RAPID RISK ASSESSMENT

Monkeypox multi-country outbreak

23 May 2022

Key messages

Cases of monkeypox (MPX) acquired in the EU have recently been reported in nine EU Member States (Austria, Belgium, France, Germany, Italy, Portugal, Spain, Sweden, and the Netherlands).

Monkeypox (MPX) does not spread easily between people. Human-to-human transmission occurs through close contact with infectious material from skin lesions of an infected person, through respiratory droplets in prolonged face-to-face contact, and through fomites. The predominance, in the current outbreak, of diagnosed human MPX cases among men having sex with men (MSM), and the nature of the presenting lesions in some cases, suggest transmission occurred during sexual intercourse.

Based on ECDC's epidemiological assessment, the likelihood of MPX spreading in persons having multiple sexual partners in the EU/EEA is considered high. Although most cases in current outbreaks have presented with mild disease symptoms, monkeypox virus (MPXV) may cause severe disease in certain population groups (young children, pregnant women, immunosuppressed persons). However, the likelihood of cases with severe morbidity cannot be accurately estimated yet. The overall risk is assessed as moderate for persons having multiple sexual partners (including some groups of MSM) and low for the broader population.

Treatment is mainly symptomatic and supportive, including prevention and treatment of secondary bacterial infections. Smallpox vaccine can be considered for post-exposure prophylaxis of close contacts at increased risk for severe disease, however careful benefit/risk assessment should be performed for the exposed individual. Important information on the use of currently available smallpox vaccines is missing for groups at increased risk for severe disease. In addition, antivirals are potential treatment options for severe cases.

EU/EEA countries should focus on prompt identification, management, contact tracing and reporting of new MPX cases. Countries should update their contact tracing mechanisms, their diagnostic capacity for orthopoxviruses and review the availability of smallpox vaccines, antivirals and personal protective equipment (PPE) for health professionals.

An interim case definition is proposed for case reporting. Guidance for the management of MPX cases and close contacts is also included. Cases should remain isolated until their rash heals completely, avoiding contact with immunosuppressed persons and pets. Abstaining from sexual activity and close physical contact is also advised until the rash heals. Most cases can remain at home with supportive care.

Close contacts of MPX cases should self-monitor for the development of symptoms up to 21 days from the last exposure to a case.

Healthcare workers should wear appropriate PPE (gloves, water-resistant gown, FFP2 respirator) when screening suspected cases or caring for a MPX case. Laboratory personnel should also take precautions to avoid occupational exposure.

Suggested citation: European Centre for Disease Prevention and Control. Monkeypox multi-country outbreak – 23 May 2022. ECDC: Stockholm; 2022.

Close contacts of a MPX case should be deferred from blood, organ or bone marrow donations for a minimum of 21 days from the last day of exposure.

Proactive risk communication and multiple community engagement activities should be carried out to increase awareness, provide updates and guidance to those at increased risk and the wider public. Risk communication messages should stress that MPXV is spread through close contact between people, especially in the same household, potentially including the sexual route. A balance should be kept between informing those most at risk but also communicating that the virus does not spread easily between people the risk to the broader population is low.

There is a potential risk of human-to-animal transmission in Europe, therefore close intersectoral collaboration between human and veterinary public health authorities working from a 'One Health' perspective is needed to manage exposed pets and prevent the disease from being transmitted in wildlife. EFSA is not aware to date of any reports on infections in animals (pets or wild animals) in the EU.

Several unknowns still exist regarding this outbreak and ECDC will continue to monitor developments closely and update the risk assessment as new data and information become available.

Event background

On 7 May 2022, the United Kingdom (UK) reported an imported case of monkeypox (MPX) in a person travelling from Nigeria. The case reported developing a rash-like illness on 29 April 2022 and travelled from Lagos to London on 3-4 May. The diagnosis was confirmed by monkeypox virus (MPXV) PCR on a vesicular swab on 6 May by the UK Health Security Agency (UKHSA) Rare and Imported Pathogens Laboratory.

On 13 May 2022, the UK reported two further cases of MPX who are part of the same family and not linked to the single imported case from Nigeria which was notified on 7 May. The cases were confirmed by PCR testing on vesicle swabs. A third family member had previously developed a rash but recovered fully. None of the individuals in this cluster had travelled or had contact with anyone with a relevant travel history [1].

On 15 May 2022, the UK reported four additional cases of MPX, confirmed by PCR. None of these cases have known epidemiological links to the imported case from Nigeria (notified on 7 May) or to the family cluster (notified on 13 May). The four cases were men who have sex with men (MSM) and presented with a vesicular rash-like illness. They were identified through attendance at genitourinary medicine (GUM) clinics. The cases are being managed in high consequence infectious diseases units in the UK [1].

On 18 May 2022, two additional cases (also MSM) were reported, one in London and one in the South-East of England[1].

On 20 May 2022, 11 additional cases were reported by the UKHSA, bring the total number of MPX cases confirmed in England to 20 [1]. All cases reported in the UK have been confirmed as caused by the MPXV West African clade.

Starting from the 18 May, multiple EU/EEA Member States reported additional suspected or confirmed cases:

- On 18 May, **Portugal** reported 14 cases of MPXV confirmed by real-time PCR in the Lisbon and Tagus River Valley Region. All cases were men with a clinical presentation of rash (some ulcerative), fever, myalgia and asthenia. None of the cases needed hospitalisation [2]. On 20 May, nine additional confirmed cases were reported, bringing the total number of confirmed cases to 23. In two cases, the west African clade was identified.
- On 19 May, **Spain** reported seven confirmed and 23 suspected cases of MPX, all among men. On 20 May, 16 additional confirmed cases were reported [3]. On 22 May, seven more cases were confirmed, with 39 new suspected cases under investigation [4].
- On 19 May, **Belgium** reported a confirmed case in a man with travel history to Lisbon, Portugal. His partner developed similar symptoms and was confirmed on the 20 May. As of 22 May, a total of four confirmed cases had been reported [5,6].
- On 19 May, **Germany** confirmed its first case in a man with travel history to Spain and Portugal. On 20 May, two more confirmed cases were reported. [7].
- On 20 May, **France** reported its first confirmed case in a man with no travel history, with three additional cases under investigation [8].
- On 20 May, **Italy** reported one confirmed case of MPX in a man who required hospitalisation and had travel history to Spain. On 21 May, two further confirmed cases were reported [9].
- On 18 May, **Sweden** reported a confirmed case in a man [10]
- On 20 May, the **Netherlands** reported one confirmed case, a man with travel history to Belgium [11].
- On 22 May, **Austria** reported its first confirmed case [12].

As of 23 May 2022, 67 confirmed cases had been reported in nine EU/EEA Member States and at least an additional 42 suspected cases were under investigation.

Cases have also been reported outside Europe: on 18 May 2022, Canada reported two confirmed and 20 suspected cases who were seen at sexually transmitted infection(STI) clinics, all men and currently undergoing laboratory testing in Montreal, Quebec[13]; one confirmed case in Boston, United States, in an adult male with recent travel history to Canada [14] and one probable case in New York City [15]. On 19 May 2022, Australia reported two confirmed cases, one was a man with travel history to the UK [16]. On 20 May 2022, Israel reported a confirmed case and additional suspected cases [17]. On 22 May, Switzerland reported a confirmed case with travel history to Europe [18].

