

Living Evidence Profile #6.11

(14 October 2022)

Question

What is the best available evidence related to the monkeypox outbreak?

What we found

To inform current knowledge related to monkeypox, we identified evidence, as well as experiences from 11 countries (Australia, Belgium, France, Germany, Italy, Netherlands, Portugal, Spain, Sweden, United Kingdom (U.K.), and the United States (U.S.) (see Box 1 for a description of our approach), and from all Canadian provinces and territories. While this living evidence profile focuses on monkeypox in humans, a complementary living evidence profile summarizes the best available evidence related to monkeypox in animals. We organized our findings using the framework below, which has not changed from the first version of our LEP.

Organizing framework

- Biology
- Epidemiology (including transmission)
- Prevention and control
- Diagnosis
- Clinical presentation
- Prognosis
- Treatment

In this and the previous interim update, we identified 59 new evidence documents since the last interim update of this LEP, of which 32 were deemed highly relevant. The newly added highly relevant evidence documents from this and the interim update include:

- five systematic reviews;
- two rapid reviews;
- 10 protocols for systematic reviews; and
- 15 single studies.

This LEP also includes evidence documents from the previous versions that we deemed to still be highly relevant, for a total of 158 highly relevant documents.

We outline in narrative form below our key findings related to the question from highly relevant evidence documents identified in both the interim update and this update, as well as the experiences from other

Box 1: Our approach

We identified evidence published from 2017 onwards (to capture any evidence related to recent outbreaks outside Africa) addressing the question by searching Health Systems Evidence (HSE), Health Evidence, ACCESSSS, PROSPERO (review protocols and registered titles), PubMed and MedRxiv on 28 September 2022 for the last interim update and 11 October 2022 for this update.

We identified jurisdictional experiences by hand searching government and stakeholder websites. We selected 11 countries (Australia, Belgium, France, Germany, Italy, Netherlands, Portugal, Spain, Sweden, United Kingdom, and the United States) that are non-endemic for monkeypox and that have had recent documented cases.

We searched for guidelines, full systematic reviews (or review-derived products such as overviews of systematic reviews), rapid reviews, protocols for systematic reviews, and titles/questions for systematic reviews or rapid reviews that have been identified as either being conducted or prioritized to be conducted.

We appraised the methodological quality of full systematic reviews and rapid reviews that were deemed to be highly relevant using AMSTAR. Note that quality appraisal scores for rapid reviews are often lower because of the methodological shortcuts that need to be taken to accommodate compressed timeframes. AMSTAR rates overall quality on a scale of 0 to 11, where 11/11 represents a review of the highest quality. It is important to note that the AMSTAR tool was developed to assess reviews focused on clinical interventions, so not all criteria apply to systematic reviews pertaining to delivery, financial or governance arrangements within health systems or to broader social systems. We appraised the quality of the highly relevant guidelines using three domains in AGREE II (stakeholder involvement, rigour of development, and editorial independence) and classified guidelines as high quality if they were scored as 60% or higher on each domain.

This update to the living evidence profile was prepared in the equivalent of three days of a ‘full-court press’ by all involved staff.

countries. This is accompanied by Table 1 that provides a summary of the total number of evidence documents in each domain of the organizing framework (with the number of new documents identified in brackets) and Table 2, which provides more details about key findings from each of the newly identified evidence documents and new insights from the jurisdictional scans. In Table 3, we provide findings from highly relevant evidence documents and jurisdictional scans from the previous version of our LEP.

A detailed summary of our methods is provided in Appendix 1, and the full list of newly identified evidence documents (including those deemed of medium and low relevance) is in Appendix 2a. The previously included documents are listed in Appendix 2b. Note that we summarized key points from each of the highly relevant evidence documents in Appendix 2b, but only the title and the URL are listed for those deemed to be medium or low relevance. We included the hyperlinks of excluded documents (at the final stage of reviewing) in Appendix 3. We also provide detailed summaries of knowledge related to monkeypox from other countries in Appendix 4, and from Canadian provinces and territories in Appendix 5.

Key findings from highly relevant evidence sources

Since the last update, new monkeypox cases have increased, with the [WHO global trends epidemiological report and health-emergency dashboard](#) reporting 72,947 confirmed cases and at least 28 deaths, and the [U.S. CDC global map](#) reporting a total of 73,288 confirmed cases as of 14 October 2022.(1; 2) For this update, we identified highly relevant evidence on the biology, epidemiology, clinical presentation, prevention and control, clinical presentation, and treatment of monkeypox.

Biology

In terms of new evidence on the biology of the monkeypox virus, we identified one [medium-quality systematic review](#) that reported three clades of the virus after estimating the serial interval (SI) and incubation period (IP), and concluded that there is a need to adjust for control measures and the length of a quarantine following the changes in these two epidemiological metrics throughout an epidemic.(3) We also found a [single study](#) that determined that the role of the first known monkeypox virus-encoded proteome structure, A42R, in the replication of poxviruses may not be readily determined by comparing its structure to cellular proteins, but increasing efforts to develop high-resolution imaging of monkeypox proteins could be beneficial to combating potential monkeypox epidemics in the future.(4)

Epidemiology

We identified two low-quality systematic reviews, one rapid review, and several single studies that addressed epidemiology of the monkeypox virus. One of the [systematic reviews](#) compared the historical evidence of monkeypox outbreaks and echoed prior reviews saying that human monkeypox has historically been more contagious and limited to African countries where it was spread by animals, but now infections spread internationally (first emerging from West Africa) by secondary affliction and sexual contact.(5) The review also indicated that all age groups are affected by the current pattern of monkeypox transmission compared to historical monkeypox transmission patterns primarily affecting children. The other [systematic review](#) examined the risk factors, transmission routes, and clinical characteristics of 3,097 monkeypox patients aged 30-40 years across 14 studies, and found that 98.7% of the patients were men who have sex with men, 37.9% had a pre-existing positive HIV diagnosis, and 22.1% of patients had a concurrent sexually transmitted infection.(6) Notably, the authors of the [low-quality rapid review](#) highlighted that the evidence regarding the persistence of the monkeypox virus in human male semen is scarce and at times, contrasting.(7)

A [single study](#) that examined monkeypox cases from 10 countries (including Canada) at the end of August 2022 found that despite outbreaks occurring across the globe, they are largely contained and under control in most countries (with the exception of the United States and Peru).(8) Another [single study](#) (pre-print) estimated the global risk of monkeypox importation through the airline travel network in 176 countries and territories, and found that while travel restrictions had a minor impact on the global airline importation risk of monkeypox, estimates showed that most locations will have an intensified importation risk of monkeypox, regardless of the geographic region, by 31 December 2022.(9) In relation to environmental transmission of the virus, another [single study](#) assessing surface swabs of areas in isolation rooms of confirmed monkeypox patients, personal protective equipment of healthcare workers, and air samples in a U.K. hospital found that 56 (93%) out of 60 samples were found to be positive, indicating widespread environmental contamination, especially after clinical contact and changing of bedding.(10)

We identified several studies conducted over the last few months that explored the epidemiological characteristics of monkeypox patients. The characteristics of 226 male patients with monkeypox who identified as gay, bisexual or as having sex with men were analyzed in [one study](#) conducted from 1 May to 1 July 2022, which found that 40% of cases reported close contact with someone who had confirmed monkeypox, and 13% were admitted to the hospital of whom 53% had severe illness.(11) Researchers of a September 2022 [study](#) in France compared monkeypox viral loads from 50 men with PCR cycle thresholds over 14 days and found that on day zero, monkeypox was detected more frequently on the skin, anus and throat, and viral loads were more expressed on skin lesions and anal samples rather than within blood and urine.(12) An [observational study](#) assessed the demographics and clinical presentation of 48 confirmed monkeypox cases in Madrid, Spain and concluded that 87.5% of the cisgender men included in the study were men who have sex with men, 39.5% were people living with HIV, 89.5% had unprotected sex in the three weeks before symptom onset, 50% had chemsex, and none had travelled to or had contact with people from endemic regions.(13) Lastly, researchers of a [single study](#) conducted in Colorado, U.S. from 1 May to 31 July 2022 determined that the risk of monkeypox transmission to healthcare personnel from symptomatic monkeypox patients could be classified as 'low', and emphasized the importance of infection-prevention measures, including appropriately educating and training the workforce.(14)

Prevention and control

A [low-quality rapid review](#) published in September 2022 evaluated the literature on the protective immunity elicited by vaccinia virus-based smallpox vaccines and found that studies confirmed a high degree of protection and immunity against monkeypox virus from various smallpox vaccines, with the Jynneos vaccine being identified as the safest vaccine available for pre-exposure and post-exposure use in preventing monkeypox.(15) However, in some cases, smallpox vaccines caused side effects and contraindications, and third-generation smallpox vaccines that require two doses were found to be an impediment to rapid outbreak response. One [single study](#) found that monkeypox incidence in 6,471 confirmed cases in 32 U.S. jurisdictions was found to be 14 times higher among unvaccinated individuals compared to those who had received their first dose of Jynneos vaccine ≥ 14 days earlier.(16) The effects of the Modified Vaccinia Ankara-Bavarian Nordic vaccine were observed in another U.S. [study](#) of 7,339 monkeypox-infected patients immediately after receiving a single dose.(17) The researchers found that 90 patients tested positive for monkeypox after the first day of administering the vaccine, eight monkeypox cases occurred more than 28 days after the first dosage, and two of these occurred more than 14 days after receiving the second dose. Behavioural changes in men who have sex with men (MSM) and transgender women in the U.S. were examined in another [study](#) which found that the most common mitigation strategies used by these groups included limiting the number of sexual partners they had and limiting their exposure by avoiding crowded social venues where skin-to-skin contact is likely to occur.(18)

Diagnosis

We identified five studies that focused on diagnosis of monkeypox. Serial laboratory testing of lesion and oropharyngeal swabs and blood testing were performed on 16 male monkeypox patients in one [single study](#), and researchers determined that infectious virus was successfully isolated from lesion swabs, but not from oropharyngeal swabs and blood samples, suggesting that oropharyngeal swabs and blood samples alone carry the risk of false negative results.(19) In a [mixed-methods study](#), a saliva-based polymerase chain reaction (PCR) assay for monkeypox in Los Angeles, San Francisco and Palm Springs, California was analyzed and a systematic review was conducted to examine how saliva-based tests compared to lesion swabs.(20) The PCR assay showed in silico inclusivity of 100% for all 97 strains of the monkeypox virus assessed, and the systematic review found that early detection of lesion swabs may indicate transmissibility through lesion development while saliva-based testing may identify cases earlier than lesion-based tests. The two best-performing fine-tuned deep-learning models for monkeypox virus detection (Xception and DenseNet-169) were selected from 13 models in a [single study](#) to develop an ensemble method with an accuracy of 87.1%.(21) The ensemble can discriminate measles and monkeypox as well as highly discriminate chickenpox.

A [prospective evaluation study](#) (pre-print) recruited 50 individuals to evaluate the accuracy of patient self-collected skin lesions, pharyngeal, and rectal swabs, and found that the performance of self-collected and physician-collected samples was similar, suggesting that self-sampling is a reliable strategy for diagnosing monkeypox.(22) Finally, another [study](#) (pre-print) examined the epidemiological characteristics, specimen collection practices, and cycle threshold values for monkeypox virus PCR tests performed at two reference laboratories in the U.S., and found that the viral load of positive specimens was comparable between both laboratories. In addition, when multiple specimens were collected for a single individual, the overall concordance rate was greater than 95%.(23) However, submitting multiple specimens in separate tubes increased the workload of the laboratory staff and costs.

Clinical presentation

We found two low-quality systematic reviews and two single studies related to clinical presentation of monkeypox. One [systematic review](#) that examined the risk factors, transmission routes, and clinical characteristics of 3,097 monkeypox patients across 14 studies found that patients commonly reported mucocutaneous lesions (98.8%), a fever (63.5%), inguinal lymphadenopathy (55.4%), and asthenia (47.4%).(6) The review also found that 7.2% of these cases required hospitalization. The other [systematic review](#) evaluated 4,080 cases of monkeypox virus and found nearly identical results for clinical manifestations of the virus.(24) This review suggested that the mildness of the current outbreak might be attributed to a better quality of care offered to patients who live in high-income countries, and to the fact that patients in this outbreak are younger.

The [observational study](#) mentioned previously that assessed the demographics and clinical presentation of 48 confirmed monkeypox cases in Madrid, Spain concluded that the first symptoms of the observed patients included skin lesions (53.8% of individuals), fever (17.9%), and respiratory symptoms (12.8%), and one out of 10 patients who had receptive anal sex had genital lesions compared to 12 out of 13 who had insertive anal sex.(13) Lastly, researchers of [the single study](#) that analyzed the characteristics of 226 confirmed cases of monkeypox infection in 29 countries found that patients with HIV were more likely to experience diarrhea, perianal rash or lesions, and rash burden.(11)

Treatment

With respect to evidence on monkeypox treatment, we identified one U.S.-based [study](#) examining the characteristics of patients in the U.S. treated with tecovirimat for monkeypox virus infection. Out of 369 patients who were treated with tecovirimat for monkeypox virus infection in the study, 93.1% were not hospitalized and the median interval from initiation of tecovirimat treatment to subjective improvement in patients was three days.(25) Adverse events were reported in 3.5% of patients, and all but one adverse event were considered non-serious.

Key findings from the jurisdictional scan

Epidemiology

Across countries analyzed in our jurisdictional scans, case counts continue to increase, though the rate of increase is slowing down. The UK Health Security Agency released an eighth [technical briefing about the monkeypox outbreak](#) in England on 23 September 2022.(26) A new observation was noted that *Shigella* spp and lymphogranuloma venereum (infections that also disproportionately affect men who have sex with men) diagnoses also began decreasing around the time that monkeypox diagnoses began slowing, which suggests that changes in sexual behaviour may have contributed to previously observed reductions in incident monkeypox cases. In Canada, as of 12 October 2022, the Public Health Agency of Canada (PHAC) reported a total of [1,411 cases of monkeypox in nine Canadian provinces and territories](#), representing only a 90-case increase from 9 September 2022.(27)

As of [6 October 2022](#), there have been 1,221 cases of monkeypox in the Netherlands.(28) In the U.K., the case count was [3,523](#) confirmed and 150 highly probable as of 10 October 2022.(29) As of 11 October 2022, there have been 138 confirmed and probable cases reported by the [Government of Australia](#) and 3,651 confirmed cases of monkeypox across all 16 federal states in [Germany](#).(30; 31) As of 12 October 2022, there have been [779](#) cases in Belgium (including one death), [4,064 confirmed cases](#) in France, [856 monkeypox cases](#) in Italy, [930 confirmed cases](#) in Portugal, [202](#) cases in Sweden, and [27,022](#) cases in the U.S.(2; 32)

Prevention and control

Vaccine eligibility appears to be expanding and the availability of second doses is increasing as supply constraints ease across most jurisdictions. In Canada, vaccine eligibility and availability has expanded in Saskatchewan, Manitoba, Québec, New Brunswick, Nova Scotia, P.E.I., Newfoundland and Labrador, the Yukon, and the Northwest Territories (see Appendix 5). As of 15 September 2022, Ontario's Chief Medical Officer Dr. Kieran Moore reported that Ontario has [administered 32,175 first doses](#) of monkeypox vaccine, and as of 6 October 2022, Québec has already begun administering [second doses](#).(33; 34)

To help ensure the continued supply of vaccines in Canada, the National Advisory Committee on Immunization (NACI) updated its [interim guidance on the use of Imvamune](#) on 16 September 2022 after considering the impact of dose-sparing strategies during periods of limited vaccine supply.(35) The guidance emphasizes priority groups, highlights those who may not need the vaccine, and the importance of supplying first doses to meet demand before second doses are offered.

Other countries continue to advance their vaccination campaigns, both in terms of increasing the number of vaccines administered and attempting to ensure equity. Vaccine eligibility has been expanded in Belgium as of [23 September 2022](#), and total vaccines doses administered include [120,128 doses](#) in France as of 10 October 2022, [20,278](#) in the Netherlands as of 29 September 2022 (increasing from 10,440 as of 25 August

2022), and 906,325 across 54 U.S. jurisdictions as of [11 October, 2022](#).(36-39) The CDC in the U.S. has also initiated [collaborative vaccination projects](#) to reduce vaccination disparities and updated its [Monkeypox Vaccine Equity Toolkit](#) which provides strategies, actions, and resources to increase vaccination among populations most affected by monkeypox, but less likely to be vaccinated.(40; 41)

As vaccination efforts ramp up, some countries, such as the U.K. and the Netherlands, have or are in the process of estimating the total eligible population to better understand vaccine supply and overall vaccination progress. The UK Health Security Agency has used surveillance data, survey findings, and expert opinion to estimate that approximately [110,000 individuals are eligible for monkeypox vaccination](#).(26) As some countries begin to offer second doses, guidance about spacing requirements between doses have varied considerably. More recently, intradermal injection of vaccines has been under consideration across countries, with policies and approaches varying considerably. In France, intradermal injection is only advised for second doses in some groups. Similarly, in Canada, off-label intradermal injection is recommended for [second doses among immunocompromised adults](#).(35) Conversely, in the U.K., intradermal injection is being increasingly used as a strategy to [enable efficient dose administration](#).(42) In Germany and the U.S., clinical data about intradermal injection is being reviewed, with Germany continuing to [recommend subcutaneous over intradermal injection](#), and the U.S. awaiting findings from a [clinical trial](#).(43; 44)

Finally, many countries, including Canada, as well as provinces and territories within Canada, are updating information and guidance regarding infection prevention, vaccination, vaccine transport and other topics related to prevention and control. For example, [Saskatchewan](#) and [Ontario](#) have updated guidelines and information on vaccines.(45; 46) In Germany, on [19 September 2022](#), Robert Koch Institute (RKI) updated their recommendations regarding the close contact management of monkeypox cases, which states that a quarantine mandate is no longer in place for contact persons, and housemates with no intimate contact with positive individuals or infectious material have been reclassified as category two contacts.(47) In the U.K., monkeypox clade IIb (B.1 lineage), which is largely circulating during the current outbreak, has [not been classified as a high consequence infectious disease](#) by the UK Health Security Agency; however, the other clades of monkeypox are classified as high consequence infectious diseases and may be subject to different clinical and public-health responses.(48)

Prognosis

Trends of case severity and characteristics of those diagnosed have remained consistent since our previous updates. As of 4 [October, 2022](#), of the 674 confirmed cases of monkeypox in Ontario, 99.3% are male and 0.7% female, 2.8% have been hospitalized, 0.3% have been in the ICU, and no deaths have been reported.(49) A particularly unique co-infection case was identified in Italy. According to a [case report](#), an Italian man was diagnosed with COVID-19, monkeypox, and HIV at the same time. After testing positive for COVID-19 on 2 July 2022, he noticed a rash on his left arm which became more painful and spread across his body over the next few days.(50) By 13 July 2022, he no longer tested positive for COVID-19, the monkeypox rash was mostly healed, and he began standard HIV treatment.

Treatment

Across jurisdictions, research and interest on tecovirimat as a treatment option for monkeypox continues. For example, a U.S. [clinical trial](#) is currently evaluating the antiviral and the [government of Australia](#) indicates that there are two therapeutic options for monkeypox: tecovirimat and vaccinia immunoglobulin.(51; 52) The CDC has also updated Interim Clinical Considerations for management of ocular monkeypox virus infection on 7 [October, 2022](#) and Clinical Considerations for monkeypox in children and adolescents less than 18 years old on 4 [October, 2022](#). (53; 54)

Table 1: Overview of topics related to monkeypox addressed by all included evidence documents (newly added documents in brackets)

Type of evidence document	Total*	Biology	Epidemiology (including transmission)	Prevention and control	Diagnosis	Clinical presentation	Prognosis	Treatment
Guidelines (non-robust)	2	-	-	(1)	-	1	1	1
Full systematic reviews	14	1(1)	7(2)	-	3(1)	7(2)	1	1
Rapid reviews	4	-	1(1)	3(2)	-	-	-	-
Non-systematic reviews	21	5	14	8	8	5	2	3
Protocols for reviews or rapid reviews that are underway	30	1(1)	3(2)	5(2)	1(1)	13(5)	-	4(3)
Titles/questions for reviews that are being planned	0	-	-	-	-	-	-	-
Single studies	212	31(4)	91(20)	48(8)	28(9)	33(4)	8	19(2)

*Some documents were tagged in more than one category so the column total does not match the total number of documents.

