Evers Y, Widdershoven V, Davidovich U, Adam PC, Op de Coul EL, et al. Mpox vaccination willingness, determinants, and communication needs in gay, bisexual, and other men who have sex with men, in the context of limited vaccine availability in the Netherlands (Dutch Mpox-survey). Frontiers in Public Health. 2023;10:1058807. Available at: https://www.frontiersin.org/journals/public-health/articles/10.3389/fpubh.2022.1058807/full

46. Reyes-Urueña J, D'Ambrosio A, Croci R, Bluemel B, Cenciarelli O, Pharris A, et al. High monkeypox vaccine acceptance among male users of smartphone-based online gay-dating apps in Europe, 30 July to 12 August 2022. Euro Surveill. 2022;27(42):2200757. Available at: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2022.27.42.2200757

47. Jonas K. PROTECT study www.protect-study.eu. Message to: Pharris A. 8 August 2024.

48. Schmidt AJ. Unpublished data. Message to: Pharris A. 8 August 2024.

49. Sulaiman SK, Isma'il Tsiga-Ahmed F, Musa MS, Makama BT, Sulaiman AK, Abdulaziz TB. Global prevalence and correlates of mpox vaccine acceptance and uptake: a systematic review and meta-analysis. Communications Medicine. 2024;4(1):136. Available at: https://www.nature.com/articles/s43856-024-00564-1

50. Centers for Disease Control and Prevention (CDC). Mpox Caused by Human-to-Human Transmission of Monkeypox Virus in the Democratic Republic of the Congo with Spread to Neighboring Countries. Atlanta: CDC; 2024. Available at: https://emergency.cdc.gov/han/2024/han00513.asp

51. European Centre for Disease Prevention and Control (ECDC). Mpox (Monkeypox). Stockholm: ECDC; 2024. Available at: https://www.ecdc.europa.eu/en/mpox-monkeypox

52. European Commission (EC). European Commission coordinates procurement and donation of 215,000 vaccine doses from Bavarian Nordic to support Africa CDC in addressing the Mpox outbreak in affected countries in Africa. Brussels: EC; 2024. Available at: https://ec.europa.eu/commission/presscorner/detail/en/ip_24_4244