Figure 1. Geographical distribution of confirmed cases of MPX in EU/EEA countries, as of 23 May 2022 (11:00)

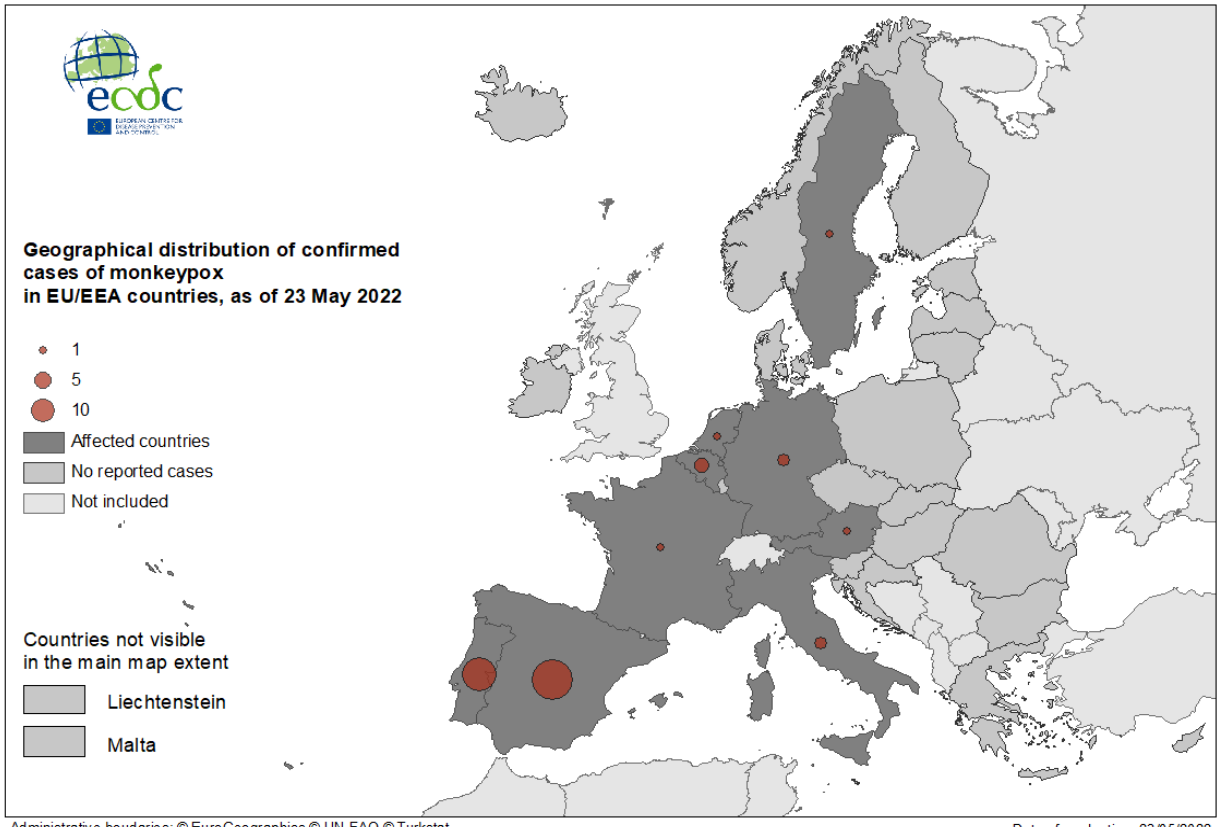
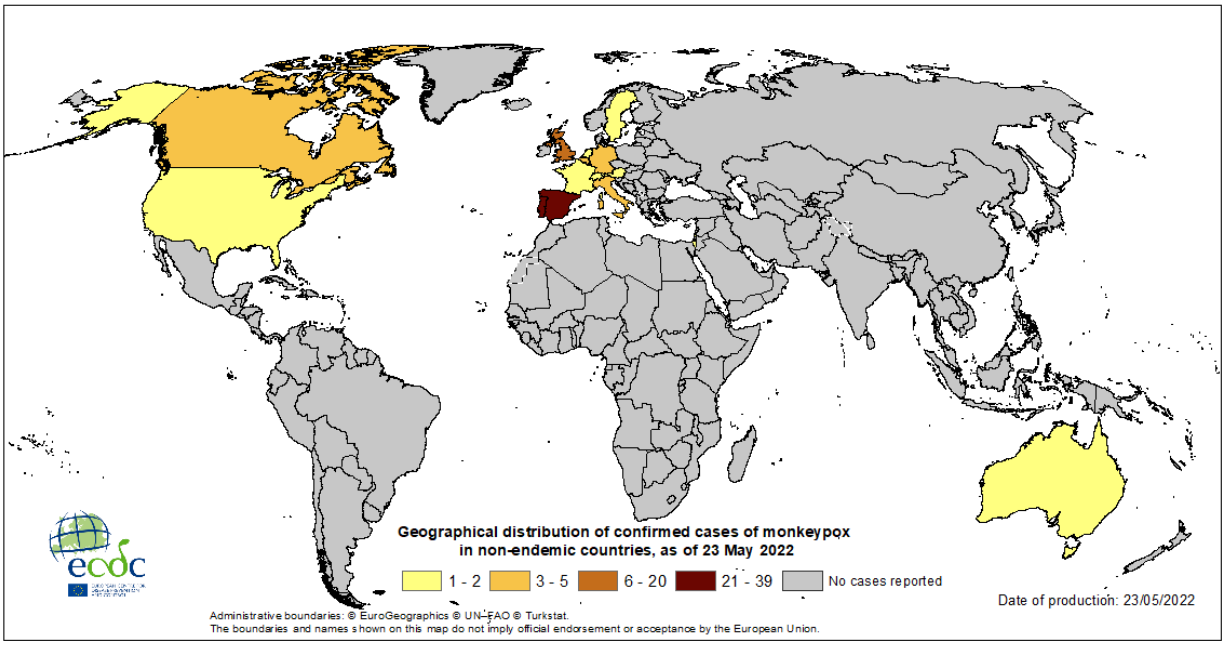


Figure 2. Geographical distribution of confirmed cases of monkeypox in non-endemic countries, as of 23 May 2022 (11:00)



Situation in west and central Africa in 2022

Generally, outbreaks of MPX continue to be reported in countries from west and central Africa [19]. Cameroon reported an outbreak of MPX in December 2021 and, as of 17 February 2022, three confirmed and 25 suspected cases have been reported, including two deaths. Cases have been reported from countries in central, north-western and south-western regions of the continent. Cases of MPX are sporadically reported in Cameroon, with more than half of the geographical regions in Africa reporting at least one case between 2020 and 2022.

The Central African Republic (CAR) reported six confirmed cases of MPX including two deaths on 14 March 2022.

Between 1 January and 17 April 2022, 1 152 suspected cases of MPX including 55 deaths (case-fatality rate of 4.8%) were reported in 54 health zones in 14 provinces of the Democratic Republic of the Congo (DRC). In the equivalent 2021 time period, 138 suspected cases and 14 deaths were reported (case-fatality rate of 10.1%). According to studies, the MPXV circulating in the DRC and CAR belong to the more virulent Congo Basin (CB) clade of the virus.

Nigeria reported 46 suspected (of which 15 confirmed) cases of MPX between 1 January and 30 April 2022. Between 2017-2022 Nigeria reported 241 confirmed cases (range 8-88 per year) including eight deaths (case-fatality ratio, CFR 3.3%) [19,20].