(n) = newly added evidence documents

Table 2: Highlights from new highly relevant evidence documents and jurisdictional experiences

Organizing framework domain	New evidence	New experiences
Biology	<ul style="list-style-type: none"> Estimates of the serial interval (SI) and incubation period (IP) of the monkeypox virus were reported for three clades of the virus in a medium-quality systematic review, which concluded that there is a need to adjust for control measures (e.g., entry restrictions) and the length of a quarantine following the changes in these two epidemiological metrics throughout an epidemic A single study that investigated the first known monkeypox virus-encoded proteome structure, A42R, found that the role of A42R in the replication of poxviruses may not be readily determined by comparing its structure to cellular proteins, but increasing efforts to develop high-resolution imaging of monkeypox proteins could be beneficial 	<ul style="list-style-type: none"> None identified
Epidemiology (including transmission)	<ul style="list-style-type: none"> A low-quality systematic review that examined the risk factors, transmission routes, and clinical characteristics of 3,097 monkeypox patients aged 30-40 years across 14 studies found that patients commonly reported mucocutaneous lesions (98.8%), a fever (63.5%), inguinal lymphadenopathy (55.4%), and asthenia (47.4%) <ul style="list-style-type: none"> 7.2% of the monkeypox cases led to hospitalization A low-quality systematic review compared the historical evidence of monkeypox outbreaks and found that human monkeypox has historically been more contagious and limited to African countries where it was spread by animals, but now infections spread internationally (first emerging from West Africa) by secondary affliction and sexual contact <ul style="list-style-type: none"> All age groups are affected by the pattern of transmission compared to previously, when monkeypox primarily affected children After examining the literature surrounding the sexual transmission of the monkeypox virus, authors of a low-quality rapid review noted that the evidence is scarce and at 	<ul style="list-style-type: none"> The Public Health Agency of Canada (PHAC) reported a total of 1,411 cases of monkeypox in nine Canadian provinces and territories as of 12 October 2022 As of 4 October 2022, Spain has 7,188 cases, which is the highest in the European region, and second highest around the globe As of 6 October, 2022, there have been 1,221 cases of monkeypox in the Netherlands In the U.K., the case count is 3,523 confirmed and 150 highly probable as of 10 October 2022 As of 11 October 2022, the government of Australia has reported 138 confirmed and probable cases As of 12 October 2022, Belgium has reported a total of 779 monkeypox cases and one death within the country As of 12 October 2022, there have been 4,064 confirmed cases of monkeypox in France; 91 of these cases have since required hospitalization As of 11 October 2022, there have been 3,651 confirmed cases of monkeypox across all 16 federal states in Germany; 18 female, three adolescent, and two children have been reported to have contracted monkeypox

Organizing framework domain	New evidence	New experiences
	<p>times, contrasting, regarding the persistence of the monkeypox virus in human male semen</p> <ul style="list-style-type: none"> • After monitoring 313 healthcare professionals who had contact with monkeypox patients in Colorado, U.S. from 1 May to 31 July 2022, one single study found that the risk of transmission could be classified as ‘low’, as none of the staff had contracted the virus <ul style="list-style-type: none"> ○ The authors emphasized the importance of infection-prevention measures, including appropriately educating and training the workforce • A single study that examined monkeypox cases from 10 countries (including Canada) at the end of August found that despite outbreaks occurring across the globe, they are largely contained and under control in most countries (with the exception of the United States and Peru) • One single study (pre-print) estimated the global risk of monkeypox importation through the airline travel network in 176 countries and territories and found that while travel restrictions had a minor impact on the global airline importation risk of monkeypox, estimates showed that most locations will have an intensified importation risk of monkeypox, regardless of the geographic region, by 31 December 2022 • Researchers of one study analyzed the epidemiological and clinical characteristics of 226 confirmed cases of monkeypox infection in 29 countries from 1 May to 1 July 2022 and found that 99% of male patients who identified as gay, bisexual or as having sex with men and reported sexual or close intimate contact within the 21 days before symptom onset, and that patients with HIV were more likely to experience diarrhea, perianal rash or lesions, and rash burden <ul style="list-style-type: none"> ○ 40% of cases reported close contact with someone who had confirmed monkeypox, and 13% were admitted to the hospital, 53% of whom had severe illness 	<ul style="list-style-type: none"> • As of 12 October 2022, Italy has reported 856 monkeypox cases • As of 12 October 2022, Portugal has reported 930 confirmed cases • According to the U.S. Centers for Disease Control and Prevention’s 2022 Monkeypox Outbreak Global Map, Sweden has confirmed 202 cases of monkeypox and no deaths as of 12 October 2022 • As of 12 October 2022, the U.S. has reported a total of 27,022 confirmed monkeypox cases • The UK Health Security Agency released an eighth technical briefing about the monkeypox outbreak in England on 23 September 2022 • It was observed that Shigella spp and lymphogranuloma venereum (infections that also disproportionately affect men who have sex with men) diagnoses also began decreasing around the time that monkeypox diagnoses began slowing, suggesting that changes in sexual behaviour may have contributed to reductions in incident monkeypox cases in August 2022

Organizing framework domain	New evidence	New experiences
	<ul style="list-style-type: none"> ○ The researchers recommend that pre-exposure monkeypox vaccination guidelines should be expanded to include those at high risk of infection and who plan to engage in sexual or close intimate contact ● One study observed the effects of the Modified Vaccinia Ankara-Bavarian Nordic vaccine on 7,339 monkeypox-infected patients in the U.S. immediately after receiving a single dose and found that 90 patients tested positive for monkeypox after the first day of administering the vaccine, eight monkeypox cases occurred more than 28 days after the first dosage, and two of these occurred more than 14 days after receiving the second dose; post-vaccination monkeypox occurred two weeks after administering the first dose ● Researchers of a September 2022 study in France compared monkeypox viral loads from 50 men with PCR cycle thresholds over 14 days and found that on day zero monkeypox was detected more frequently on the skin, anus, and throat, and viral loads were more expressed on skin lesions and anal samples rather than within blood and urine <ul style="list-style-type: none"> ○ At diagnosis, 83% of patients were detected with monkeypox which suggested male sexual secretion as a possible pathway for transmission ○ High monkeypox viral loads in skin and mucosa (including genital and anal sites) suggests that transmission occurs through body contact rather than respiratory droplets or contact with bodily fluids ● An observational study assessed the demographics and clinical presentation of 48 confirmed monkeypox cases in Madrid, Spain and concluded that 87.5% of the cisgender men included were men who have sex with men, 39.5% of individuals were people living with HIV, 89.5% had unprotected sex in the three weeks before symptom onset, 50% had chemsex, and none had travelled to or had contact with people from endemic regions 	

Organizing framework domain	New evidence	New experiences
	<ul style="list-style-type: none"> ○ Phylogenetic analysis showed that the virus belongs to the Western African clade and is closely related to strains circulating in Europe 	
Prevention and control	<ul style="list-style-type: none"> ● A low-quality rapid review from September 2022 that discussed the literature evaluating protective immunity elicited by vaccinia virus-based smallpox vaccines found that studies showed a high degree of protection and immunity against monkeypox virus from various smallpox vaccines <ul style="list-style-type: none"> ○ In some cases, smallpox vaccines caused side effects and contraindications, and third-generation smallpox vaccines that require two doses can be an impediment to rapid outbreak response ○ The Jynneos vaccine was identified as the safest vaccine available for pre-exposure and post-exposure use in preventing monkeypox ● The effects of the Modified Vaccinia Ankara-Bavarian Nordic vaccine was observed in a study of 7,339 monkeypox-infected patients in the U.S. immediately after receiving a single dose; the researchers found that 90 patients tested positive for monkeypox after the first day of administering the vaccine, eight monkeypox cases occurred more than 28 days after the first dosage and two of these occurred more than 14 days after receiving the second dose <ul style="list-style-type: none"> ○ Post-vaccination monkeypox occurred two weeks after administering the first dose ● One study examined behavioural changes in men who have sex with men (MSM) and transgender women in the U.S., and found that the most common mitigation strategies used by these groups included limiting the number of sexual partners they had, and limiting their exposure by avoiding crowded social venues where skin-to-skin contact is likely to occur <ul style="list-style-type: none"> ○ Approximately a quarter of participants became abstinent or avoided having any type of sex, asked their sexual partners if they have symptoms of monkeypox, or inspected their sexual partners for symptoms 	<ul style="list-style-type: none"> ● In Canada, the National Advisory Committee on Immunization (NACI) updated its interim guidance on the use of Imvamune on 16 September 2022 after considering the impact of dose-sparing strategies during periods of limited vaccine supply <ul style="list-style-type: none"> ○ The new guidance recommended that specific groups should be considered for vaccination, including men who have sex with men, individuals who self-identify as sex workers regardless of their self-identified sex/gender, and staff or volunteers who are in sex-on-premises venues where workers may have contact with fomites that are potentially contaminated with monkeypox ○ It also recommends that in the context of limited vaccine supply, those with prior history of monkeypox infection do not need to be vaccinated, first doses should be prioritized to meet demand for vaccinations before second doses are offered, and off-label intradermal administration can be used for immunocompetent adults as a second dose ● In Saskatchewan, an information sheet on Imvamune, including general information about the vaccine, its administration (including intradermal injection), and eligibility criteria, was updated on 3 October 2022 ● As of 6 October 2022, Manitoba health has expanded the eligibility criteria for monkeypox vaccination ● On 15 September 2022, Ontario’s Chief Medical Officer Dr. Kieran Moore reported that Ontario has administered 32,175 first doses of monkeypox vaccine ● Second doses of monkeypox vaccine began to be administered on 6 October 2022 in Quebec following a new supply of vaccines ● Vaccine eligibility and availability has also expanded in New Brunswick, Nova Scotia, P.E.I., Newfoundland and Labrador, the Yukon, and the Northwest Territories

Organizing framework domain	New evidence	New experiences
	<ul style="list-style-type: none"> • Researchers of a single study assessing surface swabs of areas in isolation rooms of confirmed monkeypox patients, personal protective equipment of healthcare workers and air samples in a U.K. hospital found that 56 (93%) out of 60 samples were found to be positive, indicating widespread environmental contamination, especially after clinical contact and changing of bedding • Another single study found that monkeypox incidence in 6,471 confirmed cases in 32 U.S. jurisdictions was found to be 14 times higher among unvaccinated individuals compared to those who had received their first dose of Jynneos vaccine ≥ 14 days earlier <ul style="list-style-type: none"> ○ The authors concluded that while the extent and durability is unknown, the Jynneos vaccine in single dosage has been shown to provide some protection against monkeypox infection 	<ul style="list-style-type: none"> • As of 23 September 2022, the vaccine eligibility criteria in Belgium have expanded and now permit individuals without a STI diagnosis in the last 12 months to be eligible for monkeypox vaccination • In France, as of 11 October 2022, 168,000+ doses have been delivered by the agency to the territories, and as of 10 October 2022, 120,128 doses have been administered to those at risk across the country • According to the National Institute for Public Health and the Environment in the Netherlands, 20,278 vaccine doses have been administered as of 29 September 2022 <ul style="list-style-type: none"> ○ This is up from 10,440 administered doses on 25 August 2022 ○ It takes up to six weeks for the full immune response to vaccination to take effect • According to the Portuguese Directorate-General for Health, as of 12 September 2022, a total of 437 people have been vaccinated • On 15 September, 2022, the CDC announced a new opportunity for jurisdictions to submit proposals for collaborative vaccination projects intended to expand access to disproportionately affected populations experiencing vaccination disparities • As of 11 October, 2022 906,325 vaccine doses were administered in 54 U.S jurisdictions • On 23 September, 2022 CDC updated the Monkeypox Vaccine Equity Toolkit which provides strategies, actions and resources to increase vaccination among populations most affected by monkeypox, but less likely to be vaccinated • On 11 October 2022, the High Authority of Health in France finalized the last of its recommendations regarding monkeypox vaccines <ul style="list-style-type: none"> ○ Its previous recommendation that both doses be administered within a 28–35-day interval is still in effect; however, it is now acknowledged that the second dose can be postponed should shortages in supply arise

Organizing framework domain	New evidence	New experiences
		<ul style="list-style-type: none"> ○ If an individual contracts monkeypox after administration of the first dose, the administration of a second dose is not necessary given the natural immunity conferred by infection ○ A recommendation has been put forth to include women who are occasional partners of, or live with at-risk men for pre-exposure vaccinations ○ Intradermal administration is only recommended for the second dose, and specifically in adults who received their first dose subcutaneously and had little to no side effects; it is not recommended for immunocompromised individuals, pregnant women, children, and those with a history of keloid scars ● Upon evaluating the data on intradermal application of monkeypox vaccinations, STIKO in Germany continues to recommend the subcutaneous administration of the Jynneos/Imvanex vaccine as opposed to delivering them intradermally ● In the U.K., second doses of the Jynneos vaccine are now being offered to those at highest risk and for whom two to three months have elapsed since their first dose <ul style="list-style-type: none"> ○ This is enabled by securing more vaccine doses as well as an expansion in using intradermal administration ● The UK Health Security Agency has used surveillance data, survey findings, and expert opinion to estimate that approximately 110,000 individuals are eligible for monkeypox vaccination in the U.K. ● A U.S. clinical trial is evaluating intradermal delivery of Jynneos monkeypox vaccine to expand vaccine supply ● In British Columbia, second doses are being offered as either a subcutaneous or intradermal injection ● On 19 September 2022, RKI in Germany updated their recommendations regarding the close contact management of monkeypox cases, which states that a quarantine mandate is no longer in place for contact persons

Organizing framework domain	New evidence	New experiences
		<ul style="list-style-type: none"> ○ Furthermore, housemates that have had no intimate contact with positive individuals or infectious material in the home have now been reclassified as category two contacts ● In the U.K., Monkeypox clade IIb (B.1 lineage), which is largely circulating during the current outbreak, has not been classified as a high-consequence infectious disease by the UK Health Security Agency; however, the other clades of monkeypox are classified as high-consequence infectious diseases and may be subject to different clinical and public-health responses
Diagnosis	<ul style="list-style-type: none"> ● In a mixed-methods study, saliva-based PCR tests for monkeypox were analyzed using an in vitro test performance assay for monkeypox alongside a systematic review examining saliva-based tests compared to lesion swabs <ul style="list-style-type: none"> ○ The assay showed in silico inclusivity of 100% for all (n= 97 strains) of the monkeypox virus, and the systematic review found that early detection of lesion swabs may indicate transmissibility through lesion development, while saliva-based testing may identify cases earlier than lesion-based tests ○ Adapting to SARS-Cov-2 testing sites may increase testing accessibility and capacity ● A prospective evaluation study (pre-print) recruited 50 individuals to evaluate the accuracy of patient self-collected skin lesions, pharyngeal, and rectal swabs, and found that the performance of self-collected and physician-collected samples was similar, suggesting that self-sampling is a reliable strategy for diagnosing monkeypox ● In another single study, serial laboratory testing of lesion and oropharyngeal swabs and blood testing were performed on 16 male monkeypox patients, and researchers determined that infectious virus was successfully isolated from lesion swabs, but not from oropharyngeal swabs and blood samples, suggesting that oropharyngeal swabs and blood samples alone carry the risk of false negative results, but may 	<ul style="list-style-type: none"> ● None identified

Organizing framework domain	New evidence	New experiences
	<p>hold value in pre-/asymptomatic cases or viral load monitoring</p> <ul style="list-style-type: none"> • One study (pre-print) examined the epidemiological characteristics, specimen collection practices, and cycle threshold values for monkeypox virus PCR tests performed at two reference laboratories in the U.S., and found that the viral load of positive specimens was comparable between both laboratories with variations being explained by differences in extraction strategies (e.g., the use of dry swabs) <ul style="list-style-type: none"> ○ When multiple specimens were collected for a single individual, the overall result concordance rate was greater than 95%, but submitting multiple specimens in separate tubes increased the workload of the laboratory staff and costs ○ Skin lesions showed the highest sensitivity • Researchers of a single study compared 13 pre-trained deep-learning models for monkeypox virus detection and selected the two best-performing fine-tuned models (Xception and DenseNet-169) for an ensemble method with an accuracy of 87.1% • The ensemble can discriminate measles and monkeypox as well as highly discriminate chickenpox 	
Clinical presentation	<ul style="list-style-type: none"> • A low-quality systematic review that examined the risk factors, transmission routes, and clinical characteristics of 3,097 monkeypox patients across 14 studies found that patients commonly reported mucocutaneous lesions (98.8%), a fever (63.5%), inguinal lymphadenopathy (55.4%), and asthenia (47.4%) <ul style="list-style-type: none"> ○ 7.2% of these cases led to hospitalization ○ Among the patients, 98.7% were men who have sex with men, 37.9% had a pre-existing positive HIV diagnosis, and 22.1% of patients had a concurrent sexually transmitted infection • An observational study assessed the demographics and clinical presentation of 48 confirmed monkeypox cases in 	<ul style="list-style-type: none"> • None identified

Organizing framework domain	New evidence	New experiences
	<p>Madrid, Spain and concluded that first symptoms included skin lesions (53.8%of individuals), fever (17.9%), and respiratory symptoms (12.8%), and one out 10 patients who had receptive anal sex had genital lesions compared to 12 out of 13 who had insertive anal sex</p> <ul style="list-style-type: none"> • Of the 4,080 cases of monkeypox virus that were evaluated in a low-quality systematic review, 7% of patients required hospitalization, and the most common clinical manifestations found were rash, fever, and lymphadenopathy <ul style="list-style-type: none"> ○ For a proper differential diagnosis, authors suggested to consider lymphadenopathy, which might differentiate monkeypox from other diseases, as well as the pattern of lesions distribution in genitalia and sexual history of confirmed cases ○ This review suggested that the mildness of the current outbreak might be attributed to a better quality of care offered to patients who live in high-income countries, and to the fact that patients in this outbreak are younger • Researchers of a single study analyzed the epidemiological and clinical characteristics of 226 confirmed cases of monkeypox infection in 29 countries from 1 May to 1 July 2022 and found that patients with HIV were more likely to experience diarrhea, perianal rash or lesions, and rash burden, and 13% were admitted to the hospital, 53% of whom had severe illness • 99% were male patients who identified as gay, bisexual or as having sex with men, and reported sexual or close intimate contact within the 21 days before symptom onset, and 40% of cases reported close contact with someone who had confirmed monkeypox 	
Prognosis	<ul style="list-style-type: none"> • None identified 	<ul style="list-style-type: none"> • As of 4 October, 2022, of the 674 confirmed cases of monkeypox in Ontario,, 99.3% are male and 0.7% female, 2.8% have been hospitalized, 0.3% have been in the ICU, and no deaths have been reported

Organizing framework domain	New evidence	New experiences
		<ul style="list-style-type: none"> • A unique case was identified in Italy where an Italian man was diagnosed with COVID-19, monkeypox, and HIV at the same time in July 2022, according to a case report <ul style="list-style-type: none"> ○ The man presented with COVID-19 symptoms nine days after he returned from a five-day trip to Spain, and after testing positive for COVID-19 on 2 July, he noticed a rash on his left arm which became more painful and spread across his body over the next few days ○ The man admitted that he had unprotected sex with other men while in Spain, and subsequently tested positive for monkeypox and HIV on 6 July • On 13 July, he no longer tested positive for COVID-19 and the monkeypox rash was mostly healed; he also began standard HIV treatment
Treatment	<ul style="list-style-type: none"> • A study examining the characteristics of patients in the U.S. treated with tecovirimat for monkeypox virus infection found that of the 369 patients observed, 99.8% were prescribed oral tecovirimat, and 93.1% were not hospitalized <ul style="list-style-type: none"> ○ The median interval from initiation of tecovirimat to subjective improvement was three days, and time to improvement of symptoms did not differ significantly with HIV infection status ○ Adverse events were reported in 3.5% of patients, and all but one adverse event were considered non-serious 	<ul style="list-style-type: none"> • On 7 October, 2022 CDC updated the Interim Clinical Considerations for management of ocular monkeypox virus infection <ul style="list-style-type: none"> ○ It provides guidance for healthcare facilities and healthcare professionals providing care for people infected with monkeypox virus • On 4 October, 2022 the CDC updated the Clinical Considerations for monkeypox in children and adolescents less than 18 years old • A U.S. clinical trial is evaluating the antiviral (tecovirimat TPOXX) for monkeypox • The government of Australia indicates that there are two therapeutic options for monkeypox: tecovirimat and vaccinia immunoglobulin <ul style="list-style-type: none"> ○ Tecovirimat has been shown to be well tolerated and active in vitro against orthopoxviruses, however, its use has not been approved for the treatment of monkeypox • Vaccinia immunoglobulin can be used alone or in combination with antivirals for the treatment of Vaccinia related complications

Table 3: Key findings from highly relevant documents and experiences from the previous versions of the LEP