Disease background

Disease characteristics

Monkeypox (MPX) is a zoonotic disease and is currently the most prevalent orthopoxvirus infection in humans after the eradication of smallpox and the cessation of universal smallpox vaccination [21-23]. Human MPX cases are increasingly reported in several African countries after its first identification as a human pathogen in the DRC in 1970, due to a combination of factors including both increased exposure (deforestation, conflict and displacement), as well as improved surveillance and laboratory capacity in the African region [24-26].

In endemic areas, MPXV is probably maintained in nature through circulation among a number of mammals, including squirrels, Gambian pouched rats *(Cricetomys gambianus*), striped mice, dormice and primates [25], with occasional spill-over events to humans [27-30]. In endemic areas, MPXV is transmitted to humans through a bite or direct contact with an infected animal's blood, meat, bodily fluids or cutaneous/mucosal lesions [21].

Sequencing has identified two distinct clades of MPXV [31]. The West African clade is known to occur from western Cameroon to Sierra Leone and carries a <1% CFR, whereas the Congo Basin clade has been detected from central and southern Cameroon to the DRC and is considered more virulent with a CFR >10% [32,33].

The largest West African clade MPX outbreak identified to date was in Nigeria in 2017, with 146 suspected and 42 confirmed cases [20,34]. In 2018, three unlinked travel-related MPX cases were identified in Israel, the UK, and Singapore [35-37]. These exportations represent the first time that a human host was documented to transfer MPXV from the African continent. However, MPX outbreaks in animals in laboratories and zoos, with no clearly identified source of infection, have been reported outside the African continent [38-40].

In 2003, the US Centers for Disease Control (CDC) reported a total of 81 human MPX cases after close contact with pet mammals, predominantly rodents. No human-to-human transmission was identified, and none resulted in death. The cases were connected to the importation of small mammals from Ghana to Texas as the probable source of introduction of the virus into the US. The spread of the virus between federal states was connected to infected pet prairie dogs that were-housed with rodents of African origin [41].

Monkeypox does not spread easily between people. Between humans, the virus can be transmitted by respiratory droplets during direct and prolonged face-to-face contact. In addition, monkeypox virus can be transmitted by direct contact with body fluids of an infected person, contact of mucosa or non-intact skin with open rash lesions or with virus-contaminated objects, such as bedding or clothing [22,25]. Sexual transmission of monkeypox has been described, but infrequently, in the literature. Ogoima et al. [42], in reporting the 2017 human MPX outbreak in Nigeria, hypothesised that sexual transmission was a plausible route of infection as it involved close skin-to-skin contact during sexual intercourse or transmission via genital secretions.

Infection of sexual partners, both female and male, has been previously reported for vaccinia virus, another virus of the *Orthopoxvirus* genus, post smallpox vaccination [43,44]. Vaginal lesions occurred in the female partner of a recently vaccinated military man who removed bandages covering his vaccination site, four days after unprotected sexual intercourse, preceded by digital vaginal contact [43]. A painful perianal rash and a lesion on the upper lip were reported by a male patient ten days after sexual intercourse with a recently vaccinated man who did not cover his vaccination site [45]. Further transmission from this patient, while he was experiencing perianal rash, occurred in a male sexual contact who experienced general symptoms and papular lesions on his penis two days after sexual intercourse.

The incubation period for MPX is usually 6 to 13 days but can range from 5 to 21 days [25]. The illness typically lasts for two to four weeks. Disease usually begins with fever, myalgia, fatigue and headache [36]. Within three days from the onset of the prodrome symptoms, a centrifugal maculopapular rash starts from the site of primary infection and rapidly spreads to other parts of the body. Palms and soles are involved in cases of the disseminated rash, which is a characteristic of the disease. The lesions progress, usually within 12 days, simultaneously from the stage of macules to papules, vesicles, pustules, crusts and scabs before falling off [46]. The lesions may be centrally depressed and can be extremely itchy and secondary bacterial infection may occur if scratching occurs. Lesions on oral or ophthalmic mucosa (enanthem) may also be present. Prior to and concomitant with the rash, lymphadenopathy is observed in many patients, which is usually not observed in smallpox or varicella [22,47]. It should be noted that the clinical manifestations in travel-related cases detected in western countries were usually mild, sometimes with very few lesions. The onset of the rash is considered the start of the infectious period; however, it is believed that persons with prodrome symptoms can also transmit MPXV [48].

The majority of human MPX cases experience mild to moderate symptoms. Complications in endemic countries include encephalitis, secondary skin bacterial infections, dehydration, conjunctivitis, keratitis, and pneumonia. The case-fatality rate of MPX ranges from 0% to 11% in outbreaks in endemic areas with mortality mostly affecting young children [25]. Little information is available on MPX in immunocompromised patients. In the 2017 Nigeria outbreak, patients with concurrent HIV-infection had more severe morbidity with more skin lesions and associated genital ulcers as compared with HIV-negative individuals. No deaths were reported among HIV-positive patients [42]. Major disease sequelae are usually disfiguring scars and permanent corneal lesions [47].

The route of infection (invasive, such as animal bite, vs. exposure to fomites) plays a role, with invasive modes of exposure causing more severe disease and shorter incubation period [49].

Considering varicella as the most relevant differential diagnosis, electron microscopy was traditionally used in the past to distinguish herpesviruses from orthopoxviruses. Currently, MPXV real-time polymerase chain reaction (Real Time-PCR) on suspected skin lesions is used. Scabs, swabs and aspirated lesion fluid should be preferably used for PCR over blood due to limited duration of viremia. These samples can be transported at room temperature and without transport media; blood and serum for serological tests can be transported at room temperature, however, tissue biopsies should be shipped frozen on dry ice. Formalin-fixed samples can be sent at room temperature [50]. Results from scabs, swabs and aspirated lesion fluid specimens show the best correlation with both infectivity and the clinical course of infection. Recent Real Time-PCR approaches can also discriminate the two MPXV clades described above. Serology has limited value due to the immunological cross-reactivity between human-pathogenic orthopoxviruses, but it is used to monitor antibody response in vaccinated individuals. However, for contact investigations, IgM and IgG detection is available in some laboratories. Immunohistochemistry can potentially be used to identify antigens in biopsy samples.

Treatment is primarily symptomatic and supportive (alleviation of fever and pruritus, hydration), including prevention and treatment of secondary bacterial infections. Antivirals tecovirimat, brincidofovir and cidofovir are potential options for severe cases [25]. Only Tecovirimat has market authorisation in the EU for the treatment of orthopoxvirus infection, including MPX. Limited data on efficacy and safety exist currently, while clinical studies are ongoing in Africa [51].

Previous vaccination against smallpox can confer cross-protection against monkeypox, which was estimated from older studies to be as high as 85% [22]. The protective effect of smallpox vaccination wanes with time, although serosurveys indicate that it can last more than20 years. However, it is believed that despite the waning effect smallpox vaccine confers, lifelong protection against severe disease can occur due to memory B and T cells therefore some degree of protection should be expected in the population of adults in the EU/EEA currently over 50 years of age [52]. No vaccine is currently authorised in the EU against MPX, but early post-exposure vaccination (within four days of exposure to a MPX case) with smallpox vaccine may prevent the disease or make its course less severe [53,54]. A third generation, non-replicating smallpox vaccine (Imvanex™ - Modified Vaccinia Ankara) was authorised under exceptional circumstances by EMA in 2013 for use against smallpox [55]. This vaccine has indication for use in patients with HIV infection for smallpox, but currently has no authorisation for use against MPX [56]. Earlier generation smallpox vaccines have been used for years (Dryvax™ and ACAM2000™), however they are associated with severe side effects, including cardiac side effects, and they are no longer licensed in the EU.

Monkeypox virus is not considered a biological agent of concern for biosecurity according to the U.S. CDC list of bioterrorism agents [57], while it is considered an 'agent with high threat for deliberate release' using the matrix developed by the EU task force on Bioterrorism (BICHAT) [58]. Although the case-fatality rate of the pathogen is low, its relative environmental stability and persistence (see below) and transmission pathways, in addition to the lack of immunity in the population, the limited availability of effective treatments and vaccination, make it an agent which could represent a biological threat in case of accidental spill or intentional release.

ECDC risk assessment for the EU/EEA

This assessment is based on evidence available to ECDC at the time of publication. It follows the ECDC rapid risk assessment methodology, where the overall risk is determined by a combination of the probability of infection and the impact of the disease on the affected population [59]. ECDC will keep monitoring the event and will reassess the risk depending on its evolution and the implemented response measures.

What is the risk of further spread of monkeypox in EU/EEA countries?

Risk in persons with multiple sexual partners, including some MSM

Human-to-human transmission of MPX occurs through close contact with infectious material from skin lesions of an infected person, and also through respiratory droplets in prolonged face-to-face contact and through fomites. The predominance, in the current outbreak, of diagnosed human MPX cases among MSM, and the nature of the presenting lesions in some cases, suggest that transmission occurred during sexual intercourse. Transmission through intact skin contact is less likely but cannot be excluded. Although sequencing data are not yet available to indicate that the outbreak is the result of one introduction, the cases of MPX within parts of the MSM community whose sexual networks[1] are inter-connected could be considered a possible source of introduction.

Particular sexual practices (e.g. having multiple casual sexual contacts and/or multiple sexual partners, attending chemsex parties) that may be present within some parts of the MSM community could further facilitate the transmission of monkeypox. Outbreaks of other sexually transmitted infections among MSM can be linked to travel abroad and to social and mass gathering events (e.g., pride events) [60-62]. Several such events are taking place in Europe over the spring and summer months, which can contribute to further accelerate the transmission of MPXV. In addition, smallpox vaccination, which confers cross-protection, has been discontinued since the 1980s and only a small percentage of military and frontline health professionals have been vaccinated in recent years. Therefore, a large part of the population is vulnerable to MPXV. The probability of further spread of MPXV among persons with multiple sexual partners in interconnected sexual networks (including some groups of MSM) in EU/EEA countries and globally, in the coming months, is therefore assessed as high.

While most MPX cases reported thus far in this outbreak have been described as mild, the number of reported cases is too low to reliably estimate rates of severe morbidity and mortality, and a clear overview of the clinical presentations in the reported cases is currently lacking. Severity estimates in the literature exist from endemic countries and the 2003 USA outbreak. In Nigeria, the CFR is estimated at 3.3% for cases diagnosed between 2017-2022, however, it is a different health care and population setting, where the disease is endemic and is probably transmitted through different routes (e.g., more frequent contact with animals). In the 2003 outbreak in the USA, which was exclusively driven by contact with infected pets (rodents), five out of 34 confirmed cases (15%) were defined as severely ill, and no deaths were reported. Patients under 18 years of age did not develop severe illness more frequently, compared to older patients [63]. These severity estimates are probably biased upwards. Immunocompromised patients are believed to be more at risk for severe disease and the prevalence of HIV among MSM is higher than in the broader population [64]. However, most people living with human immunodeficiency virus (PLWHIV) in EU/EEA (range 67–87%) are receiving antiretroviral treatment, and are not severely immunocompromised [65]. Moreover, some treatment options are available for severe MPX cases. Therefore, the impact of MPX is assessed as low, which combined with the high probability of infection leads to an overall moderate risk for persons with multiple sexual partners.

It should be noted that the above-mentioned moderate risk may be higher for older people who have multiple sexual partners or people with untreated HIV infection. ECDC will reassess the risk as more information (including clinical presentation and outcomes) becomes available.

Risk for the broader population

Based on the evidence from the cases in this outbreak detected to date, overall, the probability of further spread of MPXV among the broader population in EU/EEA countries and globally in the coming months, is assessed as very low leading to an overall low risk for the general population. However, the individual risk for very young children, pregnant women, elderly or immunocompromised individuals among close contacts of MPX cases may be high due to the higher impact of the disease in these groups.

[1] Sexual networks are groups of people who are connected to one another sexually. The different behaviour of those within the group can, for example, affect how quickly STIs can spread through a network.

Risk for health professionals

Healthcare workers

Transmission to HCWs exposed to patients with MPX is possible, given the risk of transmission of other orthopoxviruses, such as smallpox, and has been reported in outbreaks in endemic countries [42,66]. In a study of 57 HCWs exposed to patients with MPX, including nursing staff, radiology technicians, emergency department staff and physicians, no case of infection was documented [67]. One HCW in this study had evidence of recent orthopoxvirus seroconversion but had also received smallpox vaccination four months before being exposed. In another outbreak report, monkeypox was transmitted to a HCW, whose only identified exposure was the changing of potentially contaminated bedding of a hospitalised patient with MPX [35].

The probability of MPX transmission to HCWs wearing appropriate personal protective equipment (a disposable gown, disposable gloves, disposable shoe or boots covers, respiratory protection (Filtering Face Piece (FFP) 2 respirator), and eye splash protection (goggles or visor) is very low, with the disease having an estimated low impact, leading to an overall low risk.

The risk to HCWs with unprotected close contact with MPX cases (e.g. contact face-to-face for prolonged time, contact with open lesions without gloves, intubation or other invasive medical procedure) is assessed as moderate, equivalent to that of a close contact.

Laboratory personnel

Occupational exposure and infection from orthopoxviruses have been occasionally reported among laboratory personnel handling virus-containing specimens [68,69].

The risk of occupational exposure is estimated to be low for trained laboratory personnel following appropriate biosafety procedures [70].

Unprotected occupational exposure in a laboratory, particularly involving spillage or aerosolisation with exposure of mucosa, carries high probability of infection and moderate risk of the disease (due to the direct exposure of mucosae to potentially significant quantity of virus). The risk for unprotected laboratory personnel is assessed as high.

Due to an expected higher impact, the risk may be higher for exposed HCWs and laboratory personnel who are older or immunocompromised.

Table 1. Summary of risk assessed for the different population categories

	Persons with multiple sexual partners, including some MSM	Broader population	Health professionals			
			HCWs		Laboratory personnel	
			Proper PPE	Unprotected exposure	Proper procedure and PPE	Unprotected exposure
Probability	High	Very low	Very low	High	Very low	High
Impact	Low	Low	Low	Low	Low	Moderate
Overall risk	**Moderate**	**Low**	**Low**	**Moderate**	**Low**	**High**

The risk may be higher for certain people in some of the above categories, particularly very young children, pregnant women, elderly, or immunocompromised persons.