Organizing framework domain	Evidence from previous version	Experiences from previous version
Biology	<ul style="list-style-type: none"> • Researchers of a primary study (pre-print) analyzed the monkeypox viral sequences that belong to the B.1 clade from the period of 1 January to 20 July 2022 and found that the 2022 monkeypox viral population has diverged into four lineages and 11 subgroups that were identified in Slovenia, Australia, Italy, Germany, and Spain • A pre-print single study described the first evidence of recombination of the monkeypox genome in natural transmission, which the authors concluded meant the monkeypox genome is evolving and expanding quickly (last updated 13 August 2022) • A pre-print single study identified a large number of mutations within the current outbreak clade, and indicated that there is a need for a fast response with genomic analysis of the newly detected strains to develop better prevention and treatment methods (Last updated 25 July 2022) • A single study found that the monkeypox virus strain isolated in 2018 is the same lineage as the current 2022 virus strains; however, 46 new mutations were observed in the monkeypox virus 2022 strains, concluding that the current monkeypox virus is prone to novel mutations (Published 29 July 2022) • One single study that explored the population transmission of Monkeypox virus (monkeypox virus) in West Africa (WA) (clade 2/3), and the Congo Basin (CB) (clade 1) revealed that based on phylogenetic evidence, the WA clade is the origin of all monkeypox strains, with clade CB splitting off 560-860 years ago <ul style="list-style-type: none"> ○ The study also found that there was virtually no mixing between the WA and CB clade, and that clade WA diverged less from an ancestral population than clade CB (published 14 July 2022) • In a single study phylogenomic analysis of available monkeypox virus genomes found that all monkeypox virus genomes were grouped into three clades: two previously characterized clades and 	<ul style="list-style-type: none"> • Countries and provinces examined characterize monkeypox as a viral zoonotic disease caused by an orthopoxvirus

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<p>a newly emerging clade that has genomes from the ongoing 2022 multi-country outbreak (published 12 July 2022)</p> <ul style="list-style-type: none"> • A single study reported that a mutational analysis showed signs of potential monkeypox human adaptation in ongoing microevolution (Published 24 June 2022) • A single study evaluated the performance and added value of the MinION real-time TGS sequencing device for sequencing the complete genome of a monkeypox virus strain, and concluded that the data obtained from directly sequencing DNA extracted from a lesion is sufficient to complete the genome of the virus (Published 24 June 2022) • A medium-quality systematic review and a non-systematic review reported that monkeypox is a zoonotic disease caused by the monkeypox virus which is a member of the orthopoxvirus genus (6/11 AMSTAR rating; literature last searched 15 August 2018; Published 12 November 2020) • A medium-quality systematic review and non-systematic review described that the monkeypox virus falls into two distinct strains, based on genetic, geographic, and phenotypic variation, these being the West African and the Congo Basin groups, with defined epidemiological and clinical differences (6/11 AMSTAR rating; literature last searched 15 August 2018; Published December 2019) 	
Epidemiology (including transmission)	<ul style="list-style-type: none"> • A U.S. CDC MMWR examined monkeypox, HIV, and sexually transmitted infections (STI) from eight jurisdictions in the U.S. and concluded that persons with HIV infection or STIs are disproportionately represented among persons with monkeypox, and that consideration should be given to prioritizing persons with HIV infection and STIs for monkeypox vaccination plans (published 7 September 2022) • A single study reported that high risk of infection with monkeypox usually comes from close contacts with skin lesions, and that skin lesions swabs are the most effective at detecting monkeypox DNA using PCR testing (published 7 September 2022) 	<ul style="list-style-type: none"> • The Public Health Agency of Canada (PHAC) reported a total of 1,321 cases of monkeypox in nine Canadian provinces and territories as of 9 September 2022 • In recent weeks, the province of Ontario has become the epicentre of the monkeypox disease in Canada, with 631 monkeypox cases being reported as of 9 September 2022 • As of September 6, 2022, of the 631 confirmed cases of monkeypox in Ontario, with 74.8% of confirmed cases reported by Toronto Public Health, 99.4% are male and 0.6% female <ul style="list-style-type: none"> ○ There are nine probable cases (100% are male) • The Director-General of the WHO, Tedros Adhanom Ghebreyesus, said at a press conference on 31 August 2022 that

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<ul style="list-style-type: none"> • A U.S. CDC MMWR reported that MSM have taken prevention measures (e.g., reduction in one-time sexual partners), which can have important implications for the trajectory of the monkeypox outbreak (published 2 September 2022) • A U.S. CDC MMWR surveyed 824 men about their willingness to reduce their chances of monkeypox infection in response to public-health messaging, of which 48% of survey respondents reported reducing their number of sex partners, 50% reported reducing one-time sexual encounters, and 50% reported reducing sex with partners met on dating apps or at sex venues since learning about the monkeypox outbreak <ul style="list-style-type: none"> ○ Survey data suggests racial, ethnic, and geographic differences in vaccination are partially attributed to issues surrounding equitable access • A primary study that used a capture-recapture method to estimate the true number of monkeypox infections in 10 of the most affected countries (Brazil, Canada, France, Germany, Italy, Netherlands, Portugal, Spain, the United Kingdom, and the United States) found that: <ul style="list-style-type: none"> ○ The number of infections in Brazil, France, Spain, and the U.K. could reasonably be more than three times the observed number ○ The estimated numbers of cases in Canada, Germany and Italy are above two times the observed ones, and Portugal shows an estimated ratio below two • An observational study evaluating clinical characteristics and complications of patients with a monkeypox infection in Bichat Claude Bernard university hospital in Paris, France identified 245 of 264 patients as men who have sex with men (MSM) and 90 who practised chemsex in the last three months <ul style="list-style-type: none"> ○ 112 patients had a contact with a confirmed monkeypox case, and the contact was of a sexual nature for 95% of the contacts ○ The majority of patients had fever (68%) and adenopathy (69%), and skin lesions mostly affected the genital (54%) and perianal (40%) areas 	<p>the “sustained downward trend” of monkeypox cases in Canada is an encouraging sign, and highlighted that despite several countries in the Americas seeing increased case counts, Canada appears to be an outlier</p> <ul style="list-style-type: none"> • As of 7 September, 2022, there have been 1,195 cases of monkeypox reported in the Netherlands • As of 8 September 2022, the government of Australia has reported 129 confirmed and probable cases of monkeypox, including 67 in Victoria, 50 in New South Wales, five in Western Australia, three in Queensland, two in the Australian Capital Territory, and two in South Australia • As of 13 September 2022, Belgium has reported a total of 744 monkeypox cases and one death within the country • As of 13 September 2022, there have been 3,833 confirmed cases of monkeypox in France • Among the new cases reported in France on 8 September 2022, 73 monkeypox cases were detected in females and nine were reported in children • As of 13 September 2022, there are 3,547 confirmed cases of monkeypox across all 16 federal states in Germany; only 14 female and three adolescent cases have been reported to date • As of 13 September 2022, Italy has reported 813 cases • As of 13 September 2022, Portugal has reported 898 confirmed cases • As of 13 September 2022, the U.S. has reported a total of 22,629 confirmed monkeypox cases • As of 9 September 2022, Spain has 6,884 cases, which is the highest in the European region, and second highest around the globe • Sweden has confirmed 165 cases of monkeypox and no deaths as of 13 September 2022 • The case count in the U.K. is 3,407 confirmed and 145 highly probable as of 12 September 2022 • Data collection on monkeypox cases and epidemiology is conducted through information entered in the Ontario Ministry

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<ul style="list-style-type: none"> • A now published single study (previously a pre-print) provided evidence of potential asymptomatic transmission of monkeypox between close contacts in Belgium (published 12 August 2022) • A single study conducted in a home within Texas, U.S. found a statistical difference detected for viable virus in cultures of porous versus nonporous surfaces after at least 15 days (published 11 August 2022) • A pre-print modelling study found that the number and duration of monkeypox infections were strongly affected by self-reporting behaviour of the primary case and the delay in the detection of the index case in South Korea (published 11 August 2022) • A medium-quality systematic review synthesized the evidence on the reproduction number and incubation period for the monkeypox virus in six countries from May and July 2022 <ul style="list-style-type: none"> ○ The incubation period ranged from five to 41 days for the West African clade of the monkeypox virus and from eight to 14 days for the Congo basic clade ○ Of the six countries with increasing confirmed cases, the United States had the highest reproductive number, estimated to be 1.55, and in 70 countries with cases, the estimated reproductive number of all aggregated cases was 1.29 ○ The study highlights that compared to earlier reproduction number estimates, transmission of the monkeypox virus may have slowed down recently due to increased awareness of the epidemic (5/10 AMSTAR from McMaster Health Forum; Published 26 July 2022) • A network modelling study (pre-print) simulated a monkeypox epidemic among the men who have sex with men (gbMSM) community, and found that unrecognized infections have an important impact on the epidemic, and could be reduced by contact tracing and vaccinating individuals with high risk of infection (Published 31 July 2022) • One single study (pre-print) found that as of 18 June 2022, 2,551 cases of monkeypox were confirmed from 56 populations, with England (n=550), Spain (n= 497), and Portugal (n=276) having the highest cumulative number of confirmed cases 	<p>of Health (MOH) integrated Public Health Information System (iPHIS) database and the Public Health Ontario Laboratory Information Management System</p> <ul style="list-style-type: none"> • A rapid communication in Italy reported 33 PCR-confirmed cases of monkeypox infection from patients attending a sexual health clinic in Milan, Italy, from 15 May to 7 July 2022 <ul style="list-style-type: none"> ○ All 33 patients were self-identified men who have sex with other men (MSM), with a median age of 38 years ○ For 32 cases, at least one analyzed anal swab was available, whereas all cases had at least one analyzed urethral swab • The Ministry of Health in Spain highlighted a reduction in the number of new cases which, according to the health authorities, cannot be attributed to vaccination efforts, given that a large vaccination campaign has not taken place in Spain, and most of the people immunized have only received a fraction of a dose • The UK Health Security Agency released a seventh technical briefing about the monkeypox outbreak in England on 2 September 2022 <ul style="list-style-type: none"> ○ The technical briefing places England at level two of four of outbreak transmission potential (transmission within a defined sub-population) ○ The risk assessment section provides an assessment of the current disease trajectory and observed severity, both in the U.K. and internationally ○ An epidemiological update is provided which presents insights from newly diagnosed cases, enhanced surveillance questionnaires completed by cases, and testing data ○ With respect to the observed reduction in incident cases, it is noted that this occurred too soon after the introduction of the vaccination program for it to be a major driver; rather, it is more likely that cases are declining due to some combination of infection saturation, changes in case ascertainment, and behavioural changes • The U.K. has confirmed the importation of one case of monkeypox with a travel link to West Africa

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<ul style="list-style-type: none"> ○ The study also found that the reproductive number (Ro) for Spain was statistically higher than those for England and Portugal between 18 May and 18 June 2022 (published 8 July 2022) <p>A single study (pre-print) described the global spatial landscape of orthopoxviruses (including monkeypox), and found significant spatial heterogeneity with population susceptibility from 57% to 96% based on demographic changes and waning of cross-protective immunity within a nation</p> <ul style="list-style-type: none"> ○ The authors indicated that lowest levels of susceptibility included parts of Finland, Bulgaria, Monaco, Japan, and Sweden, whereas the most susceptible countries were Australia, Yemen, Colombia, Guinea-Bissau, and Ethiopia <p>The authors noted that large countries such as India, China, Brazil, the U.S., and central and western Africa were notable areas for susceptibility (Published 30 July 2022)</p> <p>A single study (pre-print) deployed digital PCR assays that target genomic monkeypox virus (monkeypox virus) DNA in the routine wastewater surveillance program in the Greater Bay in the U.S. from 19 June to 20 July 2022, and found that monkeypox virus DNA was consistently detected in samples across the majority of test sites (8/9), with increasing concentrations of DNA over time</p> <ul style="list-style-type: none"> ○ Robust surveillance of monkeypox virus using wastewater testing can provide data for targeting public health resources and raise awareness among healthcare professionals so that they can better recognize and manage monkeypox cases (Last updated 26 July 2022) <ul style="list-style-type: none"> ● Crowdsourced predictions of global projections for confirmed monkeypox cases and deaths from 19 May and 24 May 2022 that were reported in a single study revealed that the probability for 30 to 100 countries reporting one or more infections by 31 July 2022 was 0.75, with fewer estimating that there would be 100 or more countries with reported infections (published 7 July 2022) ● A single study (pre-print) that investigated monkeypox cases in Bas-Uélé, Democratic Republic of Congo found that of 77 suspected cases that were tested in 106 households, 27.3% were 	<ul style="list-style-type: none"> ○ This patient has been admitted to hospital given that cases imported directly from West Africa are still considered high consequence infectious diseases <ul style="list-style-type: none"> ● The Public Health Agency of Canada (PHAC) reported a total of 1,228 cases of monkeypox in nine Canadian provinces and territories as of 26 August 2022 ● As of 25 August 2022, the government of Australia has reported 106 confirmed and probable cases of monkeypox, including 52 in Victoria, 43 in New South Wales, four in Western Australia, three in Queensland, two in the Australian Capital Territory, and two in South Australia ● As of 30 August 2022, Belgium has reported a total of 706 monkeypox cases within the country ● As of 30 August 2022, there have been 3,547 confirmed cases of monkeypox in France ● As of 30 August 2022, there are 3,455 confirmed cases of monkeypox across all 16 federal states in Germany; only 13 female and three adolescent cases have been reported to date ● As of 30 August 2022, Italy has reported 760 cases ● As of 25 August 2022, there have been 1,136 cases of monkeypox in the Netherlands ● As of 30 August 2022, Portugal has reported 846 confirmed cases ● As of 30 August 2022, Spain has 6,543 cases, which is the highest in the European region, and second highest around the globe ● According to the U.S. Centers for Disease Control and Prevention's 2022 Monkeypox Outbreak Global Map, Sweden has confirmed 157 cases of monkeypox and no deaths as of 30 August 2022 ● The case count in the U.K. is 3,279 confirmed and 134 highly probable as of 29 August 2022 ● As of 30 August 2022, the U.S. has reported a total of 18,416 confirmed monkeypox cases ● The British Columbia Centre for Disease Control publishes a weekly monkeypox epidemiological summary to provide insights into the populations affected by monkeypox in the province

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<p>positive for monkeypox, 58.4% for chickenpox, and 14.3% negative for both</p> <ul style="list-style-type: none"> ○ While no combination of identified symptoms – monomorphic skin lesions on the palms of hands and soles of feet – had a strong confirming power for decisive diagnosis, the study’s authors concluded that intensified surveillance of monkeypox in Africa is critical considering the current outbreak outside of Africa (published 6 July 2022) ● A single study that explored the population transmission of Monkeypox virus (monkeypox virus) in West Africa (WA) (clade 2/3), and the Congo Basin (CB) (clade 1) revealed that based on phylogenetic evidence, the WA clade is the origin of all monkeypox strains, with clade CB splitting off 560-860 years ago <ul style="list-style-type: none"> ○ The study also found that there was virtually no mixing between the WA and CB clade, and that clade WA diverged less from an ancestral population than clade CB (published 14 July 2022) ● Another single study (pre-print) identified monkeypox virus genomes in multiple domestic locations from an imported case of monkeypox in a traveler that had returned from Nigeria to the United Kingdom, confirming that there is a potential for the monkeypox virus to be recovered in environmental settings associated with known positive cases (published 15 July 2022) ● One single study (pre-print) investigated the asymptomatic transmission of monkeypox from a sample of male sexual health clinic attendees in Belgium and identified three positive cases, none of whom reported symptoms (pre- and post-sampling) or contact with confirmed cases <ul style="list-style-type: none"> ○ This study provided evidence of potential asymptomatic transmission of monkeypox between close contacts (published 5 July 2022) ● An observational study that reported on confirmed cases of monkeypox diagnosed at an STI clinic in Madrid from 18 May to the beginning of June 2022 found that all 48 patients assessed were cisgender men with a median age of 35, among whom the most prevalent symptoms were the presence of vesicular- 	<ul style="list-style-type: none"> ● Current data from British Columbia points to the importance of close, intimate contact during sex in driving the spread of monkeypox ● The UK Health Security Agency released a sixth technical briefing about the monkeypox outbreak in England on 19 August 2022 <ul style="list-style-type: none"> ○ The technical briefing places England at level two of four of outbreak transmission potential (transmission within a defined sub-population) ○ The risk assessment for the U.K. provides an assessment of the current disease trajectory and observed severity, both in the U.K. and internationally ○ An epidemiological update is provided which presents insights from newly diagnosed cases, enhanced surveillance questionnaires completed by cases, and testing data ○ With respect to transmission dynamics, the briefing posits that there is negative daily case growth, but cases are increasingly geographically spread ● The fifth edition of the technical briefing provides an extensive list of priority research questions regarding the current monkeypox outbreak, as well as a list of studies underway that the UK Health Security Agency is participating in ● The case count in the U.K. is 3,081 confirmed and 114 highly probable as of 15 August 2022 ● As of 16 August 2022, Belgium has reported a total of 546 monkeypox cases within the country ● As of 16 August 2022, there are 3,186 confirmed cases of monkeypox across all 16 federal states in Germany ● As of 16 August 2022, Italy has reported 662 cases ● According to the U.S. Centers for Disease Control and Prevention’s 2022 Monkeypox Outbreak Global Map, Sweden has confirmed 130 cases of monkeypox as of 16 August 2022 ● As of 16 August 2022, the U.S. has reported a total of 12,688 confirmed monkeypox cases

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<p>umbilicated and pseudo-pustular skin lesions (93.8%), asthenia (66.6%), and fever (52.1%)</p> <ul style="list-style-type: none"> ○ 89.5% of the patients had unprotected sex in the three weeks before the onset of the symptoms, and a statistical relation was found between the location of the lesions and the role of the patients regarding sexual practices ○ Sequencing analysis indicated the virus circulating in Spain belongs to the western African clade (published 10 July 2022) ● Another observational study describing the characteristics of 54 confirmed monkeypox patients that attended open access sexual health clinics in London, UK between 14 May and 25 May 2022 identified that all patients were men who have sex with other men (gbMSM) who presented with skin lesions <ul style="list-style-type: none"> ○ Most patients reported feeling fatigue and having a fever, were white, born in the UK, and were a median age of 41 (published 1 July 2022) ● A systematic review is currently underway on monkeypox as a sexually transmitted disease ● A single study reported on the creation of an open-access database to track the incidence of monkeypox across multiple countries <ul style="list-style-type: none"> ○ Working with the WHO Hub for Pandemic and Epidemic Intelligence, the team is defining a contact data schema allowing countries and researchers to estimate key epidemiological parameters such as incubation period and serial interval across various settings (Published 1 July 2022) ● A modelling study (pre-print) simulated the spread of monkeypox in a hypothetical metropolitan area (including high- and low-risk transmission among humans and animals to humans), which found that the monkeypox virus may spill over from high-risk groups to broader populations if transmission increases within the high-risk group but could be reduced by at least 65% through public-health measures (e.g., quarantine, contact tracing) (Published 29 June 2022) ● A modelling study simulated a population of 50 million people with socioeconomic and demographic characteristics of a high-income European country 	<ul style="list-style-type: none"> ● In recent days, the province of Ontario has become the epicentre of the monkeypox disease in Canada ● On 13 August 2022, the Saskatchewan Health Authority warned the public about an “elevated risk” of contracting monkeypox through anonymous sexual contact as a result of the recently identified cases associated with this source of transmission ● The UK Health Security Agency released a fifth technical briefing about the monkeypox outbreak in England on 12 August 2022 ● A report by the CDC suggests that among the cases with reported classification by health departments, 74% of cases were locally acquired ● The percentage of locally acquired cases increased from 51% to 82% from 17 May to 2 July and from 3 July to 22 July 2022, respectively ● According to Dr. Tam’s recent remarks at a press conference on 27 July 2022, over 99% of the monkeypox cases in Canada for whom additional information is available are male with a median age of 36 years ● The National Institute for Public Health and the Environment report published on 2 August 2022 in the Netherlands indicates that anyone can get monkeypox and infections with the virus occurs in all age categories; however, most of the recent infections have involved gbMSM contact, with the highest risk of infection being among men who have sex with multiple partners <ul style="list-style-type: none"> ○ Monkeypox is transmitted through intimate contact (kissing, making love, and sexual intercourse) with an infected person, and can also be transmitted occasionally through unprotected contact with contaminated materials ○ The virus can spread via droplets of fluid from the blisters or from the mouth and nose, though the risk of this is low ○ The scabs from the blisters can also transmit the virus ○ Blisters may form in less visible locations, including the mouth or inside the rectum, where they may look like ulcers ● The UK Health Security Agency released a technical briefing about the monkeypox outbreak in England on 19 July 2022