Risk of transmission through substances of human origin

No cases of monkeypox virus transmission through substances of human origin have ever been documented. However, there are reported cases of virus transmission from mother to child during pregnancy [71], and animal studies show the presence of virus in blood, tissues and organs of infected animals.[72,73] Existence of viremia (i.e. blood specimens positive for viral DNA) has been shown. The duration of viremia is unclear [74], and there are no data on viraemia in asymptomatic patients (including during the incubation period). Even though information is limited, it is likely that monkeypox virus is transmissible through substances of human origin, but the overall risk for recipients in the EU/EEA is low.

Risk of spill-over event to animal species in Europe

Currently, little is known about the suitability of European peri-domestic (mammalian) animal species to serve as a host for monkeypox virus. However, rodents, and particularly species of the family of *Sciuridae* (squirrels) are likely to be suitable hosts, more so than humans (see disease background), and transmission from humans to (pet) animals is theoretically possible. Such a spill-over event could potentially lead to the virus establishing in European wildlife and the disease becoming an endemic zoonosis. In the US, there is no evidence that the virus became enzootic in wildlife, however, animal health authorities carried out systematic surveillance and an aggressive campaign for exposed animals during the 2003 outbreak [41]. The probability of this spill-over event is very low.

Options for response

The current priority for countries should be the identification, isolation and contact tracing of MPX cases. Prompt diagnosis will allow for isolation of cases and contribute to the control of this outbreak. Reporting newly identified cases to EpiPulse and the European Surveillance System (TESSy) is also important to allow for a better overview of the epidemiological situation and development of the outbreak. Reporting in TESSy will be implemented shortly by ECDC.

These priorities require significant preparedness and response activities including:

- The review and strengthening of laboratory diagnostic capacity for orthopoxviruses;
- The availability and stockpile of PPE for health professionals;
- The review of stockpiles of smallpox vaccines and the development of vaccination strategies;
- The review of availability of antiviral treatments for severe cases;
- The collaboration with animal health services for the management of exposed pets;
- Strong risk communication and engagement with the MSM communities, as well as the broader public.

Overall preparedness and response

Laboratory diagnostics and sequencing

Countries should review their in-house molecular diagnostic testing capacities and capabilities for orthopoxviruses and in particular for monkeypox virus (including surge capacity related to reagents, consumables and available trained staff). In case of limited experience in monkeypox testing, laboratories are encouraged to refer specimens for confirmatory testing. Countries not having national reference laboratory capacity should refer at least the first suspected case(s) for reference testing to another EU/EEA country. The European laboratory network for emerging viral diseases (EVD-LabNet) will facilitate the sharing of protocols and can facilitate confirmatory testing support through their network members. The European Virus Archives (EVAg) can provide positive control materials [75].

According to the EVD-LabNet Directory, based on self-reporting of the EVD-Lab members (as of May 2022), MPXV diagnosis is possible in 19 laboratories in 13 EU/EEA countries: Denmark, Finland, France (2), Germany (4), Greece, Hungary, Ireland, Italy (2), Portugal, Romania, Slovenia, Sweden, and the Netherlands (2) [76].

Sequencing of poxvirus DNA in samples can validate the specificity of the detection and assist in understanding transmission chains and patterns of spread, therefore sharing sequences is encouraged internationally. In addition, sequencing will allow detection of potential genomic and proteomic differences of MPXV in this outbreak. Member States who need diagnostic and/or sequencing support should contact EVD-LabNet (chantal.reusken@rivm.nl) and ECDC (ECDC.Microbiology@ecdc.europa.eu).

Currently, there is no commercial MPX virus assay on the European market. The GeneXpert platform (Cepheid Sunnyvale, CA, USA) has been used for diagnosis of MPX in DRC [77]. The multiplex assay includes a MPX-specific assay, orthopoxvirus generic assay, and an internal control. The methodology decreases manipulations of the samples, thereby also limiting opportunities for contamination.

Vaccination and antivirals

Availability of smallpox vaccine should be reviewed in EU/EEA countries as regards type, doses and authorisation status. As mentioned above (see Disease Background) smallpox vaccine can be used for post-exposure prophylaxis (PEP) of close contacts at increased risk for severe disease (see Management of MPX contacts). The smallpox vaccine, if administered within the first four days after exposure to a confirmed MPX case can have significant protective effect [22]. In addition, countries may consider prophylactic vaccination of certain health professionals responding to this outbreak. To date, the vast majority of cases have mild to moderate symptoms and are all recovering well. However, numbers are still low and the severity profile of the disease cannot be reliably estimated.

No smallpox vaccine is authorised for use against MPX in the EU, but the 3rd generation smallpox vaccine Imvanex™ (Modified Vaccine Ankara-MVA) has been authorised by EMA for the EU market against smallpox [78]. MVA has shown protection in primate models challenged with lethal doses of monkeypox virus [79]. Older generation smallpox vaccines have significant side effects and in addition, are no longer authorised and should not be used. Careful needs assessment should be carried out in each country to estimate the potential need of smallpox vaccine for the management of this outbreak and collaboration between the national drug authorities and EMA is needed to clarify the authorisation status of the MVA vaccine if it is to be used against MPX. However, it is important to note that efficacy data for this vaccine against MPX in humans are missing as well as safety data for the use of this vaccine in immunocompromised persons.

Considering the above and the limited supply of smallpox vaccine doses, National Immunization Technical Advisory Groups (NITAG) should develop specific guidance for the vaccination of close contacts of MPX cases. The use of smallpox vaccination for the purpose of pre-exposure prophylaxis in the exposed communities of MSM cannot be considered at this point, considering the limited supply of vaccine and most importantly the benefit/risk ratio of smallpox vaccination in this outbreak.

As regards antivirals used for the treatment of MPX, tecovirimat is the only antiviral drug with an indication for the treatment of orthopoxvirus infections, including MPX, authorised by EMA [51]. Brincidofovir is not authorised in the EU but has been authorised by FDA for treatment of MPX. However, their availability in the EU market is quite limited in the number of doses. Clinicians and infectious disease societies also need to provide guidance for the use of this medication and ideally, follow a common treatment protocol in order to provide valuable efficacy data. Health authorities should consider prioritisation of patient groups that could be offered treatment. Use of antivirals for post-exposure prophylaxis could be additionally investigated. Cidofovir is active *in vitro* for smallpox, but has a pronounced nephrotoxicity profile that makes it unsuitable as first choice treatment.

Personal Protective Equipment

As indicated above, human-to-human transmission of MPXV can occur via droplets in prolonged close contact and contact with the infectious lesion material [22,25]. Therefore, appropriate PPE is needed for all health professionals who will screen suspected cases, care for a MPX patients or handle contaminated material (clothes, bedlinen, etc.) or laboratory specimens (gowns, FFP2 respirators, goggles). Availability of sufficient stocks of PPE at healthcare facilities and at national levels should be monitored and ensured.

Exposure of pets

Public health authorities should work together with veterinary authorities to ensure capacity is in place for quarantining and testing of mammalian pet animals that have been exposed or are at risk of exposure (i.e. pets of a close contact of a MPX case) to MPXV. Rodent pets should ideally be isolated in monitored facilities, complying with respiratory isolation (e.g. a laboratory) and animal welfare conditions (e.g. government facilities, kennels or animal welfare organisations), and tested (by PCR) for exposure before quarantine ends. Euthanasia should only be a last resort reserved to situations where testing and/or isolation are not feasible. Other mammalian pet species could be isolated at home if animal welfare conditions allow it (e.g. availability of an enclosed outdoor space for dogs, regular veterinary checks to assess the health status, preventing access to visitors, preventing pets from leaving the home).