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<ul style="list-style-type: none"> ○ The baseline scenario projected that with no public health emergency interventions, monkeypox could lead to small national outbreaks of moderate duration, but they would all subside in 23 to 37 weeks, depending on the number of cases introduced ○ Contact tracing with isolation of symptomatic cases would reduce the number of secondary cases by 72.2% following the introduction of 3 cases, 66.1% after 30 cases, and 68.9% after 300 cases ○ Adding ring vaccination to contact tracing would reduce the number of secondary cases by 77.8% following the introduction of 3 cases, 78.7% after 30 cases, and 86.1% after 300 cases (Published 23 June) ● A single study (pre-print) reported on the findings of an online survey completed by 856 U.S. residents (51% female, 41% with a college degree or higher, 38% were 55 years or older) about their knowledge, attitudes, and perceptions about monkeypox <ul style="list-style-type: none"> ○ The respondents reported that the most reliable information came from healthcare professionals, health officials (e.g., Centers for Disease Control and Prevention), and social media accounts of healthcare professionals and researchers ○ Almost half the respondents (47%) feel that their knowledge level about monkeypox is poor or very poor ○ Current COVID-19 vaccination status was a strong predictor of positive intentions of receiving a monkeypox vaccination if recommended ● The low levels of knowledge about monkeypox indicate the need for more clear communication about the outbreak (Published 23 June 2022) ● A non-systematic review reported that monkeypox transmission in healthcare settings outside of endemic regions found that although many exposures in healthcare settings have been documented, only a single transmission event has been reported (Published 9 June 2022) ● A non-systematic review conducted a pooled analysis of 124 cases in Italy, Australia, Czech Republic, Portugal, and the United 	<p>which places the monkeypox outbreak at level 2 of potential transmission (transmission within a defined sub-population)</p> <ul style="list-style-type: none"> ● The technical briefing also includes sections about risk assessment for several outbreak dynamics, an epidemiological update, findings from enhanced surveillance questionnaires, transmission dynamics, and clinical experiences ● The Public Health Agency of Canada reported a total of 604 cases of monkeypox in Canadian provinces and territories as of 20 July 2022, with 320 cases confirmed in Québec, 230 cases in Ontario, 12 cases in Alberta, two cases in Saskatchewan, and 40 cases in British Columbia ● Confirmed cases of monkeypox in Canada are reported to the Public Agency of Canada (PHAC) and updated weekly by province or territory on their website ● Monkeypox cases in Canada have spiked in recent days, with Québec continuing to be the epicentre of the disease in Canada <ul style="list-style-type: none"> ○ The spread of monkeypox continues to be primarily among men who have sex with men, but experts continue to remind the public that the characteristics of the virus do not restrict it to one group ● Cases have generally risen sharply across other jurisdictions as well, with as of 19 July 2022, 41 cases reported in Australia, 311 in Belgium, 1,435 in France, 374 cases in Italy, 656 cases in the Netherlands, 3,125 cases in Spain, 71 in Sweden, 2,137 in the UK, and 2,107 in the U.S. <ul style="list-style-type: none"> ○ 2,110 cases have been reported in Germany as of 20 July 2022 ● The Institute of Tropical Medicine in Belgium is conducting a study to investigate “asymptomatic shedding” and the risk of Monkeypox infection ● The Directorate-General for Health in Portugal has noted that the use of condoms is not likely to provide effective protection from monkeypox and the CDC in the U.S. notes that efforts are still underway to determine whether monkeypox can spread through semen or vaginal fluids

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<p>Kingdom, and found that the current monkeypox epidemic differs from previous outbreaks in terms of age (54.29% of individuals in their 30s), gender (most cases being males), risk factors and transmission route, with sexual transmission being highly likely</p> <ul style="list-style-type: none"> ○ Risk factors included being male, having sex with other men, human immunodeficiency virus positivity, and a history of previous sexually transmitted infections (Published 8 June 2022) ● A single study (pre-print) reported on the incubation period for monkeypox in the Netherlands and found that the average incubation period was 8.5 days and can reach up to 17 days, which the authors concluded that these findings supports the use of 21 days for monitoring or quarantining close contacts to limit the spread of monkeypox infection (Published 13 June 2022) ● A single study assessed the effect of an enhanced surveillance approach to detect monkeypox virus (monkeypox) cases in Nigeria, which involved community volunteers who were trained to conduct active case searches and follow-up in addition to surveillance support, and found that this approach improved reporting of monkeypox in hotspots (Published 25 May 2022) ● A single study (pre-print) reported on a branching process transmission model and found that the basic reproduction number for monkeypox could be substantially larger than one among men who have sex with men (gbMSM) sexual contact network, and recommended that ongoing support and public health messaging should be implemented for prevention and early detection within the gbMSM network who have a large number of partners (Published 13 June 2022; Pre-print) ● As of 2 June 2022, 780 laboratory confirmed cases have been notified to WHO under the International Health Regulations (IHR) or identified by WHO from official public sources in 27 non-endemic countries in four WHO regions (Published 4 June 2022) <ul style="list-style-type: none"> ○ Preliminary data from PCR assays indicate that the monkeypox virus strains detected in Europe and other non-endemic countries belong to the West African clade 	<ul style="list-style-type: none"> ● In an announcement on 4 July 2022, the Public Health Agency of Canada (PHAC) noted that the possibility and extent of respiratory transmission is of monkeypox is “unclear at this time” ● The public health agencies of the four UK nations have agreed that the current outbreak clade of monkeypox does not classify as a high consequence infectious disease given that there has been no observed mortality in the UK and there are interventions available <ul style="list-style-type: none"> ○ However, importation of monkeypox directly from West Africa and cases caused by the Congo basin clade will still be classified as high consequence infectious diseases ● The UK Health Security Agency is publishing an updated epidemiological overview of the current monkeypox outbreak every Tuesday and Friday; the report includes information regarding the nation, region, and age of new cases ● The UK Health Security Agency has published a technical briefing investigating the monkeypox outbreak in England which contains sections about the following: <ul style="list-style-type: none"> ○ Assessed level of the outbreak in England ○ Research and evidence gaps prioritisation ○ Epidemiologic update, including findings from rapid sexual health questionnaires completed by cases ○ Transmission dynamics ● In Portugal, the Directorate-General for Health suggested that transmission is occurring through close contact, including sexual intercourse ● The UK Health Security Agency has published a technical briefing investigating the monkeypox outbreak in England which addresses: <ul style="list-style-type: none"> ○ Assessed level of the outbreak in England ○ Research and evidence gaps prioritisation ○ Epidemiologic update, including findings from rapid sexual health questionnaires completed by cases ○ Genomic information ○ Transmission dynamics

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<ul style="list-style-type: none"> ○ Currently, the public-health risk at the global level is assessed as moderate, however the public-health risk could become high if the virus establishes itself in non-endemic countries as a widespread human pathogen ● WHO provides the following interim advice: <ul style="list-style-type: none"> ○ All countries should be on the alert for signals related to people presenting with a rash that progresses in sequential stages that may be associated with fever, enlarged lymph nodes, back pain, and muscle ache ○ Increasing awareness among potentially affected communities, as well as healthcare providers and laboratory workers, is essential for identifying and preventing further cases and effective management of the current outbreak ○ Caring for patients with suspected or confirmed monkeypox requires early recognition through screening protocols adapted to local settings; prompt isolation and rapid implementation of appropriate infection, prevention and control measures; testing to confirm diagnosis; symptomatic management of patients with mild or uncomplicated monkeypox; and monitoring for and treatment of complications and life-threatening condition ● A non-systematic review reported that monkeypox cases have been growing across an expanding number of non-endemic countries in recent months <ul style="list-style-type: none"> ○ Future outbreaks are likely to increase in size and frequency due to the cessation of smallpox vaccine programs, which provide cross-protection ○ Based on global travel trends, traveller volumes originating from flights from countries where monkeypox is endemic are greatest to Paris, London, Dubai, Johannesburg, and Brussels ○ Supporting endemic countries by strengthening laboratory capacity and increasing timely access to smallpox vaccination for close contacts can help mitigate further chains of transmission (Published 31 May 2022) ● A non-systematic review by the European Centre for Disease Prevention and Control (ECDC) reported monkeypox cases 	<ul style="list-style-type: none"> ● Monkeypox cases have continued to spread in non-endemic countries in Europe, Australia, the United States and Canada ● Canada’s Chief Public Health Officer, Dr. Theresa Tam reported at a news conference on 3 June 2022 that a disproportionate number of the confirmed cases in Canada are among gay and bisexual men, but warned that anyone can be potentially susceptible to the disease <ul style="list-style-type: none"> ○ Dr. Tam encouraged public-health officials to learn from the experience of the HIV/AIDS epidemic and to involve communities that have the most impacts right from the start. ● To date, transmission within and across countries appears to be circulating below the detection of surveillance systems. In the U.K., contact-tracing investigations have linked transmission to gay bars, saunas, and the use of dating applications in the U.K. and abroad, but no single factor or exposure linking all cases has been identified ● Human monkeypox was first identified in the Democratic Republic of the Congo in 1970 and has since been reported across several other central and western African countries and occasionally in countries outside of Africa including in the United States (47 cases in 2003 and one in 2021), the United Kingdom (four cases in 2018-19 and three in 2021), Israel (one case in 2018), and Singapore (one case in 2019). As of Wednesday 25 May 2022, there were 219 confirmed cases outside of countries in which monkeypox is endemic ● Monkeypox can spread to humans via animals (rodents and primates) as well as other humans and contaminated objects such as bedding. Animal-to-human transmission may occur by bite or scratch, bushmeat preparation, direct contact with body fluids or lesion material, or indirect contact with lesion material, such as through contaminated bedding ● Human-to-human transmission is thought to generally occur through large respiratory droplets requiring prolonged face-to-face contact

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<p>across nine countries (Austria, Belgium, France, Germany, Italy, Portugal, Spain, Sweden, and the Netherlands)</p> <ul style="list-style-type: none"> ○ Countries should update their contact-tracing mechanisms and review availability of smallpox vaccines, personal protective equipment, and antivirals ○ Healthcare workers should wear gloves, water-resistant gowns, and FFP2 respirator when screening suspected cases or caring for monkeypox cases ○ Proactive risk communication and multiple community-engagement activities should be implemented to provide updates and increase awareness for those at risk and the wider public (Published 23 May 2022) <ul style="list-style-type: none"> ● A single study reported two cases of monkeypox within two white British men <ul style="list-style-type: none"> ○ The study indicated that skin lesions at the point of sexual contact were likely the primary location of infection, which was followed lymphadenopathy, fever, headache, and diarrhea ● The authors concluded that healthcare workers should use appropriate PPE and receive education on clinical pathways to manage possible monkeypox cases, and encouraged collaborative efforts with clinicians and patients to ensure sensitive community engagement/education to avoid stigmatization ● A medium-quality systematic review reported that outside of the Democratic Republic of Congo (DRC), there has been a notable increase in number of individual monkeypox outbreak reports between 2010 and 2018, particularly in the Central African Republic, but the authors noted that this does not necessarily translate to an increase in annual cases over time in these areas <ul style="list-style-type: none"> ○ In Nigeria, geographical patterns of infections suggest a possible new and widespread zoonotic reservoir (6/11 AMSTAR rating; literature last searched 15 August 2018) ● A single study pre-print conducted in the Democratic Republic of Congo found that 70% of cases reported a generalized skin eruption within three weeks of contact with a person infected with monkeypox (Last updated 5 June 2022; Pre-print) 	<ul style="list-style-type: none"> ● An infected pregnant women may also pass monkeypox on to their developing fetus

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<ul style="list-style-type: none"> • A low-quality systematic review reported that from 2009-2019 there have been almost 20,000 suspected or confirmed cases of monkeypox and of those cases, one case was in Israel in 2018, three in the UK in 2018 and one in 2019, and one in Singapore in 2019 <ul style="list-style-type: none"> ○ The median age at presentation has increased from four to five years old from 1970-1989 to 21 years in 2010-2019, with cases outside of Africa even higher and occurring most frequently in adult males ○ The authors hypothesize that this increase may be due to the cessation of smallpox vaccinations, which provided some cross-protection against monkeypox (4/11 AMSTAR rating; literature last searched 7 September 2020) • A non-systematic review reported that the two possible means of monkeypox virus transmission are animals-human transmission and human-human transmission, and respiratory droplets and contact with body fluids, contaminated patient’s environment or items, skin lesion of an infected person associated with inter-human transmission (Published 12 November 2020) <ul style="list-style-type: none"> ○ Animal-to-human transmission occurs through direct contact with the above viral hosts or by direct contact with blood ○ Human-to-animal transmission has not been reported • A non-systematic review reported that the frequency and geographic distribution of human monkeypox cases across West and Central Africa have increased in recent years <ul style="list-style-type: none"> ○ Monkeypox is largely found in rodents and has been detected in squirrels, rats, mice, and monkeys ○ Indirect or direct contact with live or dead animals is assumed to be the main source of human monkeypox infections ○ Secondary human-to-human transmission is considered common and presumably occurs through respiratory droplets or indirect or direct contact with body fluids, lesion material and contaminated surfaces or other material (Published December 2019) 	

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<ul style="list-style-type: none"> • A non-systematic review indicated that transmission to humans is primarily by exposure to animal reservoirs (primary zoonotic transmission), such as squirrels (Published April 2019) • A non-systematic review reported that the current evidence indicates that an outbreak is caused by multiple sources emerging into the human population, and is not sustained by human-to-human transmission; however, most cases are reported individually which prevents an accurate picture of the overall transmission <ul style="list-style-type: none"> ○ There are current knowledge gaps in the epidemiology, host reservoir, emergence, transmission, pathogenesis, and prevention of monkeypox • A single study described an imported case of monkeypox from Nigeria to the United Kingdom, whereby secondary transmission occurred within the family <ul style="list-style-type: none"> ○ After arrival, case one developed a vesicular lesion, day 19 an 18-month old child within the family developed lesions, and by day 33, an adult member developed a vesicular rash and confirmed with monkeypox through PCR testing ○ 30 contacts were identified for active surveillance as they had direct exposure of broken skin or mucous membrane to a symptomatic patient (Published 21 August 2021) • A single study found that in the Democratic Republic of the Congo, the incidence of monkeypox from 2011-2015 was lower among those presumed to have received smallpox vaccination than among those presumed unvaccinated <ul style="list-style-type: none"> ○ The highest incidence was among 10-19-year-old males, the cohort reporting the highest proportion of animal exposures (37.5%) ○ The authors concluded that the increase in the incidence of monkeypox might be linked to declining immunity provided by smallpox vaccination (Published 4 June 2021) • A single study used historical data from the Democratic Republic of the Congo to estimate the reproduction number (R) and basic reproduction number (R0) of smallpox and monkeypox in a population with imperfect immunity 	

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<ul style="list-style-type: none"> ○ With data from 2011-2012 that indicate a 60% population immunity against orthopoxvirus species, the R value for monkeypox was calculated to be 0.85 (UI: 0.51-1.25) (Published 8 July 2020) ● A single study described the transmission of monkeypox virus from an investigation that Public Health England (PHE) conducted of two unrelated cases of monkeypox that affected travelers returning from Nigeria <ul style="list-style-type: none"> ○ Transmission of monkeypox occurred between the second patient to a healthcare worker, most likely the only exposure risk identified during assessment of the infected healthcare worker was the changing of potentially contaminated bedding, when patient 2 had multiple skin lesions but before a diagnosis of monkeypox had been considered (Published April 2020) ● A single study examined the association between exposure to rodents and non-human primates with rash severity amongst confirmed cases from the monkeypox surveillance program in the Democratic Republic of the Congo <ul style="list-style-type: none"> ○ The authors reported no association found between rodent exposure and monkeypox rash severity (Published 24 December 2019) ● A single study described the the seroprevalence of orthopoxviruses amongst employees of a primate sanctuary and residents of nearby villages in Cameroon <ul style="list-style-type: none"> ○ Forty-three participants (34.4%) were IgG positive for anti-orthopoxvirus antibodies; however, amongst those born after the era of routine smallpox vaccination only four (6.3%) were positive for anti-orthopoxvirus antibodies ○ The authors concluded that presence of anti-orthopoxvirus antibodies in individuals born after the era of smallpox vaccination suggests the possibility of asymptomatic circulation of an orthopoxvirus (which was most likely monkeypox) in human populations (Published 25 November 2019) ● A single study reported the epidemiological features of the 2017 to 2018 human monkeypox outbreak in Nigeria, the largest 	

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<p>documented human outbreak of the west African strain of the monkeypox virus</p> <ul style="list-style-type: none"> ○ Data was collected with a standardized form based on a case definition of human monkeypox from previously established guidelines ○ Diagnosis of the human monkeypox virus infection was confirmed by viral identification with real-time PCR and detection of antibodies ○ The results showed that 122 confirmed or probable cases of human monkeypox was recorded in 17 states of Nigeria, infecting individuals from the ages of two to 50 years ○ All patients had rashes on all parts of the body, fever, headaches, and lymphadenopathy ○ The results suggest endemicity of monkeypox virus in Nigeria, with some evidence of human-to-human transmission (Published August 2019) ● A single study reported an outbreak investigation involving human monkeypox cases from four districts (Impfondo, Betou, Dongou, and Enyelle) in the Likouala department of the Republic of the Congo <ul style="list-style-type: none"> ○ The results showed that there were no epidemiologic links between cases from different districts, and all hypothesized human to human transmission events appeared to have been contained within the individual districts ○ There was no evidence suggesting that the virus was introduced from neighbouring countries ○ The authors noted some challenges associated with the remote regions of the districts, such as limited health and transportation infrastructure, absence of specimen collection supplies, and a well-functioning cold chain, that would have resulted in inconsistent and incomplete reporting (Published February 2019) ● A single study found that rope squirrels shed large quantities of the virus and for long periods, supporting the hypothesis that they play a potential role in monkeypox virus transmission to humans 	

Organizing framework domain	Evidence from previous version	Experiences from previous version
	and other animals in the Central African region (Published 21 August 2017)	
Prevention and control	<ul style="list-style-type: none"> • A high-quality guideline from France describes prevention and control measures for patients, healthcare workers, children, schools, and transportation (high-quality AGREE II rating; published in Clinical Microbiology and Infection) • A pre-print single study from Bangladesh indicated that while individuals were aware of monkeypox, there was limited understanding of its transmission pathways (pre-print; last updated 1 September 2022) • A pre-print single study measured antibodies among historically smallpox-vaccinated, monkeypox PCR-positive and recently vaccinated individuals with Jynneos, and found that the immunization series yielded low levels of neutralizing antibodies, but a third vaccination further boosted the response (pre-print; last updated 1 September 2022) • A single study using Natural Language Processing (NLP) techniques aimed to understand the attitudes of the public towards monkeypox on Twitter, with the authors suggesting that the public has not yet panicked about monkeypox <ul style="list-style-type: none"> ○ Negative sentiments included deaths, the severity of the virus, lesions, whether the virus is airborne, vaccines, and how the virus would affect daily and travel activities (published September 2022) • A recently published low quality rapid review found that two replication-competent (ACAM2000 and APSV) and one replication-deficient (MVA-BN) vaccinia virus vaccines were effective against orthopoxvirus, including the monkeypox virus • ACAM2000 showed immunogenic effect and efficacy against monkeypox infection, although there are adverse effects, including myocarditis/pericarditis • MVA-BN has been approved in the U.S. and Canada as a vaccine for the prevention of monkeypox infections • Of the 1,932 respondents to a cross-sectional survey (from 15 June and 27 July 2022) on the monkeypox outbreak in the U.K., 	<ul style="list-style-type: none"> • As of 13 September 2022, 902 doses of vaccine have been administered across Manitoba • On 9 September 2022, Nova Scotia announced that it aims to soon offer the monkeypox vaccine to people at highest risk of exposure, such as members of the LGBTQ community • The Halifax Sexual Health Centre will host a free pre-exposure clinic as soon as the week of 19 September 2022 • In Nunavut, the Nunavik Regional Board of Health and Social Services recommends that anyone with symptoms should call their local community service centres or Nursing Stations to ask for an appointment to confirm, and follow public-health measures such as self-isolation, wearing a mask and covering skin lesions until healed <ul style="list-style-type: none"> ○ For now, the supply of vaccines in Nunavut are reserved for those who have had close contact with someone who has tested positive, and for men who have had or will have sexual contacts with at least one new male partner • In France, as of 8 September 2022, 152,000+ doses have been delivered by the agency to the territories and 84,740 doses have been administered to those at risk across the country • The New South Wales government in Australia expects to receive up to 30,000 vaccine doses at the end of September and 70,000 doses in early 2023 • In Germany, 5,300 monkeypox doses were delivered to the federal states in July 2022 and another 19,500 were delivered during the week of 29 August 2022 • As of 6 September 2022, 461,049 vaccine doses were administered in 35 U.S jurisdictions • On 29 August 2022, The U.S. Department of Health and Human Resources (HHS) announced that it will provide approximately \$11 million to support the first U.S.-based fill and finish manufacturing of Jynneos – a vaccine approved to prevent smallpox and monkeypox

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	<p>34% reported a limited understanding of public-health information on monkeypox, 52% considered themselves at risk, 61% agreed people infected with monkeypox should isolate for 21 days, 49% reported they would first attend a sexual health clinic if infected, 86% reported they would accept a vaccine, and 59% believed monkeypox originated from animals</p> <ul style="list-style-type: none"> • The group of respondents was made up largely of white, employed men who have sex with men with university education, and the sources of information trusted most by respondents were healthcare professionals (37%), official health agencies (29%), and mainstream media (12%) • One pre-published primary study found that a monkeypox clinical decision support system (CDSS) tool that was developed and implemented into the electronic health record of a large integrated healthcare system in Massachusetts and New Hampshire identified areas to improve the efficiency of diagnostic evaluation and to alert clinicians of the monkeypox work-up in progress and infection control protocols in real-time • In another pre-published study, the monkeypox epidemic within the U.K. population was assessed by simulating control options over a 12-week projection period using a discrete population transmission model, where the researchers found that the monkeypox virus may have already infected a significant portion of men-who-have-sex-with-men (MSM) with the highest sexual activity • The case incidence flattened, and researchers predicted that a decline will follow with continued immunity through vaccination among targeted groups and a behavioural-driven decrease in the transmission rate of infected individuals • Optimal vaccine allocation was explored in a study using a deterministic compartmental model to simulate the rollout of 5,000 vaccines over 15 days among two representative gay, bisexual, and other men who have sex with men (GBMSM) networks in Ontario cities; the city sizes, epidemic potentials (R_0), mixing between cities, and distribution of imported cases between cities were varied in the modelling 	<ul style="list-style-type: none"> • As of 6 September, 2022 HHS awarded a \$20-million contract to AmerisourceBergen to expand and quicken distribution of vaccines and treatments for monkeypox • On 1 September 2022, the Institute of Tropical Medicine (ITM) in Belgium announced that moving forward, it will be administering monkeypox vaccines intradermally through a micro-dosing technique; this economical process will enable 2.5-times more vaccines to be given to those at risk • On 8 September 2022, researchers at ITM released four recommendations to help slow the spread of the monkeypox outbreak • The UK Health Security Agency has produced three leaflets targeted at patients to answer questions about the vaccine, vaccine eligibility, and intradermal injection • As of 11 August 2022, the Government of Canada has distributed over 99,000 doses of Imvamune vaccine to provinces and territories, and more than 50,000 people have been vaccinated in Canada • In Australia, the New South Wales government began vaccinating people at highest risk from monkeypox from 8 August 2022 using the Jynneos vaccine <ul style="list-style-type: none"> ○ 30,000 further doses of the Jynneos vaccine are expected at the end of September and 70,000 doses are expected in early 2023 • In Belgium, the Imvanex and Jynneos vaccines are currently the only ones to have received regulatory approval for monkeypox • Given the limited supply and availability of monkeypox vaccines, the first phase of the vaccination campaign is focused solely on vaccinating those on an invitational basis (e.g., male and transgender sex workers; men who have sex with men and are HIV positive or are taking pre-exposure prophylaxis and have had at least two sexually transmitted infections in the last year; at-risk individuals, including those with immune disorders or those at high-risk contact and increased risk of infection) or through referrals from their specialist.

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	<ul style="list-style-type: none"> • The modelling revealed that a fixed number of vaccine doses can avert more infections over the short term when they are prioritized to a network with more initial infections, a larger transmission network, and a network with greater epidemic potential • The researchers of a pre-published study explored the intentions of healthcare workers (HCWs) in France and Belgium to get vaccinated against monkeypox, and found that of the 397 HCWs who responded to the study's online survey from 15 June to 8 August 2022, 55.4% said that they would probably get the monkeypox vaccine, while 79% said that they would accept the vaccine if it was recommended for the general public • Those who had a favourable attitude towards monkeypox vaccination in HCWs were more likely to have COVID-19 vaccine eagerness and concerns about monkeypox epidemics • The authors of a medium-quality systematic review that assessed saliva-based polymerase chain reaction (PCR) for orthopoxviruses concluded that these types of tests are potential tools for outbreak control (5/10 McMaster Health Forum AMSTAR rating; published 9 August 2022) • A pre-print single study reported on the willingness and determinants of behaviour change of individuals within the gbMSM network to reduce monkeypox transmission, where the authors concluded that there was an overall intention from individuals to reduce the number of sexual partners, especially among individuals who were not on PrEP (published 3 August 2022) • A pre-print modelling study found that the critical threshold to vaccinate depends on the basic reproduction number of the monkeypox virus and on other public-health measures (published 2 August 2022) • A pre-print single study described the outcomes of vaccinating high-risk contacts receiving Imvanex smallpox vaccine as an early post-exposure ring vaccination, where authors concluded that the 	<ul style="list-style-type: none"> • Future stages of the vaccination campaign are expected to occur once there is an increase in vaccine delivery to Belgium, which is expected to take place by November 2022 • In France, as of 11 August 2022, 52,000+ doses have been delivered by the Agency to the territories • In addition to the 40,000 smallpox vaccine doses ordered by Germany, the number of vaccine doses expected to be secured later on has reached 200,000 • The government of Australia is continuing to update its guidance for the Jynneos and ACAM2000 vaccines currently in circulation • In Belgium, the second phase of the campaign, which focuses on prevention, has commenced, allowing individuals with two sexually transmitted infections in the last year to be eligible for vaccinations, and additional changes to eligibility are expected to take place by November 2022 by which time Belgium will receive an estimated 30,000 doses • In France, as of 23 August 2022, 103,000+ doses have been delivered by the Agency to the territories • According to the National Institute for Public Health and the Environment, one-third of the target group is now vaccinated against monkeypox as of 25 August 2022 in the Netherlands, with 10,440 vaccines administered • In Spain, an additional 5,000 doses of the monkeypox vaccine will arrive on 30 August 2022 and 31 August 2022 • The doses of Imvavex come from centralized purchasing from European countries, and try to control the spread of monkeypox • As of 23 August, 2022, 207,728 vaccination doses were administered in the 19 U.S. jurisdictions reporting data • Following Manitoba's first confirmed monkeypox case, the province announced on 26 August 2022 that it has expanded the criteria for vaccination eligibility • A news report indicates that a limited supply of the Imvamune vaccine has been distributed to the Northwest Territories

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	<p>vaccine was effective and well-tolerated against monkeypox (last updated 4 August 2022)</p> <ul style="list-style-type: none"> • A pre-print cohort study defined their highest-risk population as those who have used HIV-PrEP or erectile dysfunction therapy, or were diagnosed with STIs by rectal PCR, and found that this group had a 20-fold risk for monkeypox virus infection compared to moderate risk groups, and concluded that these findings may assist with prioritizing risk groups for vaccinations (Literature last published 25 July 2022) • A single study (pre-print) reported on determinants of vaccination intention and self-isolation intention after exposure among 394 people in the gbMSM community in the Netherlands <ul style="list-style-type: none"> ○ 72% of the sample population indicated their intention to get vaccinated, especially among those who were single but dating, in a polyamorous relationship, and/or retired ○ 44% of the sample population indicated their intention to self-isolate after an exposure, especially among those who identified as retired, first and second-generation migrants ○ The authors suggests that efforts to increase vaccination, intentions to isolate and ability to self-diagnose should be aimed at gbMSM with the highest risk (Published 31 July 2022) • A single study (pre-print) evaluated the humoral and cellular immune responses for up to six months after vaccination with COH04S1 two-dose vaccine in a subgroup of 20 volunteers in a phase one clinical trial <ul style="list-style-type: none"> ○ A detectable humoral and cellular response for up to six months post vaccination was found at all tested dose levels ○ Increased timing between vaccinations marginally increased the magnitude of the long-term response compared to volunteers with a shorter vaccination interval (i.e., 28 versus 56 days apart) ○ The authors concluded that the COH04S1 vaccine induces a robust and durable immunity and could be tested in non-inferiority clinical trials (Last updated 29 July 2022) • A single study (pre-print) investigated environmental contamination with monkeypox virus from infected patients 	<ul style="list-style-type: none"> ○ These doses are reserved for people who have been identified as close contacts of probable or confirmed cases of monkeypox ○ The province is following the National Advisory Committee on Immunization's guidance on administering the Imvamune vaccine • The Nunavut territorial government has received 140 doses of the vaccine from the federal government stockpile, with plans for more to follow • Newfoundland and Labrador is receiving an increased supply of Imvamune and will be expanding eligibility for doses of Imvamune, a vaccine used for smallpox that also provides protection against monkeypox <ul style="list-style-type: none"> ○ A focused vaccination campaign for those at highest risk of infection based on the current evidence and knowledge base of monkeypox will be launched ○ As of 22 August 2022, two-spirit (Indigenous people who identify as non-binary in Indigenous culture) transgender and non-transgender males who self-identify as being part of the LGBTQ2S+ community and have had intercourse with two or more partners within the last 90 days can receive vaccination • The shortage of the vaccine has led the U.S. and European health authorities to authorize the division of each available dose into five, with the aim of immunizing more people with fewer vials <ul style="list-style-type: none"> ○ Spain approved a new vaccination strategy a week ago in which it indicates applying 0.1 ml in most cases instead of 0.5 ml as before. This would mean that current shipment could translate into up to 25,000 people vaccinated • Given global vaccine shortages, the U.K. is limiting post-exposure vaccination to those at highest risk of severe complications, but the program for pre-exposure vaccination is unchanged • There are reports that given vaccine shortages the U.K. monkeypox vaccination campaign will be paused to a large extent

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	<p>admitted to isolation rooms in the UK to inform infection prevention and control measures</p> <ul style="list-style-type: none"> ○ This study identified widespread surface contamination in occupied patient rooms, on healthcare worker personal protective equipment after use, and in doffing areas ○ The results of this study indicated significant contamination in isolation facilities and the potential for aerosolization of monkeypox virus during specific activities (Last updated 21 July 2022) <ul style="list-style-type: none"> ● A single study examining the susceptibility blood samples of four populations (France, Bolivia, Laos, and Mali) to for antibodies that neutralize the vaccinia and cowpox viruses found that individuals from the four regions, (and to a larger extent, Europe, Africa, Asia, and South America) are very likely to be susceptible to monkeypox infections (published 17 July 2022) ● According to a single study, the rapid development and implementation of a mobile response tool for detection of monkeypox exposure in healthcare personnel at a Boston academic health center was able to support exposure and contact tracing investigations for monkeypox within 24 hours of identification of a suspected patient ● It was highlighted that the modernization of the response tool, efficient communications from the teams involved, and the experience of the response tool’s development team prior to and during the COVID-19 pandemic made it possible for the mobile response tools to be implemented quickly (published 11 July 2022) ● The WHO released interim guidance on vaccines and immunization for monkeypox <ul style="list-style-type: none"> ○ The organization does not recommend the use of first-generation vaccines held in national reserves related to the smallpox eradication program ○ Mass vaccination is not required or recommended at this time based on current assessment of risks and benefits, but strongly encouraged to countries to convene their national immunization advisory groups to determine relevance and context 	<p>until new vaccine doses arrive in late September; however, doses are being reserved for post-exposure vaccination</p> <ul style="list-style-type: none"> ● The UK Health Security Agency is piloting offering fractional doses (of 0.1 ml as opposed to 0.5 ml) at three vaccination sites given current global vaccine shortages ● Given current vaccine shortages, the British Columbia Centre for Disease Control notes that the monkeypox vaccine is reserved for Canadian residents and those visiting British Columbia for extended periods of time, and people should not travel to the province for the purpose of obtaining the vaccine ● A report by the Ontario Ministry of Health dated 29 August 2022 provides updated Imvamune guidelines for healthcare providers <ul style="list-style-type: none"> ○ Given the current supply constraints, Ontario is using a single dose of Imvamune to limit transmission; two doses are recommended for moderately to severely immunocompromised individuals and certain laboratory employees ○ Individuals who have had a confirmed case of monkeypox are not recommended to receive the monkeypox vaccine at this time due to the limited utility of the vaccine ○ Imvamune may contain trace amounts of antibiotics (gentamicin and ciprofloxacin) and egg products, so these individuals should be monitored for an extra 15 minutes after getting vaccinated ○ People with atopic dermatitis may have more frequent and intense reactions after vaccination ● According to a report by the Government of Quebec dated 25 August 2022, people suspected of having monkeypox will be contacted by the public-health authority and will be required to cover the lesions, avoid contact with people who are more at risk (pregnant women, children under 12, immunocompromised people), avoid sexual contact, wear a mask when less than one metre from another person indoors and outdoors, avoid sharing any items, avoid any activities in which uncovered lesions may be in contact with the skin, mucous membranes, or objects or another person, adopt general hygiene measures, inform sexual

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	<ul style="list-style-type: none"> ○ Most interim vaccination recommendations are related to off-label use (i.e., smallpox vaccines off-label for monkeypox) and vaccines approved for monkeypox such as MVA-BN, LC16, or ACAM2000 ○ Pre-exposure prophylaxis (PrEP) is recommended for health workers at high risk, laboratory personnel working with orthopoxviruses, clinical laboratory personnel performing diagnostic testing for monkeypox, and any outbreak response team members ○ Vaccination program should be accompanied with strong communication and conduct of vaccine effectiveness studies (Published 14 June 2022) ● A single study described the development and implementation of a mobile response survey for notification of possible exposure, risk assessment and stratification, and symptom monitoring for healthcare personnel after exposure to the monkeypox virus at Massachusetts General Hospital <ul style="list-style-type: none"> ○ These tools were deployed within 24 hours of identification of a patient with suspected monkeypox, with the full suite in production within 4 days of confirmation of the diagnosis of monkeypox (Published 16 June 2022; Pre-print) ● The WHO developed the following interim guidance on risk communication and community engagement (Published 2 June 2022): <ul style="list-style-type: none"> ○ “Identify target groups relevant to the monkeypox outbreak in Europe (i.e., population groups at risk need to be alerted about specific risks and protective measures; broader public needs to be informed about disease and preventive measures) ○ Tailor risk communication through channels and spokespersons that target groups trust ○ Acknowledge uncertainty by labelling public-health advice as preliminary and based on current evidence, and committing to provide further information and guidance as it becomes known ○ Package messages and health advice relevant to specific settings and circumstances 	<p>partners with whom they have been in contact with since the onset of symptoms</p> <ul style="list-style-type: none"> ● The Netherlands has begun testing for monkeypox DNA in sewage and has so far identified monkeypox in all eight locations that were sampled <ul style="list-style-type: none"> ○ This approach is being used to help track the spread of monkeypox and act as an early-warning system ● As of 23 August 2022, France’s free confidential telephone line information service has received 6,400 calls ● In the Netherlands, 5,441 vaccinations have been administered against monkeypox as of 10 August 2022, with 70,000 vaccines currently available for those at high risk for contracting monkeypox ● In Portugal, according to the Directorate-General for Health, as of August 8, 133 contacts (71.1%) of all those eligible have been vaccinated ● The Government of Spain has distributed 5,000 vaccines to health clinics, with an anticipated 7,000 more arriving to the country this week ● The U.K. has procured 150,000 doses of the smallpox vaccine from Bavarian Nordic to offer to those eligible for vaccination, and as of 10 August 2022, roughly 50,000 have arrived in the U.K. and 27,000 doses have been administered ● A report by the CDC of 2,891 monkeypox cases reported in the U.S. from May 17 to July 22 by 43 states, Puerto Rico and the District of Columbia, indicated that among 339 persons with vaccination status available, 48 (14%) reported previous receipt of smallpox vaccine, including 11 (23%) who received one of two Jynneos doses during the current outbreak, 11 (23%) who received pre-exposure prophylaxis at an unknown time before the current outbreak, and 26 (54%) who did not provide information about when vaccine was administered ● On 12 August 2022, the Government of Canada announced funding from the HIV and Hepatitis C Community Action Fund

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	<ul style="list-style-type: none"> ○ Provide public-health advice specific to the monkeypox outbreak without comparing it with or leveraging other health issues ○ Use pictures of monkeypox symptoms to increase understanding but not generate fear ○ Community-engagement approaches should be used to support targeted risk communication messages to populations or groups more likely to be exposed to the virus, which would require that public-health authorities at national and sub-national level identify and actively work with relevant civil society organizations, community-based organizations and stakeholders, and leverage the trust they have to ensure that the affected communities are properly informed and empowered to protect themselves from the disease” ● The WHO released guidance on surveillance, case investigation, and contact tracing (Published 22 May 2022) <ul style="list-style-type: none"> ○ If there is a suspect case of monkeypox virus, case investigation should consist of clinical examination of the patient with appropriate personal protective equipment (PPE), questioning the patient about possible sources of infection, and safe collection and dispatch of specimens for laboratory examination to be confirmed for monkeypox ○ As soon as a suspected case is identified, contact identification and contact tracing should be initiated, and contacts should be monitored at least daily for the onset of any signs or symptoms for a period of 21 days from last contact with a patient or contaminated materials ○ Quarantine or exclusion from work are not necessary during the contact-tracing period if there are no symptoms present or begin to develop ● The authors of a single study pre-print conducted in the Democratic Republic of Congo recommended that rapid field diagnostics should be implemented for early detection and surveillance (Last updated 5 June 2022; Pre-print) ● A non-systematic review noted that vaccination against smallpox provides cross-protection against other OPV species including 	<p>to support community-based organizations in Vancouver and Edmonton in addressing the monkeypox outbreak</p> <ul style="list-style-type: none"> ● An environmental scan by Public Health Ontario published in August 2022 on guidance for monkeypox waste disposal indicates that items contaminated in the care of a monkeypox patient should be considered infectious waste and discarded according to jurisdictional protocols ● This is part of a \$1 million commitment to support community-based organizations across the country ● France’s digital campaign has been further supplemented with broadcasting efforts on community radios and the distribution of over 2,800 posters and 94,000 flyers ● On 4 August 2022, the U.S. Department of Health and Human Services declared the U.S. monkeypox outbreak to be a public-health emergency ● On 28 July 2022, New Brunswick announced that it has 140 doses of vaccine and is continuing to develop guidance on how to manage cases and contacts, and surveillance activities as Newfoundland announces its first probable case ● Currently, Alberta residents who self-identify as meeting specific criteria are eligible for vaccination ● The Nunavik Regional Board of Health and Social Services indicated that vaccines are available in the territory; however, there is limited available information on which and what type of vaccine ● The UK has now procured a total of 130,000 doses of the smallpox vaccine from Bavarian Nordic to offer to those eligible for vaccination ● Two vaccines are available in Australia for the prevention of monkeypox, the 3rd generation JYNNEOS and the 2nd generation ACAM2000 <ul style="list-style-type: none"> ○ The Australian Technical Advisory Group on Immunization has identified key risk groups recommended to receive vaccination

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	<p>monkeypox and many patients were born after the cessation of smallpox eradication program (Published 12 November 2020)</p> <ul style="list-style-type: none"> • A separate non-systematic review similarly highlighted that most confirmed monkeypox cases are younger than 40-years old, a population born only after the discontinuation of the smallpox vaccination campaign, possibly reflecting a lack of cross-protective immunity (Published December 2019) <ul style="list-style-type: none"> ○ Prevention measures for animal-to-human transmission include avoiding contact with rodents and primates, limiting direct exposure to blood and inadequately cooked meat, and using personal protective equipment when handling potential animal reservoir species ○ Prevention measures for human-to-human transmission include avoiding close contact with anyone infected and healthcare providers using personal protective equipment when treating infected patients • A non-systematic review highlighted that other key public health measures, such as case isolation, contact tracing, avoiding contact with animals or materials suspected of being infected, use of personal protective equipment and good hand-hygiene practices, remain the best measures for preventing and controlling human monkeypox (Published April 2019) • A single study of an outbreak of monkeypox mentions the use of contact tracing and active surveillance of 30 contacts identified as having had direct exposure of broken skin or mucous membranes to a symptomatic patient (Published 21 August 2021) • A cross-sectional single study of strategies used, and challenges faced when responding to a monkeypox outbreak noted (Published 17 April 2019): <ul style="list-style-type: none"> ○ To respond to the outbreak, the hospital established a make-shift isolation ward for case management by a monkeypox response team and provided infection and control resources ○ Challenges included some healthcare workers being reluctant to participate in the outbreak with some avoiding suspected patients; stigma and discrimination experienced by patients and their family members; and refusal of isolation and 	<ul style="list-style-type: none"> • As of 27 July 2022 in France, more than 32,000 doses have been delivered by the Agency to the territories • In France, pre-exposure vaccination is completed through the third generation MVA-BN (Imvanex and Jynneos) vaccines, which the High Authority of Health has listed as being interchangeable • A total of 40,000 Jynneos vaccine doses are available for use in Germany, with another 200,000 scheduled to arrive in the third quarter of 2022 • A news report indicates that the Imvanex vaccine has been administered in Portugal since July 16 • On 25 July 2022, France began a digital campaign on preventive vaccinations • The CDC indicates that the only FDA-approved dosing regimen for the JYNNEOS vaccine is a two-dose series, with few exceptions • The CDC advises that JYNNEOS may be administered regardless of the timing of other vaccines <ul style="list-style-type: none"> ○ However, because of the observed risk for myocarditis after the ACAM2000 and mRNA COVID-19 vaccines, people might consider waiting four weeks after orthopoxvirus vaccination before receiving a Moderna, Novavax, or Pfizer-BioNTech COVID-19 vaccine • Quebec reported that vaccine side effects for less than 10% of people include pain, redness, swelling, induration, itching at the injection site, nausea, headache, fatigue, and muscle pains <ul style="list-style-type: none"> ○ Side effects for less than 1% of people include heat, nodule, hematoma, discolouration at the injection site, limb pain, joint pain, fever and chills ○ Side effects for less than 0.001% of people include swollen gland, skin peeling, nose or throat injection, difficulty sleeping, dizziness, and numbness • To reduce the risk of becoming infected or spreading monkeypox, an updated set of PHAC recommendations on limiting contact, hygiene and safe sex practices has been released