Surveillance and EU/EEA reporting

Monkeypox is currently not listed as a disease under surveillance [80] in the EU/EEA , nor is the virus notifiable in animals under Commission Implementing Regulation 2018/1882. Orthopoxvirus infection is a mandatory notifiable disease in some countries, and some have now made MPX notifiable as part of the response to this outbreak. The rapid evolution of the current outbreak involving multiple EU/EEA countries, the limited data available on disease severity and the previously unreported context of transmission among groups of MSM highlight the need for setting up a European surveillance system aiming to describe the epidemiology and evolution of the outbreak and to support control measures.

The following interim case definition is proposed:

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 1st March 2022

Probable case

(1) A person with an unexplained rash* on any part of their body

AND one or more other symptom(s) of monkeypox infection** with symptom onset since 1st March 2022

AND one of the following:

- has a positive laboratory test result on orthopoxvirus 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 generalised or localised maculopapular or vesiculopustular rash with centrifugal spread, with lesions showing umbilication or scabbing, lymphadenopathy and one or more other MPX-compatible symptoms**.

** 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 characterise the rash: 'unexplained localised or generalised maculopapular or vesiculopustular rash potentially with umbilication or scabbing'.*
***Fever (usually high >38.5°C), headache, back ache, fatigue, lymphadenopathy (localised or generalised).*

Patients who fulfil the criteria for probable cases should be tested with a monkeypox virus specific PCR assay or an orthopoxvirus specific PCR assay which is then confirmed through sequencing. If negative, these patients should be excluded.

ECDC in liaison with the World Health Organization (WHO) asks countries to report newly-identified cases in the line listing document in EpiPulse [access only to nominated users]. Reporting in TESSy will be implemented shortly by ECDC.

Management of cases

Newly identified cases of MPX should undergo a medical assessment for severity and risk factors (e.g. underlying conditions or medications affecting immune competence, untreated HIV infection etc.). Those at increased risk of severe disease from MPX may require hospitalisation and/or treatment with antivirals (see Overall preparedness and response section). People at increased risk for severe disease include infants and young children, pregnant women, elderly and severely immunocompromised persons. A common treatment protocol should be considered for patients treated in EU/EEA countries in order to provide much needed efficacy data. Tecovirimat also has the potential to cause resistance to pox viruses, therefore, careful monitoring of treated patients should be undertaken, particularly the immunosuppressed. Potential combination with brincidofovir can also be explored. The majority of MPX cases reported so far in this outbreak have been mild with localised disease and self-limiting symptoms. Therefore, hospitalisation is not necessary, unless the patient's clinical condition requires it. Patients can remain isolated at home with supportive care (analgesia, hydration). If isolation is not possible at home, then hospitalisation or other arrangement can be considered.

MPXV can be transmitted to anyone, regardless of sexual orientation or gender identity, through contact with body fluids, monkeypox sores, or shared items. Therefore, cases should be instructed to isolate until the rash scabs fall off, which indicates the end of infectiousness. Cases should remain in their own room, when at home, and use designated household items (clothes, bed linen, towels, eating utensils, plates, glasses), which should not be shared with other members of the household (see the next section for information on cleaning and disinfection of such materials). Cases should also avoid contact with immunocompromised persons until their rash heals. A MPX case should be monitored daily by public health authorities (e.g. via telephone calls) and can temporarily leave their home (e.g. for medical appointments and necessary exercise for their mental health stability), provided they wear a medical face mask and their rash is covered (e.g. long sleeves and pants). They should also be instructed

to avoid close or intimate contact (hugging, kissing, prolonged face-to-face contact in closed spaces) with other people until their rash heals completely.

Careful hand and respiratory hygiene are recommended for the case and everyone in the household; a medical face mask should be used when in contact with other people. Cases should abstain from sexual activity until scabs fall off. While the use of condoms is consistently encouraged during sex for prevention of HIV and other STIs, cases should be made aware that the use of condoms alone cannot provide full protection against MPXV infection, as contact with skin lesions is involved for its transmission. Because transmission through droplets is possible, avoidance of close, physical contact is recommended until the scabs fall off.

Health authorities and policy makers should consider that sex workers may be disproportionately affected by this outbreak and may need incentives to be able to comply with the full recommendation of isolation until the rash heals completely which may last up to four weeks.

Finally, instructions should be given to MPX cases to avoid contact with any mammal pets, and in particular pet rodents (mice, rats, hamsters, gerbils, guinea pigs, squirrels etc), due to the possibility of human-to-pet transmission. Any recent contact with such pets should be noted and animal health services should be contacted for advice.

Environmental persistence and disinfection

Poxviruses show extraordinary resistance to drying [81], and increased temperature and pH tolerance when compared with other enveloped viruses. These characteristics strongly impact their environmental persistence: materials from infected patients (e.g., dermal crusts) or fomites (e.g., bed linens) remain infective for months to years.

Despite these characteristics, poxviruses are sensitive to common disinfectants, although they can be less sensitive to organic disinfectants compared to other enveloped viruses, due to their reduced envelope lipid content.

Cleaning of the room where a MPX case stayed should be done without stirring a lot of dust or causing the formation of aerosols and should use regular cleaning products followed by disinfection using a 0.1 % sodium hypochlorite (NaClO) (dilution 1:50, if household bleach is used, usually at an initial concentration of 5%). Particular attention should be paid to toilets and frequently touched surfaces. Contaminated clothing and linens should be collected and washed at 60°C cycles. Carpets, curtains and other soft furnishings can be steam-cleaned.[82].

Single-use disposable cleaning equipment (e.g. disposable towels) is recommended. If disposable cleaning equipment is not available, the cleaning material (cloth, sponge etc.) should be placed in a disinfectant solution effective against viruses, or 0.1% sodium hypochlorite. If neither solution is available, the material should be discarded.

Gauzes or other material soaked with lesion fluid or containing scabs from the MPX case should be preferably handled in a healthcare facility as infectious waste, or according to instructions from the local public health authority.

Management of monkeypox contacts

Close contacts of the currently reported MPX cases include mainly sexual partners and people living in the same household or anyone sharing the same bedding or clothing with an MPX case. Sharing the same workspace for several hours seated within one to two metres or being a co-passenger in longer flights, train or bus rides may also qualify as a close contact in certain situations, but this would require a case-by-case assessment. (see Table 2). From outbreaks in Africa, the secondary attack rate is estimated at 9-12% among unvaccinated contacts within households, however other estimates are as high as 50%, while in the 2003 US outbreak it was 0% [34,58]. Although some of the reported cases are epidemiologically linked, no further onward transmission to close contacts that are not sexual partners has been documented yet in this outbreak.

Contact tracing of newly identified MPX cases should be performed carefully and exhaustively, building on long-standing good practices implemented for the management of STIs and the HIV epidemic and the ongoing COVID-19 pandemic. Partner notification should be rapidly initiated; however, this might be challenging in the case of anonymous sexual partners. Involvement of sexual health services, who are experienced in partner notification for sexually-transmitted diseases is recommended to ensure the best possible outcome.