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	<ul style="list-style-type: none"> ○ Training was offered and using a collaborative approach among all involved stakeholders addressed some of these challenges and eventually led to successful containment of the outbreak ● A single study examining thresholds to trigger a public-health response to monkeypox identified three different statistical thresholds that were used: Cullen, c-sum, and a World Health Organization (WHO) method based on monthly incidence (20 December 2018) <ul style="list-style-type: none"> ○ The study concluded that using signals detected by a single method may be inefficient and overly simplistic for triggering public-action for monkeypox ● Instead, a response algorithm is proposed which integrates the WHO method as an objective threshold with contextual information about epidemiological and spatiotemporal links between suspected cases 	<ul style="list-style-type: none"> ● On 21 July 2022, the federal government announced that it is providing funding for community-based organizations in regions most affected currently by the monkeypox outbreak to reach at-risk populations on how to protect themselves ● The Alberta Health Service has produced infection prevention and control measures for healthcare providers working with patients suspected to have monkeypox ● Monkeypox testing is recommended for individuals with acute rash or ulcers with or without systemic symptoms and in the past 21 days had one or more of the following risk factors: <ul style="list-style-type: none"> ○ Sexual contact with a new, anonymous, or multiple partners ○ Sexual contact with someone who had a new, anonymous, or multiple partners ○ Significant contact with someone who has skin lesions with no known alternate cause ○ Contact with a known or probable case of monkeypox ● The Coalition for Epidemic Preparedness Innovations has awarded the UK Medicines and Healthcare products Regulatory Agency and the UK Health Security Agency funding to advance research into tools for assessing current and future vaccines against monkeypox ● At a recent press conference, Dr. Theresa Tam responded to questions about whether governments are looking at how to financially support those who need to isolate by saying that she is encouraging provinces and territories to implement these types of supports ● On 26 July 2022, Australia's Chief Medical Officer, Professor Paul Kelly, declared the monkeypox (monkeypox) situation a Communicable Disease Incident of National Significance ● The Public Health Agency of Canada has provided resources on their website for health professionals administering IMVAMUNE vaccinations ● The Provincial Infection Control Network of British Columbia has issued interim infection prevention and control guidance for monkeypox in health care setting which covers patient

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		<p>placement, hand hygiene, personal protective equipment, patient transport, cleaning and disinfection, laundry, and waste management</p> <ul style="list-style-type: none"> • In Ontario, a City of Toronto report dated 19 July 2022 discussed the side effects of the Imvamune vaccine, including redness, pain or swelling at the injection site, tiredness, headaches, and muscle aches • According to Prince Edward Island’s Chief Public Health Officer, the province has 140 doses of vaccine to be given four weeks apart for anyone who is identified as a close contact to a confirmed or suspected case, and multiple courses of antiviral treatment • In Portugal, the Directorate-General for Health indicated that as of July 12th, Portugal has received 2700 doses of the JYNNEOS vaccine, produced by the Bavarian Nordic company • The Spanish Ministry of Health closed a bilateral purchase of 200 doses of the vaccine with the Netherlands before the European Commission sent the first shipment of 5,300 doses at the end of June. The remaining 7,120, up to complete 12,420, are expected to arrive between July and August • The European Medicines Agency (EMA) is reviewing the Bavarian Nordic vaccine for indication in monkeypox infection • Canada’s Chief Public Health Officer, Dr. Theresa Tam, indicated that negotiations are underway to procure more monkeypox vaccine from the Danish manufacturer Bavarian Nordic <ul style="list-style-type: none"> ○ The manufacturer said in early June that PHAC had agreed to a US\$56 million, five-year contract to purchase IMVAMUNE vaccine, with expected delivery beginning in 2023 • According to a Canadian 4 July 2022 news report, a total of 8,101 doses of IMVAMUNE vaccine have been administered in Québec since 27 May, and as of 30 June, nearly 6,000 people in Toronto have been vaccinated against monkeypox

Organizing framework domain	Evidence from previous version	Experiences from previous version
		<ul style="list-style-type: none"> • In Alberta, the Imvamune vaccine is currently being offered to those to have had close contact with someone who has monkeypox up to 14 days after exposure <ul style="list-style-type: none"> ○ As of 4 July 2022, eight people in Alberta are reported to have been immunized with the Imvamune vaccine ○ To date the EU has approved the vaccine for conventional smallpox, whereas the United States has approved for both smallpox and monkeypox • Health Direct Australia recommends vaccinations, indicated to be 85% effective in preventing monkeypox, within 4 days of having close contacts with a person infected with monkeypox • In France, a digital campaign that has been launched on the “sexosafe.fr” site has received 348,000+ clicks and 292,000+ visits; this site provides guidance on what to do if Monkeypox symptoms appear as well as additional information regarding preventive measures • On 13 July 2022, Public Health France and SIS-Association have launched a free information service to answer Monkeypox-related inquiries • The UK Health Security Agency is advising men who have confirmed monkeypox infection to use condoms during sex for 12 weeks following recovery from infection, and the agency is offering a monkeypox PCR test on semen samples after these 12 weeks have passed for patients who meet certain criteria • A report by the Ontario Ministry of Health dated 14 June 2022 provides Imvamune guidelines for healthcare providers <ul style="list-style-type: none"> ○ The report provides an overview of using Imvamune in special populations: clinical trials have included people living with HIV, there is less experience in individuals with severe immunosuppression; no clinical trials have been conducted in pregnant individuals, although approximately 300 pregnancies have been reported to the manufacturer with no safety issues, and there is no data on whether the vaccine is excreted in breastmilk although this is unlikely since the vaccine is nonreplicating; the vaccine has not been studied in youth under 18 although it has been given to children as PEP in the

Organizing framework domain	Evidence from previous version	Experiences from previous version
		<p>U.K. for monkeypox; people with atopic dermatitis may have more intense and frequent reactions after vaccination</p> <ul style="list-style-type: none"> • The Provincial Infection Control Network of British Columbia has released interim infection prevention and control guidance for monkeypox in health care settings <ul style="list-style-type: none"> ○ The document outlines specific guidance regarding patient placement, hand hygiene, personal protective equipment, patient transport, cleaning and disinfection, laundry, and waste management • The government of Australia has made the ACAM2000™ smallpox vaccine available to be used for PEP (e.g., healthcare workers, household contacts, or contacts in other settings) and PrEP (e.g., healthcare workers, laboratory worker), but cannot be used in individuals with severely immunocompromised conditions, people who are pregnant, people with active eczema or other active skin conditions, people with allergies, and children under 12 months • An Emergency Committee of the World Health Organization will convene on June 23 to determine if orthopoxvirus is an international threat • In Canada, on 8 June 2022, the National Advisory Committee on Immunization (NACI) released interim guidance on the use of Imvamune, a third-generation smallpox vaccine, for post-exposure prophylaxis (PEP) against monkeypox: <ul style="list-style-type: none"> ○ A single dose of Imvamune may be offered to individuals with high-risk exposures of a probable or confirmed case of monkeypox, or in setting where transmission is occurring, ideally within four days of exposure ○ PEP should not be offered to individuals who already have a monkeypox infection ○ A second dose of Imvamune may be offered after 28 days of the first dose if continued risk of exposure is indicated • NACI also recommended Imvamune pre-exposure prophylaxis (PrEP) for adults at high risk of occupational exposure in a laboratory research setting and for special populations, such as individuals who are immunocompromised, pregnant, lactating,

Organizing framework domain	Evidence from previous version	Experiences from previous version
		<p>children and youth who are less than 18 years old, and individuals with atopic dermatitis based on exposure risk</p> <ul style="list-style-type: none"> • In Germany, The Standing Committee on Vaccination (STIKO) has put forth a recommendation to vaccinate individuals against the Monkeypox virus with Imvanex <ul style="list-style-type: none"> ○ This includes vaccinations for certain population groups, including 1) post-exposure prophylaxis upon Monkeypox exposure in asymptomatic individuals aged 18 years and older (e.g., those who have had close physical contact with individuals with Monkeypox); 2) individuals with an increased risk of exposure and infection during a potential outbreak (e.g., men aged 18 years and older with same-sex sexual contacts or multiple partners); and 3) immunocompromised individuals ○ For those who have not previously been vaccinated against smallpox, immunization with Imvanex is a two-dose regimen separated 28 days apart, while a single dose is sufficient for those with a previous smallpox vaccine (barring immunocompromised individuals who would still receive two doses in either case) • The Public Health Agency of Canada has issued a travel health notice, last updated 20 June 2022, to practise enhanced health precautions when traveling to certain countries <ul style="list-style-type: none"> ○ Enhanced health precautions may include using personal protective equipment, delaying travel until risk is lower, avoiding higher risk activities, and additional vaccinations for certain groups ○ Talking to sexual partners about sexual health and using barriers such as gloves and condoms ○ Avoid sharing toothbrushes, sex toys, and drug use supplies ○ Avoid prolonged face-to-face contact, especially indoors ○ Stay home if you are sick, and encourage others to do the same • Asymptomatic patients can be managed in a primary care setting, vaccination clinics and other outpatient settings such as sexual health clinics

Organizing framework domain	Evidence from previous version	Experiences from previous version
		<ul style="list-style-type: none"> • A report by Public Health Ontario dated 13 June 2022 indicated that self-isolation must be maintained until all scabs have fallen off, new skin is present, and they have been cleared by their public health unit (no longer considered infectious) <ul style="list-style-type: none"> ○ An AIIR is not required for specimen collection ○ It is recommended that hand hygiene facilities be available in laundry areas, and that clothes from monkeypox cases be machine washed using 70-degree Celsius hot water and regular laundry detergent ○ Routine environmental disinfection must occur in emergency rooms and outpatient settings, inpatient rooms, and shared showering facilities • A technical report by Public Health Ontario dated 28 May 2022 describes interim case and contact management guidelines for local public health units based on information from selected public health organization such as the CDC, the United Kingdom Health Security Agency, and the WHO <ul style="list-style-type: none"> ○ For those self-isolating, it is recommended to cover skin lesions by wearing long clothing, designating one person to care for the person who is self-isolating ○ It is recommended to wear gloves when handling laundry, to not shake or agitate soiled laundry dispersing infectious particles ○ Contaminated dressings and bandages should not be disposed of with household garbage or in landfills, so consider using a biohazard/environmental remediation company to transport waste safely to the hospital for safe processing ○ A detailed guide to assessing risk of exposure is provided in the document • The UK passed legislation to make monkeypox a notifiable disease in law as of 8 June 2022 <ul style="list-style-type: none"> ○ This legislation means that doctors are required to notify their local council or Health Protection Team if they suspect a patient has monkeypox and laboratories must notify the UK Health Security Agency if they identify monkeypox virus in a sample

Organizing framework domain	Evidence from previous version	Experiences from previous version
		<ul style="list-style-type: none"> ○ To ensure anyone concerned about monkeypox seeks appropriate healthcare, the National Health Service regulations were amended to make monkeypox treatment and diagnosis free from charge for all overseas visitors ● The government of Australia has convened national expert groups to develop treatment and vaccine guidelines ● The Italian Ministry of Health issued a variety of recommendations: case notification, protective measures for healthcare workers, contact tracing, possibly implementing quarantine measures, as well as providing non-stigmatizing information to at-risk populations ● In Portugal, the Directorate-General for Health disseminated communication materials related to transmission, prevention, and hygiene measures to reduce the risk of monkeypox ● Dissemination activities include raising awareness at public and private events ● The UK Health Security Agency has produced guidance regarding the cleaning of sex-on-premises venues in light of the monkeypox virus outbreak ● The UK Health Security Agency has produced guidance regarding home isolation for people who have been diagnosed with monkeypox infection ● Cases are being asked to isolate at home, if they are well enough, and to avoid contact with others until lesions have healed and scabs have dried ● In some jurisdictions, new recommendations and guidelines have been put in place to help prevent and control the spread of monkeypox <ul style="list-style-type: none"> ○ For example, the UK Health Security Agency alongside the public-health agencies of England, Scotland, Wales and Northern Ireland have released a consensus statement regarding principles for monkeypox control in the U.K. to guide the public-health response to ensure there is a proportionate response that encourages engagement with health services, prevents stigma, and controls spread

Organizing framework domain	Evidence from previous version	Experiences from previous version
		<ul style="list-style-type: none"> ○ As part of these guidelines, the smallpox vaccine is being offered to health workers who will care for monkeypox patients as well as those who work in sexual-health centres and may have assessed suspected cases ○ In Germany, RKI released a recommendation on 30 May 2022 about hygiene measures for the treatment and care of patients diagnosed with Monkeypox in healthcare facilities, which includes the use of hand disinfectant, disposable medical gloves, personal protective equipment, and providing spatial accommodation (i.e., single rooms for infected patients) ○ The country has also planned for an additional 200,000 smallpox vaccine doses to follow the original order of 40,000 smallpox vaccine doses ○ In France, a recommendation was released on 24 May 2022 to launch a targeted vaccination strategy to help reduce the transmission of the monkeypox virus ○ The recommendation includes providing smallpox vaccinations for at-risk adults (e.g., exposed healthcare professionals) who have been in contact with infected individuals ○ Vaccinations should occur within the first two weeks of exposure (ideally within the first four days) and using a two-dose regimen given 28 days apart ○ Immunocompromised individuals should receive three doses ● Several jurisdictions have also noted efforts to manage community engagement and provide targeted communication about the monkeypox virus <ul style="list-style-type: none"> ○ In Spain and Portugal, public-health authorities are engaging with LgbTQI+ communities ○ Further, the UK Health Security Agency is working with partners to communicate with sexual-health service partners as well as the gay, bisexual, or other men who have sex with men community about monkeypox and how to stay safe

Organizing framework domain	Evidence from previous version	Experiences from previous version
		<ul style="list-style-type: none"> • Broadly, jurisdictions align with the recommendations from the U.S. CDC, which recommends that the following measures be taken to prevent infection with monkeypox virus: <ul style="list-style-type: none"> ○ Avoid contact with animals that could harbour the virus (including animals that are sick or that have been found dead in areas where monkeypox occurs); ○ Avoid contact with any materials, such as bedding, that has been in contact with a sick animal; ○ isolate infected patients from others who could be at risk for infection; ○ Practice good hand hygiene after contact with infected animals or humans (e.g., washing your hands with soap and water or using an alcohol-based hand sanitizer); and ○ Use personal protective equipment (PPE) when caring for patients • The countries reviewed also noted that high-risk contacts such as sexual partners, family members, and others in contact with skin blisters should also quarantine <ul style="list-style-type: none"> ○ If they take a test that has a negative result, they may end their quarantine and if the result is positive, they should continue isolating. Across jurisdictions, recommended isolation periods include periods of at least 21 days or others that recommend until the scabs have fallen off and their skin is completely healed ○ Belgium was the first country to announce a mandatory 21-day isolation period for individuals infected with monkeypox • Many jurisdictions have source and contact-tracing measures in place in the event of a confirmed case <ul style="list-style-type: none"> ○ The UK Health Security Agency produced a monkeypox contact tracing classification and vaccination matrix to help guide follow-up and vaccination advice for individuals who have had varying levels of exposure risk with confirmed cases of monkeypox ○ The Ontario Monkeypox Investigation Tool was created to record patient information and prevent future illness caused by monkeypox.

Organizing framework domain	Evidence from previous version	Experiences from previous version
		<ul style="list-style-type: none"> ○ Germany ordered 40,000 smallpox vaccine doses as a preventive measure and the U.K. has purchased supplies of Imvanex (a smallpox vaccine) to be offered to close contacts of those diagnosed with monkeypox to reduce their risk of symptomatic infection and severe illness
Diagnosis	<ul style="list-style-type: none"> ● One research report demonstrated that recombinant soluble truncated forms of A35R and H3L can be used in enzyme-linked immunosorbent assay (ELISA) as diagnostic tools for the detection of recently infected monkeypox patients ● A non-systematic review by the European Centre for Disease Prevention and Control outlined optimal approaches for conducting PCR tests, where the authors concluded that laboratories should evaluate published protocols by using control materials or specimens with their own reagents and instruments, and contamination of assays should be monitored by individual laboratories with whole-process negative pathogen controls that contain human genomic DNA (published 11 August 2022) ● A pre-print single study evaluated the PCR assay currently recommended by the U.S. CDC and seven other real-time PCR assays for monkeypox, and found wide variations in the primer and probe sequences compared to the genome of the current circulating monkeypox strains ● The authors concluded that it is critical to develop updated assays for the detection of monkeypox so that accurate and specific data is used to inform public-health risk mitigation strategies (last updated 11 August 2022) ● A single study adapted existing PCR test kits from SARS-CoV-2 for the use in monkeypox diagnoses, which the authors found 100% clinical performance to detect monkeypox and concluded that timely use of PCR tests are important for limiting transmission (Published 29 July 2022) ● A single study reporting on the laboratory testing methods of the Laboratory Response Network (LRN) in the US to detect Orthopoxvirus revealed that from 17 May to 30 June 2022, LRN 	<ul style="list-style-type: none"> ● On 7 September 2022, the HHS secretary signed a declaration under section 564 of the Federal Food, Drug, and Cosmetic Act to allow the U.S. Food and Drug Administration (FDA) Commissioner to issue emergency-use authorizations for in vitro diagnostics to expand the availability of tests for monkeypox ● Among the new cases reported in France on 23 August 2022, 39 monkeypox cases were detected in females and eight were reported in children ● As case counts rise and strain testing capacity, some jurisdictions are adjusting testing protocols <ul style="list-style-type: none"> ○ To support the monkeypox response in Canada and conduct testing for jurisdictions that are not performing their own, PHAC’s Health Portfolio Operations Centre, Incident Management Structure and the National Microbiology Laboratory (NML) have been activated to Level 2 ○ The Government of Northwest Territories released an algorithm for health professionals to identify suspect cases of monkeypox ○ A report by Public Health Ontario updated on 25 July 2022, outlines monkeypox testing indications ○ Vancouver Coastal health has produced standard operating procedures for health professionals for the clinical assessment, testing, and public health follow up of monkeypox ○ To increase testing capacity in the UK, some suspected monkeypox samples are now being tested with an orthopox polymerase chain reaction test, with those testing positive deemed as highly probable cases ○ laboratories, however, clinicians continue to face difficulties in ordering tests

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<p>was able to assess 2,009 samples, 36.6% (n=395 individuals) of which were non-variola Orthopoxvirus positive</p> <ul style="list-style-type: none"> ○ The expansion to five commercial laboratories starting the week of 15 July 2022 is anticipated to make testing more accessible, increase convenience for providers and patients, and further augment national capacity (published 15 July 2022) ● According to a single study, the rapid development and implementation of a mobile response tool for detection of monkeypox exposure in healthcare personnel at a Boston academic health center was able to support exposure and contact tracing investigations for monkeypox within 24 hours of identification of a suspected patient (published 11 July 2022) ● A single study (pre-print) described the potential use of a real-time PCR assay in the multi-national outbreak given its ability to detect positive test samples (Last updated 23 June 2022) ● A non-systematic review highlighted that of monkeypox can occur through genetic methods (i.e., PCR or RT-PCR), phenotypic methods based on clinical diagnosis, immunological methods including IgG and IgM antibody detection and immunohistochemistry for viral antigen detection, and electron microscopy (Published 12 November 2020) <ul style="list-style-type: none"> ○ For diagnosis, optimal clinical specimens for laboratory analyses include those from skin lesions, exudate, or crusts stored in a dry, sterile tube (without viral transport media) and kept cold ● A single study noted that that a confirmed monkeypox case requires detection of Orthopoxvirus or monkeypox virus DNA with real-time polymerase chain reaction (PCR) or isolation of monkeypox virus in culture from ≥1 specimen (Published 4 June 2021) ● swab eluates, crust homogenates, or blood from suspected cases were used to test monkeypox infection 	<ul style="list-style-type: none"> ○ Outsourcing tests to commercial laboratories is expected to clear up the backlog in the US ● According to a Health Agencies Update in the US, over 8000 tests have been available weekly through more than 67 public health ● In Italy, the rapid communications report dated 26 May 2022, noted four patients were positive for monkeypox DNA in real-time PCR using samples from skin, genital and anal lesions, serum, plasma, seminal fluid, feces, and the nasopharynx <ul style="list-style-type: none"> ○ Viral DNA was extracted by Qiamp Viral RNA mini kit (Qiagen) and two real-time PCRs using a Real-Star Orthopoxvirus PCR kit, and a G2R_G assay which was used as a confirmatory PCR ○ Sanger sequencing was used to identify which of the two clades the virus belonged to ● Diagnosis of the monkeypox virus primary occurs first through clinical assessment and then confirmed through laboratory testing of biological specimens ● Clinicians can recognize potential monkeypox infection based on the similarity of its clinical course to that of smallpox ● The main feature that distinguishes infection with monkeypox from that of smallpox is the development of swollen lymph nodes (lymphadenopathy) ● The spectrum of monkeypox disease ranges from mild to severe and fatal ● The virus can be detected using polymerase chain reaction (PCR) and the particles can further be detected through an electron microscope. The UK Health Security Agency has produced guidance for collecting, submitting, and processing of samples for the diagnosis of monkeypox
Clinical presentation	<ul style="list-style-type: none"> ● A single study conducted in 42 health centres and clinics from 17 German cities reported that all 546 monkeypox infections were men who have sex with men (MSM), almost half of them were 	<ul style="list-style-type: none"> ● In Belgium, ITM researchers identified three positive samples of monkeypox within asymptomatic patients who were initially