Awareness raising in MSM communities about the ongoing MPX outbreak is extremely important and should happen with the engagement of the community (see section risk communication and community engagement). Contact tracing should pay particular attention to identifying MPX contacts who are immunocompromised. Working with associations supporting people living with human immunodeficiency virus (PLWHIV) and immunocompromised patients would be valuable. Public health resources for these activities are very important. Although the number of contacts to be traced is not expected to be very large, the case complexity will be high. That the public health workforce is already affected by the continuous pressure of the response needs to the COVID-19 pandemic should also be considered.

All identified close contacts (see Table 2) of a MPX case should be instructed to self-monitor for fever and MPX symptoms daily for 21 days after their last exposure. Instructions should be provided, if they develop any symptoms during this period, to self-isolate except for attending medical assessments or testing. In general, symptomatic contacts should be isolated during their investigation until MPX is excluded. Close contacts should be advised to avoid close physical contact with young children, pregnant women and immunocompromised persons until MPX is excluded.

Sexual contacts of MPX cases should abstain from sex for a duration of at least 21 days or until the infection is excluded. While all persons are encouraged to use condoms consistently during sexual activity for prevention of HIV and other STIs, they should be made aware that the use of condoms alone cannot offer full protection against transmission of MPXV. Because transmission through droplets in prolonged face-to-face contact is also possible, avoidance of close, physical contact is recommended for the duration of 21 days following exposure. Sex workers may be a group potentially exposed to MPX and consideration should be given to the fact that they would need financial support to comply with the recommended duration of self-monitoring.

Close contacts of MPX cases would benefit from an exposure assessment, including history of past smallpox vaccination, and should be carefully evaluated for the potential need of post-exposure prophylactic (PEP) smallpox vaccination. Use of PEP smallpox vaccination should only be offered after a careful risk/benefit ratio assessment for the individual person, including the type and timing of last exposure, their age group, their medical history particularly as regards their immune status and other underlying conditions that would indicate that they are at increased risk for severe MPX disease. The time from vaccination until developing the expected antibody protection also plays a role. In addition, the profile, indication and availability of the nationally available smallpox vaccine should be considered (which generation of vaccine is available, number of doses etc.). Use of the smallpox vaccine up to four days after exposure to MPX can prevent the onset of symptoms, while after that and until 14 days post-exposure prophylactic vaccination may modify the disease course [83]. If the currently authorised 3rd generation MVA vaccine for smallpox would be used, then two doses would be needed 28 days apart.

For passengers in an aircraft, bus or train sitting within a radius of two metres of a symptomatic case (i.e. seated one-two seats around the case), an exposure assessment by health authorities should be carried out and monitoring implemented accordingly. Exposure on longer flights or rides (more than eight hours) can be considered as riskier [84]. From when smallpox was circulating, no transmission on aircraft was documented [85]. Table 2 presents the overview of the advice for the management of contacts of a MPX case.

Table 2. Summary of management approach for contacts of a MPX case

Type of contact	Description	Management guidance
Close contact	• Sexual partner • Person(s) living in same household, or similar setting (e.g camping, overnight sleeping etc) • Person(s) sharing clothing, bedding, utensils etc, while the patient had a rash • Person(s) sharing the same closed workspace/office for long periods of time • Caregivers of MPX case, while symptomatic • HCW who had contact with MPX case (lesions or prolonged face-to-face contact) without appropriate PPE • HCW or other person who suffered a sharps injury or was exposed to MPX case body fluids or aerosol generating procedure without PPE • Laboratory staff suffering exposure to occupational accident with virus-containing sample (splash, sharp or aerosol exposure etc) • Co-passenger seated one -two seats distance around case while they were symptomatic, in airplane, bus or train ≥ 8 hours duration	• Careful benefit/risk assessment for the need for PEP smallpox vaccination • Self-monitor for fever or other MPX symptoms (headache, back ache etc) or new unexplained rash for 21 days from last exposure. In that case self-isolate and abstain from sexual activity until MPX is excluded. • Careful hand hygiene and respiratory etiquette. • Abstain from sexual activity and avoid close physical contact for 21 days or until MPX is excluded. • Avoid contact with mammal pets for 21 days or until MPX is excluded
All other contacts	• Brief social interactions • Work colleagues not sharing same office • Persons sharing fitness equipment or sharing the same sauna or bath, without sexual contact • Social encounters/ acquaintances • HCW contact with appropriate PPE	• Depending on the certainty of contact, some of these contacts may be asked to self-monitor for fever or other MPX symptoms (headache, back ache etc) or new unexplained rash for 21 days from last exposure.

Healthcare settings and diagnostic laboratories

Raising awareness of health professionals is important for case identification and contact tracing in this MPX outbreak. Countries are urged to provide information about the ongoing situation to their clinicians at various levels in the health system, with a particular focus to general practitioners, sexual clinics, genito-urinary practitioners, walk-in clinics providing care to MSM and sex workers, dermatology departments and emergency departments in general. Cases with localised unexplained rash with inguinal lymphadenopathy and other MPX-compatible symptoms should be referred to specialised services per national guidelines for decision on testing.

In healthcare settings, prevention of transmission is based on appropriate infection prevention and control measures. MPX is considered to be mainly transmitted through respiratory droplets and direct contact with body fluids or lesion material[66,86]. Therefore, both contact and airborne precautions should be applied when providing care for patients with monkeypox. Patients who need to be hospitalised should preferably be placed in an isolation room with anteroom and negative pressure, or if not available in a single room. Healthcare workers entering the isolation room should wear gloves, a water-resistant gown and an FFP2 respirator [25].

WHO suggests that national health authorities should consider immunisation against smallpox for healthcare workers treating or exposed to patients with MPX or their samples [25]. Careful risk/benefit ratio assessment should also be carried out for the individual health professionals offered the smallpox vaccine as pre-exposure prophylaxis in this outbreak.

Clinical specimens suspected to contain MPXV are considered category A (UN 2814) – Infectious Substances Affecting Humans. They should be packaged and transported following the relevant regulation, unless previously treated to neutralise or inactivate the pathogen [87,88].

Diagnostic specimens suspected to contain MPXV should be ideally processed using a certified Class II Biological Safety Cabinet. Laboratory staff handling specimens suspected to contain MPXV who are not vaccinated within the last 10 years should use appropriate PPE under more stringent biosafety-3 work practices to reduce the risk of exposures. Vaccinated laboratory staff could work using BSL-2 practices. Centrifugation of infected materials must be carried out in closed containers placed in sealed safety cups, or in rotors that are loaded or unloaded in a Class II biological safety cabinet. Laboratory waste containing monkeypox virus should be decontaminated before disposal (e.g., by autoclaving). Due to the short duration of viraemia, testing specimens in clinical chemistry laboratories is probably not a high-risk activity. However, using the precautionary principle, they should be handled as described above. If the appropriate safety conditions are not available, referral to a certified laboratory should be considered [89].

Cleaning and disinfection in healthcare facilities should follow the rules as outlined above (see environmental cleaning and disinfection). In addition, staff performing cleaning and disinfection in a MPX case's room should wear a minimum set of PPE:

- a disposable water-resistant gown;
- disposable gloves;
- disposable shoe or boots covers;
- respiratory protection (Filtering Face Piece (FFP) 2 respirator);
- eye splash protection (goggles or visor).

Donning and doffing of PPE should be carefully performed by trained staff, and hand hygiene should be performed every time PPE, such as gloves, are removed.