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<p>living with HIV infection, but there were no apparent clinical presentation differences between MSM with or without HIV infection (published 4 September 2022)</p> <ul style="list-style-type: none"> • An observational study evaluating clinical characteristics and complications of patients with a monkeypox infection in Bichat Claude Bernard university hospital in Paris, France identified that the majority of the 264 patients had fever (68%) and adenopathy (69%), and skin lesions mostly affected the genital (54%) and perianal (40%) areas • Overall, 17 patients were hospitalized and none of them were immunocompromised • A high-quality systematic review assessed the clinical features, hospitalizations, complications and deaths of monkeypox confirmed or probable cases <ul style="list-style-type: none"> ○ The most prevalent clinical features included rashes, fever, pruritus, and lymphadenopathy ○ The authors concluded that countries must urgently prepare human resources and infrastructure to treat patients according to the most reliable clinical information (8/11 McMaster Health Forum AMSTAR rating; published 10 August 2022) • A low-quality systematic review reported on the evidence regarding neurological complications associated with monkeypox <ul style="list-style-type: none"> ○ The authors identified the following neurological complications among 12 individuals with monkeypox: low mood, seizures, encephalitis, respiratory failure, and encephalopathy ○ Seven cases of encephalitis were identified; three of these patients died, two made a full recovery, and two did not have a reported outcome status ○ The authors emphasize the importance of appropriately identifying monkeypox in young children given their increased susceptibility to monkeypox-associated encephalitis (2/10 McMaster Health Forum AMSTAR rating; literature last searched 19 June 2022) • A single study characterized cases of monkeypox in Germany based on an anonymous survey completed by the German AIDS 	<p>testing for sexually transmitted infections (e.g., gonorrhea and chlamydia)</p> <ul style="list-style-type: none"> • In the Netherlands, the National Institute for Public Health and the Environment updated its report on 16 August 2022 <ul style="list-style-type: none"> ○ A number of people have had proctitis, an inflammation of the lining of the rectum, which is sometimes the only symptom ○ The report provides images of monkeypox on the finger ○ A person may already be contagious before developing any visible symptoms ○ Some people develop flu-like symptoms or a skin rash before blisters ○ Blisters may be in the mouth or rectum, where they may resemble ulcers ○ Some people with monkeypox only have one blister ○ Scabs from blisters can also transmit the virus • The UK Health Security Agency has produced guidance regarding case definitions of possible, probable, highly probable, and confirmed cases of monkeypox with guidance for clinicians about actions to take when presented with possible, probable, highly probable, or confirmed cases • In the Netherlands, The National Institute for Public Health and the Environment report published on 30 June 2022 reported that 84% of patients have systemic symptoms such as fever, tiredness, muscle pain or swollen lymph nodes • The agency of health surveillance in Spain (SiViES) has complete data of 2,368 patients, 2,348 are men and 20 are women <ul style="list-style-type: none"> ○ Ages range from 3 to 76, with a median age of 37 years ○ Among the 1,199 patients with characterization of their symptoms, they mainly presented fever (56.6%); exanthema [skin eruption] anogenital (49.8%), oral-buccal (39.9%) and in other locations (40.4%); localized lymphadenopathy (45.5%); and asthenia (38.0%) • A total of 54 patients (4.5%) presented complications throughout their clinical process; the most frequent were secondary bacterial infections and mouth ulcers

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<p>Society and the German Association for Outpatient Physicians for Infectious Diseases and HIV Medicine</p> <ul style="list-style-type: none"> ○ All cases were gbMSM (n=301), including 141 individuals with HIV and 135 individuals with pre-exposure prophylaxis ○ More than half of the individuals had a diagnosis of an STI in the six months before their monkeypox infection (published 12 August 2022) <ul style="list-style-type: none"> ● A single study analyzed clinical and virological characteristics of monkeypox cases at three sexual health clinics in Spain where all presented skin lesions, and where 15 of the 181 individuals were found to be heterosexual men or women <ul style="list-style-type: none"> ○ The authors recommended that due to the variability of the clinical presentations, physicians should have a low threshold for suspicion of monkeypox (published 8 August 2022) ○ A single study described 185 monkeypox cases in Spain, where the authors concluded that sexual contact was the most likely mechanism of monkeypox transmission (published 2 August 2022) ● A single study reported on the clinical features and treatment responses of seven individuals with monkeypox from 2018 to 2020 <ul style="list-style-type: none"> ○ Three patients were treated with Brincidofovir (200 mg once a week orally), all of whom developed elevated liver enzymes resulting in therapy cessation; one patient was treated with Tecovirimat (600 mg twice daily for two weeks orally) and experienced no adverse effects, had a shorter duration of viral shedding and illness (10 days of hospitalization) compared with the other patients; and one patient had a mild relapse six weeks after hospital discharge (Published August 2022) ● A single study characterized the clinical presentation of monkeypox among 197 patients at infectious disease centres and sexual health centres in London, U.K. from May to July 2022 <ul style="list-style-type: none"> ○ All 197 patients were men with a mean age of 38 years and identified as gay, bisexual, or gbMSM, which all presented with mucocutaneous lesions, mostly on genitals or in the perianal area 	<ul style="list-style-type: none"> ● Of the cases investigated in France, the most commonly reported symptoms are a genito-anal rash, eruption on another part of the body, fever, and lymphadenopathy ● In Italy, a letter to the editor dated 9 June 2022 reported a total of 29 PCR-confirmed cases <ul style="list-style-type: none"> ○ 28/29 cases were males, and 16/18 reported having sex with other men ○ The median age of patients was 36 years ○ All presented with a rash, and in 18/21 cases, the rash was localized in the genital/perianal area ○ Fever was reported in 12/22 cases for whom information was available ● In the Netherlands, as of 31 May 2022, all 31 cases were men and identified as gbMSM with an age range of 23-64 years <ul style="list-style-type: none"> ○ 18 cases had reported symptom onset and the most likely date of exposure related to attending an event ○ The 97.5 percentile for the incubation period is estimated to be 19.9 days, and an estimated 2% of all cases would develop symptoms more than 21 days after being exposed ● The literature indicates that incubation periods differ by route of transmission (non-invasive exposure through skin or droplets is 13 days, and complex and invasive exposure through contact with broken skin or mucous membranes is 9 days), which is consistent with smallpox ● A recent Eurosurveillance case report described a case of monkeypox infection in an individual returning to Australia from Europe, with the individual reporting a genital rash, followed by a fever and lymphadenopathy, which then led to diffuse rash with few lesions present on the face and extremities ● The incubation period can range from five to 21 days ● At the onset of the infection, symptoms are described as mild and include fever, headache, muscle ache, swollen lymph nodes, chills, and fatigue ● Between one and five days after the onset of fever, a rash develops, often starting on the face and then spreading to other

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<ul style="list-style-type: none"> ○ 170 participants reported systemic illness, with the most common symptoms being fever, lymphadenopathy, and myalgia ○ 20 patients were admitted to hospital for the management of symptoms, most commonly rectal pain and penile swelling (Published 28 July 2022) ● A single study reported on an international case series that describe the presentation, clinical course, and outcomes of PCR-confirmed monkeypox <ul style="list-style-type: none"> ○ 528 infections were studied from 27 April to 24 June 2022, at 43 sites in 16 countries ○ 98% were gay or bisexual men, 75% were White, and 41% had human immunodeficiency virus infection ○ 95% presented with a rash, 73% had anogenital lesions, and 41% had mucosal lesions ○ Systemic symptoms before the rash included fever, lethargy, myalgia, headache, lymphadenopathy ○ Viral DNA was detected in 29 of 32 of persons in whom seminal fluid was analyzed ● Antiviral treatment was given to 5% of people; 13% were hospitalized (Published 21 July 2022) ● A medium quality systematic review (pre-print) that investigated the neurological and psychiatric presentations of monkeypox (monkeypox) virus infection found that the most frequent clinical feature of neuropsychiatric presentations of monkeypox was myalgia, followed by headache, fatigue, seizure, confusion, and encephalitis (published 11 July 2022) ● A single study (pre-print) that investigated monkeypox cases in Bas-Uélé, Democratic Republic of Congo found that of 77 suspected cases that were tested in 106 households, 27.3% were positive for monkeypox, 58.4% for chickenpox, and 14.3% negative for both ● While no combination of identified symptoms – monomorphic skin lesions on the palms of hands and soles of feet – had a strong confirming power for decisive diagnosis, the study’s authors concluded that intensified surveillance of monkeypox in Africa is 	<p>parts of the body with the rash tending to be more concentrated on the face and extremities than on the trunk</p> <ul style="list-style-type: none"> ○ Generally, the disease affects the face (in 95% of cases); the palms of the hands and soles of the feet (in 75% of cases); the oral mucosa (in 70% of cases); the genitalia (30%); and the conjunctiva and cornea (20%) ○ However, in most of the known recent cases in Europe, the rash has started around the pubic or anus region before spreading to the rest of the body <ul style="list-style-type: none"> ● The B.C. Centre for Disease Control maintains a webpage about monkeypox for healthcare providers with information about clinical presentation, transmission, management of suspected cases (including diagnosis and testing), infection prevention and control, and treatment

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<p>critical considering the current outbreak outside of Africa (published 6 July 2022)</p> <ul style="list-style-type: none"> • A non-systematic review reported that vaccinia viruses can be inactivated on artificially contaminated surfaces by 70% ethanol (≤ 1 minute), 0.2% peracetic acid (≤ 10 min) and 1% to 10% of a probiotic cleaner (1 h) <ul style="list-style-type: none"> ○ Hydrogen peroxide (14.4%) and iodine (0.04% - 1%) were effective in suspension tests, sodium hypochlorite (0.25% - 2.5%; 1 min), 2% glutaraldehyde (10 min) and 0.55% ortho-phthalaldehyde (5 min) were effective on artificially contaminated surfaces ○ Copper (99.9%) was equally effective against vaccinia virus and monkeypox virus in 3 minutes (Published 28 June 2022) • A single study (pre-print) estimated the incubation period from 22 cases (from 17 May 2022 to 6 June 2022) to be 7.6 days (from exposure to first symptom onset, 95% CI 17.1 days), which the authors concluded that it aligns with the U.S. CDC recommendation of monitoring for 21 days after last exposure (Published 21 June 2022) • A high-quality systematic review (pre-print) appraised 14 guidelines focusing on the availability, scope, quality, and inclusivity of clinical managements for monkeypox virus globally, and found that most of the guidelines were of low-quality due to a lack of detail in its methodology and narrow range of covered topics <ul style="list-style-type: none"> ○ Most guidelines focused on adults, with some providing advice for children, pregnant women, and immunocompromised individuals ○ Treatment guidance was mostly limited to advice on antivirals, in which seven out of 14 guidelines advised cidofovir ○ All guidelines recommended vaccination as post-exposure prophylaxis (PEP) (Published 14 June 2022; AMSTAR rating 7/9) • A non-systematic review conducted a pooled analysis of 124 cases in Italy, Australia, Czech Republic, Portugal, and the United Kingdom, and found that clinical presentation is also atypical, 	

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<p>being largely characterized by anogenital lesions and rashes, with fewer on the face and extremities</p> <ul style="list-style-type: none"> ○ The most common symptom reported was fever (54.29%) followed by inguinal lymphadenopathy (45.71%) and exanthema (40%) (Published 8 June 2022) ● A single study reported on two cases with exclusive genital lesions, which the authors concluded that this may suggest monkeypox virus can be sexually transmitted, and recommended increased awareness among clinicians and ring vaccination (Published 14 June 2022) ● A retrospective observational study examined the longitudinal clinical course of monkeypox in the U.K., viral dynamics, and the adverse events of novel antiviral therapies in seven patients who were diagnosed from 2018-2021 (Published 24 May 2022) <ul style="list-style-type: none"> ○ Viraemia, prolonged virus DNA detection in upper respiratory tract swabs, low mood, and PCR-positive deep tissue abscess were some of the disease features ● A pre-print of a prospective observational study conducted in the Democratic Republic of Congo reported the findings from 216 patients with monkeypox <ul style="list-style-type: none"> ○ Fetal death was reported among four of five patients who were pregnant ○ Patients who died had higher viral DNA and the maximum lesion count ○ The most common complaints were rash (96.8%), malaise (85.2%), sore throat (78.2%), and lymphadenopathy/adenopathy (57.4%) ● Patients under five years of age had the highest lesion count, and primary household cases tended to have higher lesion counts than secondary household cases (Last updated 29 May 2022; Pre-print) ● A non-systematic review reported that monkeypox symptoms can occur in three phases including: 1) an incubation period of four to 21 days; 2) prodromal illness with signs including lymph node enlargement, headache, fever, back pain, myalgia, intense asthenia, pharyngitis, sweating and malaise; and 3) followed by an exanthema phase that includes vesiculopustular rashes that appear 	

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<p>within one to 10 days spread over the body) (Published 12 November 2020)</p> <ul style="list-style-type: none"> • A non-systematic review described that monkeypox is similar to smallpox but generally less severe (Published December 2019) <ul style="list-style-type: none"> ○ Incubation period is estimated at five to 21 days, and symptoms and signs at two to five weeks ○ The illness begins with nonspecific symptoms and signs including fever, chills, headaches, lethargy, asthenia, lymph node swelling, back pain, and myalgia, followed by rashes of varying size that appear first on the face then across the body, hands, legs, and feet ○ Complications such as secondary bacterial infections, respiratory distress, broncho-pneumonia, encephalitis, corneal infection with vision loss, gastrointestinal involvement, vomiting, and diarrhea with dehydration ○ Case fatality rates have varied between 1% and 10% and occur mostly among young adults and children, especially those with immunosuppression • A non-systematic review indicated that the clinical presentation of the monkeypox virus largely resembles that of smallpox, with an incubation period of seven to 17 days, and includes fever, muscle aches, backache, lymphadenopathy, followed by lesions and rashes all over the body (Published April 2019) • A non-systematic review indicated that the clinical presentations of the monkeypox virus includes symptoms with skin and mucosal lesions which are difficult to distinguish from smallpox, and the infection starts with fever, headache, back pain, myalgia and asthenia followed by eruption of skin and mucosal lesions starting with the face (Published January 2019) • A single study reported that a suspected monkeypox case was defined as an individual with a vesicular or pustular rash with deep-seated, firm pustules, and ≥ 1 of the following symptoms: fever preceding the eruption, lymphadenopathy (inguinal, axillary, or cervical), or pustules or crusts on the palms of the hands or soles of the feet (Published 4 June 2021) 	

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<ul style="list-style-type: none"> • A single study described the clinical course and management of 40 hospitalized monkeypox cases during the 2017-2018 human monkeypox outbreak in Nigeria using retrospective records <ul style="list-style-type: none"> ○ The most common clinical features observed (in order) included skin rash, fever, lymphadenopathy, genital ulcers, body aches, headache, sore throat, pruritus, and conjunctivitis and photophobia ○ The most common first symptoms were rash and fever ○ Twenty-one (52.5%) of 40 cases developed one or more complications including (in order of frequency) secondary bacterial infection, gastroenteritis, sepsis, bronchopneumonia, encephalitis, keratitis, and premature rupture of membrane at 16 weeks' gestation and resultant intrauterine fetal death ○ Patients with HIV type 1 coinfection were significantly more likely to have larger skin rashes, genital ulcers, secondary bacterial infection, and longer duration of illness ○ Sequelae observed amongst 18 patients discharged from hospital and seen at follow-up included hyperpigmented atrophic scars, hypopigmented atrophic scars, patchy alopecia, hypertrophic skin scarring, and contracture/ deformity of facial muscles; three of the 18 patients showed complete healing after eight weeks of follow-up (Published 15 October 2020) 	
Prognosis	<ul style="list-style-type: none"> • A low-quality guideline described a clinical management algorithm for people who are pregnant with suspected monkeypox virus exposure, and recommended that all cases of monkeypox virus in pregnancy are reported to WHO and an international registry for emerging pathogens, as well as clinicians to consider Tecovirimat and vaccinia immune globulin for people who are pregnant and are severely ill (Published 2 July 2022) • A single study of 40 monkeypox cases found that 21 (52.5%) developed one or more complications including (in order of frequency) secondary bacterial infection, gastroenteritis, sepsis, bronchopneumonia, encephalitis, keratitis, and premature rupture of membrane at 16 weeks' gestation and resultant intrauterine fetal death (published 15 October 2020) <ul style="list-style-type: none"> ○ Five (12.5%) of the cases died 	<ul style="list-style-type: none"> • As of September 6, 2022, of the 631 confirmed cases of monkeypox in Ontario, 99.4% are male and 0.6% female, 2.9% have been hospitalized, 0.3% have been admitted to the ICU, and no deaths have been reported • On 9 September 2022, RKI pre-published an article that investigated the current incubation period of monkeypox during the ongoing outbreak in Germany; nearly 20% of the cases had an incubation period of one to three days • As of 22 August 2022, of the 582 confirmed cases of monkeypox in Ontario, 99.5% are male, 3.1% have been hospitalized, 0.3% have been admitted to the ICU, and no deaths have been reported • A report by Public Health Ontario dated 15 August 2022 indicates that 16 of 529 (3%) confirmed cases have been

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<ul style="list-style-type: none"> ○ Patients with HIV type 1 coinfection were significantly more likely to have larger skin rashes, genital ulcers, secondary bacterial infection, and longer duration of illness ○ Sequelae observed amongst 18 patients discharged from hospital and seen at follow-up included hyperpigmented atrophic scars, hypopigmented atrophic scars, patchy alopecia, hypertrophic skin scarring, and contracture/deformity of facial muscles; three of the 18 patients showed complete healing after eight weeks of follow-up ● A cross-sectional single study of 223 participants found that hunting of non-human primates was associated with rash severity in both unadjusted and adjusted models (OR= 2.78 (95% CI: 1.18, 6.58)), while exposure to non-human primates was associated with rash severity only in an unadjusted model (published 24 December 2019) <ul style="list-style-type: none"> ○ There was no association found between rodent exposure and monkeypox rash severity ● In an observational single study of fetal outcomes of four pregnant women with infected with monkeypox, three of four experienced fetal demise (17 October 2017) <ul style="list-style-type: none"> ○ The study concluded that maternal monkeypox infection may have adverse consequences for the fetus without apparent correlation with severity of maternal disease 	<p>hospitalized, and 0.4% have been in the ICU; no deaths have been reported</p> <ul style="list-style-type: none"> ● A report by Public Health Ontario dated 29 July 2022 indicates that 11/367 (3%) of confirmed cases have been hospitalized, and 0.5% have been in the ICU; no deaths have been reported <ul style="list-style-type: none"> ○ 99.5% of cases are male, 0.5% are female ● Spain has recorded its first two deaths in patients infected with monkeypox <ul style="list-style-type: none"> ○ The Ministry of Health of Andalusia has reported that one of the deaths is a 31-year-old man who was admitted to the Intensive Care Unit of the Reina Sofía University Hospital in Córdoba with meningoencephalitis caused by the infection ● The first victim, in the Valencian Community, was also a young man (his age has not been reported) who also suffered from encephalitis ● A report by Public Health Ontario dated 18 July 2022 indicates that 9/230 cases have been hospitalized, and 1/230 have been in the intensive care unit, and no deaths have been reported ● According to the SiViES health report in Spain, 48 cases have been hospitalized (4.0%) and none of the cases has died ● The Eurosurveillance case report describing the monkeypox infection in an individual returning to Australia from Europe concluded that normal CD4+ T-cell count and suppressed HIV viral load on antiretroviral therapy were potential important factors in preventing more severe outcomes ● Most monkeypox cases are mild and the infected person will recover within a few weeks ● Although monkeypox is generally mild, it has been reported to be potentially more severe in children and immunocompromised individuals, as there is the possibility of superinfections of skin lesions or further complications arising from existing respiratory, digestive, ophthalmological, or neurological disorders ● Complications may include secondary bacterial infections, bronchopneumonia, sepsis, encephalitis, and corneal infection with subsequent loss of vision