Waste should be assessed depending on risk and handled in accordance with healthcare facility policies and local regulations. If assessed as infectious clinical waste category A (UN3549), transport should be handled according to UN transport regulations [87]. Staff engaged in waste management should wear PPE [82].

Substances of human origin

All potential donors should be carefully interviewed regarding contacts with infected (confirmed or suspected) MPX cases, infected animals or travels to affected areas. Medical history data on these risk factors should be collected in the case of deceased donors.

Based on the incubation period of MPX, it is recommended to defer asymptomatic donors that have been in contact with (confirmed or suspected) cases from substances of human origin donation for a minimum of 21 days from the last day of exposure.

Since the MPX prodromal stage varies in duration (1–4 days [22]) and symptoms can be non-specific and mild [88-91] or absent [49], careful examination for any possible signs of infection should be performed even after the expiration of the deferral period (at least 21 days from the last day of exposure). Examination should not overlook mild and non-specific signs like headache or fatigue or anogenital skin lesions.

Risk communication and community engagement

It is important that health authorities communicate risks about this MPX outbreak, referring to the specific characteristics of the current situation, so that people at risk can adopt appropriate preventive and treatment-seeking behaviour. A balance should be kept between informing people at risk but also communicating that the virus is not spread easily between people and the risk to the broader population is low. However, much remains unknown about the event, in particular where and how index cases have acquired their infections. Authorities should make clear that while the evidence base is still quite limited, intensive work is ongoing to fill in the knowledge gaps. As such, the initial prevention strategies implemented may need to be adapted as more scientific information becomes available.

In the meantime, efforts should be made to ensure that stigmatisation does not occur based on sexual orientation and practices. Risk communication messages should stress that monkeypox virus is spread through close contact between people, especially in the same household, including during sexual contact. Transmission of vaccinia virus has been described among heterosexual partners [43] and similarly, it is expected that sexual transmission will occur in the broader population. Therefore, risk communication messages could also state that MPX infection is not indicative of someone's sexual orientation nor that the latter influences their susceptibility to the disease. In clear and accessible language, people who are infected with monkeypox virus should be advised to avoid any sort of close contact, including protected sexual contact, with other people until their rash has ended and the last scab has fallen off, no matter how long this process takes (may be up to four weeks). If they are living with other people, the importance of staying in one room for as long as they have the rash should be stressed, and ideally, they should have access to their own bathroom. Advice to avoid sharing bedding or any household items with anyone else should be disseminated. Building on approaches that were developed during the early COVID-19 pandemic [94], if full isolation is not possible, very good hygiene practices should be promoted: the monkeypox virus is able to survive on surfaces or other fomites for long periods of time (days to months [95,96]).

If high-risk close contacts of MPX patients are offered post-exposure vaccination in the form of the smallpox vaccine, they should be fully informed about the risk/benefits for them and potential side effects of the vaccine offered [95,96].

Community engagement approaches should be used to understand perceptions and concerns and to support targeted risk communication messages to populations or groups more likely to be exposed to the virus. This requires the identification of relevant community-based organisations and stakeholders and leveraging their existing networks so they can communicate with community members and raise awareness using language adapted to their community and through appropriate communication channels [97]. Public health institutions should regularly inform and exchange ideas with these organisations and groups on specific aspects of the risk communication messages to be adapted and disseminated, as well as on their impact on the target audience.

Three key groups should be considered as priority groups for community engagement strategies during the current MPX outbreak.

- Since the current event has seen several cases in MSM, this group must be made aware of the risk of infection as well as prevention measures they may take. Applications used by MSM for meeting partners can be explored to reach those most at risk and provide health promotion information. Various organisations exist at the regional, national, sub-national and local level working on health for LGBTQIA+, including activist groups and community testing organisations (i.e. checkpoints). These should be contacted, informed and asked to engage with their members, users and networks about the situation and hear their perceptions and concerns. Other organisations working on sexual health may also be mapped and contacted for similar purposes. Key messages should focus on the fact that MPXV is spread through close contact with infectious individuals, may possibly be sexually transmitted and that condoms can mitigate the risk of many sexually-transmitted infections, but cannot offer full protection against transmission of MPXV, since contact with lesions may be sufficient for transmission to occur.
- As people who are immunocompromised have been shown to be more vulnerable to severe disease [42], support organisations for immunocompromised people should also be identified, kept informed, and supported in conducting outreach to their members. Particular focus should be given to their heightened risk of severe disease, and the importance of seeking treatment should they develop symptoms of MPX infection. However, it is important to clarify that people living with HIV under appropriate treatment are not considered immunocompromised, and those with untreated HIV should be referred to HIV treatment [98].
- Healthcare workers' unions and associated professional networks should be engaged with so they can be equipped to detect and treat cases early as well as provide health advice and disseminate messages about case definitions and strategies for contact tracing. They should also be informed about the particular susceptibility to severe disease of people with untreated HIV and those who are otherwise immunocompromised so that they can provide appropriate treatment and support for such patients. Health workers should also be made aware that their own close contact with patients may put them at increased risk of infection and therefore they should protect themselves accordingly.

ECDC is working with multiple civil society organisations to reach out to MSM groups by disseminating the following message to all European countries:

'Monkeypox virus is spreading in Europe, in particular among men who have sex with men. It is transmitted through close contact, like during sexual intercourse or through contaminated bedding, sex toys. If you or any recent (last 21 days) partner have unusual sores or rash, contact your sexual health provider (find closest site here: https://www.testfinder.info) or your GP or local health provider. More info can be found here: www.ecdc.europa.eu/en/news-events/epidemiological-update-monkeypox-outbreak'

Limitations

This assessment is undertaken based on facts known to ECDC at the time of publication and has several key limitations. In particular, there are many scientific uncertainties and knowledge gaps regarding human MPX, including:

- This is the first outbreak of MPX outside Africa suggesting transmission during sexual contact/intercourse as the primary route of transmission of the disease. No comprehensive data are available on severity of illness and on transmission dynamics as well as on effective response measures.
- A lack of clear understanding of the epidemiological situation since countries are in the case-finding stage.
- A lack of understanding of the route of introduction of MPXV in MSM communities.
- Lack of sequencing results of MPXV to identify chains of transmission and connections among cases. Sequencing may also provide clues regarding a possible time and mode of introduction of MPXV in Europe. Look-back studies may also be useful in leftover samples from STI clinics to study this question.
- More accurate estimates of the risk of transmission associated with different sorts of contacts with clinical cases are needed in European settings.
- Information is needed on the current residual cross protection from smallpox vaccination in the EU/EEA population.
- Efficacy data of the currently available smallpox vaccine(s) against MPX are lacking, and safety data for the use of the smallpox vaccine in young children, pregnant women and immunocompromised are also lacking.
- Efficacy data and safety profile of the available antiviral agents for the treatment of potential severe cases are also lacking. A common treatment protocol is proposed by EMA and should be adopted.
- More information is needed on the clinical presentation of cases and their outcome, to establish the severity (morbidity and mortality) of the disease in Europe.
- More information is also needed on possible contact with animals. In addition, studies are needed to assess the vulnerability of European rodent and other mammal species to MPXV.

Source and date of request

ECDC internal decision, 17 May 2022.

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All experts have submitted declarations of interest, and a review of these declarations did not reveal any conflict 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.

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