Organizing framework domain	Evidence from previous version	Experiences from previous version
		<ul style="list-style-type: none"> The severity of illness can depend upon the initial health of the individual, the route of exposure, and the strain of the infecting virus (West African vs. Central African virus genetic groups, or clades)
Treatment	<ul style="list-style-type: none"> A high-quality guideline published in France indicated that all symptomatic cases should not be treated with a drug, but only people at higher risk should be considered for treatment with tecovirimat, brincidofovir, cidofovir, and anti-monkeypox immunoglobulins (high-quality AGREE II rating; published in Clinical Microbiology and Infection) A low-quality rapid review found that combined use of antiviral drugs, including cidofovir, brincidofovir, and tecovirimat, and vaccinia immune globulin (produced from the pooled blood of the vaccinated population by the smallpox vaccine) can enhance significant effectiveness in immunocompromised subjects According to a recent pre-published study, the rate of appearance of active lesions decreased gradually throughout treatment of 14 patients with tecovirimat between December 2021 and February 2022, with the median time for new lesions being five days following the start of treatment Tecovirimat is an antiviral drug that has been approved by the FDA for the treatment of smallpox and by the European Medicine Agency for the treatment of orthopoxvirus diseases A retrospective single study examined the longitudinal clinical course of monkeypox in the U.K., viral dynamics, and the adverse events of novel antiviral therapies in seven patients who were diagnosed from 2018-2021 <ul style="list-style-type: none"> five patients remained in isolation for more than three weeks due to PCR positivity three patients were treated with Brincidofovir (200 mg once a week orally), all developing elevated liver enzymes, which resulted in the stopping of therapy one patient received Tecovirimat (600 mg twice daily for two weeks orally) and experienced no adverse effects with a shorter 	<ul style="list-style-type: none"> As of September 6, 2022, of the 631 confirmed cases of monkeypox in Ontario, 99.4% are male and 0.6% female, 2.9% have been hospitalized, 0.3% have been admitted to the ICU, and no deaths have been reported On 9 September 2022, RKI pre-published an article that investigated the current incubation period of monkeypox during the ongoing outbreak in Germany; nearly 20% of the cases had an incubation period of one to three days The National Institute for Health and Care Research in the U.K. has commissioned the Placebo-Controlled Randomized Trial of Tecovirimat in Non-Hospitalized Monkeypox Patients (Platinum) trial to test the safety and efficacy of tecovirimat in monkeypox patients <ul style="list-style-type: none"> The trial has already begun recruiting patients The trial will examine the following outcomes: time needed for skin and mucosal lesion healing, time for throat and lesion swabs to test negative, rate of hospitalization The British HIV Association has released a statement on monkeypox which includes information regarding the impact of HIV on monkeypox, vaccine considerations, as well as pharmacokinetic and renal considerations for treatment According to the U.S. CDC, there is currently no treatment available specifically for monkeypox infections, however there are medical countermeasures available through the Strategic National Stockpile (SNS) with limited available evidence on its effectiveness for the treatment of monkeypox such as: 1) Tecovirimat; 2) Vaccinia Immune Globulin Intravenous (VIGIV); 3) Cidofovir; and 4) Brincidofovir A report by the Ontario Ministry of Health dated 28 May 2022 provides guidance for the Imvamune vaccine as post-exposure prophylaxis (PEP)

Organizing framework domain	Evidence from previous version	Experiences from previous version
	<p>duration of viral shedding and illness (10 days of hospitalization) (Published 24 May 2022)</p> <ul style="list-style-type: none"> • A non-systematic review noted that monkeypox is primarily treated through supportive care, symptomatic management, and treatment of secondary bacterial infections (Published December 2019) • A non-systematic review highlights that antivirals such as Tecovirimat, Cidofovir and Brincidofovir have shown efficacy in in vitro and animal studies, but their effectiveness in humans is unknown (Published 12 November 2020) <ul style="list-style-type: none"> ○ Cidofovir and Brincidofovir may be considered in severe cases of monkeypox ○ Brincidofovir may have an improved safety profile compared to Cidofovir ○ Human clinical trials of Tecovirimat suggested that the drug was safe and tolerable with only minor side effects • A non-systematic review noted that the recent development of Tecovirimat (and its license in Nigeria) as an antipoxvirus cure is an important achievement in antiviral therapy (Published April 2019) • A single study examining monkeypox outbreaks in Africa concluded that robust disease surveillance systems with initial and long-term financial and human resource investment are required to stop the spread of monkeypox (published 16 March 2018) <ul style="list-style-type: none"> ○ Coordination of interventions and routine sharing of information between human and wildlife sectors is necessary because monkeypox is a zoonotic disease • A single study of pregnant women infected with monkeypox in the Democratic Republic of Congo noted that during hospitalization, pregnant women received antibiotics (amoxicillin, chloramphenicol via eye drops, and erythromycin, as well as gentamycin, if necessary) for prevention or control of bacterial superinfection, paracetamol and papaverine were given as analgesics, metronidazole and mebendazole were administered for giardiasis and other intestinal parasitic infections, and quinine as given for malaria (17 October 2017) 	<ul style="list-style-type: none"> ○ Imvamune is a live third generation replication deficient smallpox vaccine, developed to provide an alternative for the vaccination of immunocompromised individuals with atopic dermatitis who could not receive replicating smallpox vaccines • In the U.K., the Health Security Agency has released interim guidance about the de-isolation and discharge of monkeypox-infected patients, which pertains both to patients admitted to hospitals as well as those who manage symptoms at homes • All jurisdictions highlight that treatment for monkeypox is mainly supportive • While most patients recover well with only supportive care, some patients may need pain medication, intravenous fluids, and viral medications for severe cases. • Recently, the European Union approved Tecovirimat to help treat monkeypox infections (but its availability is currently limited) • CDC lists antivirals Cidofovir, Brincidofovir and Tecovirimat as possible treatments for severe cases of monkeypox, but that their clinical effectiveness in humans have not yet been confirmed • Additionally, several countries note that smallpox vaccines, antivirals, and vaccinia immune globulin may be used during the first few days of someone who may have been infected as a preventive measure to help control outbreaks

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To help health- and social-system leaders as they respond to pressing challenges, the McMaster Health Forum prepares rapid evidence profiles like this one. This rapid evidence profile was commissioned by the Office of the Chief Science Officer, Public Health Agency of Canada. The opinions, results, and conclusions are those of the McMaster Health Forum and are independent of the funder. No endorsement by the Public Health Agency of Canada is intended or should be inferred.



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Appendix 1: Methodological details

We use a standard protocol for preparing living evidence profiles (LEP) to ensure that our approach to identifying research evidence as well as experiences from other countries and from Canadian provinces and territories are as systematic and transparent as possible in the time we were given to prepare the profile.

Identifying research evidence

For this LEP, we searched [ACCESSSS](#), [HealthEvidence](#), [Health Systems Evidence](#), [PubMed](#) and [MedRxiv](#) for:

- 1) guidelines (defined as providing recommendations or other normative statements derived from an explicit process for evidence synthesis);
- 2) full systematic reviews;
- 3) rapid reviews;
- 4) protocols for reviews or rapid reviews that are underway;
- 5) titles/questions for reviews that are being planned; and
- 6) single studies (when no guidelines, systematic reviews or rapid reviews are identified).

In each database we used the open search function for monkey pox OR monkeypox. In PubMed, we used the MeSH headings of monkeypox and monkeypox virus combined with open text terms of monkeypox and monkey pox. All searches were limited to literature published from 2017 onwards to capture any evidence related to recent outbreaks outside Africa.

Each source for these documents is assigned to one team member who conducts hand searches (when a source contains a smaller number of documents) or keyword searches to identify potentially relevant documents. A final inclusion assessment is performed both by the person who did the initial screening and the lead author of the rapid evidence profile, with disagreements resolved by consensus or with the input of a third reviewer on the team. The team uses a dedicated virtual channel to discuss and iteratively refine inclusion/exclusion criteria throughout the process, which provides a running list of considerations that all members can consult during the first stages of assessment.

During this process we include published, pre-print and grey literature. We do not exclude documents based on the language of a document. However, we are not able to extract key findings from documents that are written in languages other than Chinese, English, French or Spanish. We provide any documents that do not have content available in these languages in an appendix containing documents excluded at the final stages of reviewing.

Identifying experiences from other countries and from Canadian provinces and territories

For each LEP, we collectively decide on what countries to examine based on the question posed. For other countries we searched relevant government and stakeholder websites. In Canada, we search websites from relevant federal and provincial governments, ministries and agencies (e.g., Public Health Agency of Canada).

While we do not exclude countries based on language. Where information is not available in English, Chinese, French or Spanish, we attempt to use site-specific translation functions or Google translate.

Assessing relevance and quality of evidence

We assess the relevance of each included evidence document as being of high, moderate or low relevance to the question. We then use a colour gradient to reflect high (darkest blue) to low (lightest blue) relevance.

Two reviewers independently appraised the quality of the guidelines we identified as being highly relevant using AGREE II. We used three domains in the tool (stakeholder involvement, rigour of development and editorial independence) and classified guidelines as high quality if they were scored as 60% or higher across each of these domains.

Two reviewers independently appraise the methodological quality of systematic reviews and rapid reviews that are deemed to be highly relevant. Disagreements are resolved by consensus with a third reviewer if needed. AMSTAR rates overall methodological quality on a scale of 0 to 11, where 11/11 represents a review of the highest quality. High-quality reviews are those with scores of eight or higher out of a possible 11, medium-quality reviews are those with scores between four and seven, and low-quality reviews are those with scores less than four. It is important to note that the AMSTAR tool was developed to assess reviews focused on clinical interventions, so not all criteria apply to systematic reviews pertaining to health-system arrangements or to economic and social responses. Where the denominator is not 11, an aspect of the tool was considered not relevant by the raters. In comparing ratings, it is therefore important to keep both parts of the score (i.e., the numerator and denominator) in mind. For example, a review that scores 8/8 is generally of comparable quality to a review scoring 11/11; both ratings are considered 'high scores.' A high score signals that readers of the review can have a high level of confidence in its findings. A low score, on the other hand, does not mean that the review should be discarded, merely that less confidence can be placed in its findings and that the review needs to be examined closely to identify its limitations. (Lewin S, Oxman AD, Lavis JN, Fretheim A. SUPPORT Tools for evidence-informed health Policymaking (STP): 8. Deciding how much confidence to place in a systematic review. *Health Research Policy and Systems* 2009; 7 (Suppl1):S8.

Preparing the profile

Each included document is hyperlinked to its original source to facilitate easy retrieval. For all included guidelines, systematic reviews, rapid reviews and single studies (when included), we prepare a small number of bullet points that provide a brief summary of the key findings, which are used to summarize key messages in the text. Protocols and titles/questions have their titles hyperlinked given that findings are not yet available. For this profile, we only prepared bulleted summaries of key findings for documents deemed to be of high relevance. For those classified as medium or low relevance, we list the title with a link to the primary source for easy retrieval if needed. We then draft a brief summary that highlights the total number of different types of highly relevant documents identified (organized by document), as well as their key findings, date of last search (or date last updated or published), and methodological quality.

Appendix 2a: Key findings from new evidence documents that address the question, organized by document type, and sorted by relevance to the question and monkeypox

Type of document	Relevance to question	Key findings	Recency or status
Guidelines	None identified		
Full systematic reviews	<ul style="list-style-type: none"> Biology 	<ul style="list-style-type: none"> The aim of this study was to synthesize evidence on serial interval (SI) and incubation period (IP) of the monkeypox virus Estimates of SI and IP have been reported for three clades of the monkeypox virus Authors concluded that there is a need to adjust for control measures (e.g., entry restrictions) and the length of a quarantine following the changes in these two epidemiological metrics throughout an epidemic <p>Source (5/11 AMSTAR rating)</p>	Literature last searched 26 August 2022 (pre-print)
	<ul style="list-style-type: none"> Epidemiology Clinical presentation 	<ul style="list-style-type: none"> The main objective of this systematic review was to examine the risk factors, transmission routes, and clinical characteristics of monkeypox patients Data from a total of 3,097 patients was analyzed across 14 studies; the median age of patients was 30-40 years, prevalence of the virus among men was 99.9% and among men who have sex with men was 98.7%, a pre-existing positive HIV diagnosis was found in 37.9% of patients, and 22.1% of patients had a concurrent sexually transmitted infection Commonly reported symptoms or characteristics among patients were mucocutaneous lesions (98.8%), a fever (63.5%), inguinal lymphadenopathy (55.4%), and asthenia (47.4%); monkeypox cases leading to hospitalization were found to be 7.2% <p>Source (4/10 AMSTAR rating)</p>	Literature last searched 21 August 2022
	<ul style="list-style-type: none"> Clinical presentation 	<ul style="list-style-type: none"> This review included 14 papers that reported on a total of 4,080 cases of monkeypox virus The most common clinical manifestations were rash, fever, and lymphadenopathy, while arthralgia and rectal bleeding were the least common 	Literature last searched 2 September 2022

		<ul style="list-style-type: none"> • For a proper differential diagnosis, authors suggested to consider lymphadenopathy, which might differentiate monkeypox from other diseases, like varicella and smallpox • The pattern of lesions distribution in genitalia, and a history of men who have sex with man, are other important factors to guide a differential diagnosis of monkeypox • In this study, 7% of patients required hospitalization, with no ICU admissions or mortality events • This review suggests that the current outbreak is significantly milder than previous outbreaks, which might be attributed to a better quality of care offered to patients who live in high-income countries and to the fact that patients in this outbreak are younger • The reported mortality rates in some patients might be attributed to the HIV co-infection, and to atypical presentations of monkeypox, which included encephalitis, sepsis, and myopericarditis; however, the exact cause-effect of the different morbidities on the severity of monkeypox should be further studied <p>Source 3/11 AMSTAR rating</p>	
	<ul style="list-style-type: none"> • Diagnosis 	<ul style="list-style-type: none"> • This article aimed to analyze saliva-based PCR tests for monkeypox, and includes an assay performance alongside a systematic rapid review to compare saliva-based tests compared to lesion swabs • The study describes a saliva-based polymerase chain reaction (PCR) assay for monkeypox, in vitro test performance <ul style="list-style-type: none"> ○ The assay showed in silico inclusivity of 100% for all (n= 97 strains) of the monkeypox virus, with an analytic sensitivity of 250 copies/ml ○ The assay was specific to the orthopoxvirus genus and did not detect nonorthopoxvirus genera • A systematic rapid review was conducted to assess the performance of saliva tests to PCR of lesion swabs <ul style="list-style-type: none"> ○ Early detection of lesion swabs may also mean the virus can be transmissible through lesion development. ○ Salvia-based testing may identify cases earlier than lesion-based tests 	<p>Published 2 October 2022</p>

		<ul style="list-style-type: none"> ○ Adapting to SARS-Cov-2 testing sites may increase testing accessibility and capacity Source (5/10 AMSTAR rating) 	
	<ul style="list-style-type: none"> • Epidemiology 	<ul style="list-style-type: none"> • The review aimed to compare the historical evidence of monkeypox outbreaks within fatality rate, transmission, patient characteristics, and incidence <ul style="list-style-type: none"> ○ Human monkeypox has been historically more contagious and limited to African countries, but now infections spread internationally (first emerging from West Africa) • Based on a risk assessment, human monkeypox is affected by human transmission through contact and exposure to the outdoors (sleeping outside or entering rainforests) • Historically, monkeypox transmission was spread by animals, however, recent cases showed transmission of monkeypox by secondary affliction and sexual contact • All age groups are affected by the pattern of transmission compared to previously when monkeypox primarily affected children • Reviewing the history of monkeypox outbreaks can provide perspectives on prevention for present and future outbreaks Source (3/9 AMSTAR rating) 	Last updated 30 July 2022
Rapid reviews	<ul style="list-style-type: none"> • Epidemiology 	<ul style="list-style-type: none"> • The focus of this rapid review was to examine the current body of literature surrounding the sexual transmission of the monkeypox virus • The authors note that the evidence is scarce and at times, contrasting, regarding the persistence of the monkeypox virus in human male semen; further investigation is recommended to examine if and at what concentrations monkeypox can be sexually transmitted Source (1/9 AMSTAR rating) 	Published 13 September 2022
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • This rapid review described human immune responses to orthopoxviruses, provided an overview of the vaccines available for orthopoxviruses, and discussed the literature evaluating protective immunity elicited by vaccinia virus-based smallpox vaccines • The clinical effectiveness of smallpox vaccines (~85%) against monkeypox was determined from surveillance studies 	Literature last searched 8 August 2022

		<p>conducted in central Africa in the 1980s, and also later during outbreaks in the same area</p> <ul style="list-style-type: none"> ○ These studies showed a high degree of protection and immunity against monkeypox virus from various smallpox vaccines, however, smallpox vaccines in some cases cause side effects and have contraindications ● Although safer for use in immunocompromised populations, third-generation vaccines that require two doses can be an impediment to rapid outbreak response ● The Jynneos vaccine was identified as the safest vaccine available for pre-exposure and post-exposure use in preventing monkeypox <ul style="list-style-type: none"> ○ ACAM2000 and LC16m8 vaccines are also available in different countries; in addition, in some countries, antivirals might be available for treatment <p>Source (3/9 AMSTAR rating)</p>	
	<ul style="list-style-type: none"> ● Prevention and control 	<ul style="list-style-type: none"> ● In this review, 22 articles and eight vaccine recommendations were examined to understand the background of monkeypox virus vaccine development and highlight current related guidelines ● The smallpox vaccine, which is 85% effective in preventing infection, was found to be the only immunization option for monkeypox during the authors' examination ● More specifically, the Jynneos smallpox vaccine was found to be the most preferable and advised vaccine, with an emphasis on third-generation smallpox vaccines due to their minimal side effects ● The priority list to receive vaccination included healthcare providers, lab professionals, pregnant women or lactating mothers, and immunocompromised or chronically ill patients ● The study concluded that with the rapid spread of monkeypox, more clinical trials on humans should be conducted to further evaluate vaccine safety, efficacy, and adverse events <p>Source</p>	<p>Published 29 Sept 2022 (pre-print)</p>
<p>Non-systematic reviews</p>	<p>None identified</p>		

Protocols for reviews that are already underway	<ul style="list-style-type: none"> Prevention and control Treatment 	The role of vaccination and treatment in monkeypox: A systematic review	Anticipated completion 12 October 2022
	<ul style="list-style-type: none"> Diagnosis 	Diagnostic accuracy of PCR and ELISA for monkeypox infection: A systematic review and meta-analysis	Anticipated completion 6 October 2022
	<ul style="list-style-type: none"> Clinical presentation Treatment 	Spectrum of ocular manifestations and its treatment in monkeypox virus infection worldwide: Systematic review	Anticipated completion 8 October 2022
	<ul style="list-style-type: none"> Clinical presentation 	ENT manifestations in Monkeypox patients: A systematic review and meta-analysis	Anticipated completion 15 October 2022
	<ul style="list-style-type: none"> Clinical presentation 	Oral manifestations of human monkeypox (HMPX) infection: Systematic review and meta-analysis	Anticipated completion 30 November 2022
	<ul style="list-style-type: none"> Treatment 	Clinical outcomes of established and promising treatment modalities of monkeypox- A systematic review of case reports	Anticipated completion 11 December 2022
	<ul style="list-style-type: none"> Clinical presentation 	Comparison of clinical symptoms from patients in the 2022 monkeypox outbreak versus previous outbreaks – a systematic review and meta-analysis	Anticipated completion 31 Oct 2022
	<ul style="list-style-type: none"> Prevention and control 	Acceptance towards monkeypox vaccination: A systematic review and meta-analysis	Anticipated completion 31 Oct 2022
	<ul style="list-style-type: none"> Epidemiology 	Epidemiologic situation of HIV and monkeypox coinfection: Systematic review	Anticipated completion 28 Oct 2022
	<ul style="list-style-type: none"> Clinical presentation 	All presentations associated with human monkeypox virus infection: a systematic review and meta-analysis	Anticipated completion 25 Nov 2022
	<ul style="list-style-type: none"> Epidemiology 	The return of Monkeypox: Assessment of prevalence, transmission and treatment	Anticipated completion 31 Dec 2023
Titles and questions for reviews being planned	None identified		
Single studies	<ul style="list-style-type: none"> Epidemiology 	<ul style="list-style-type: none"> Upon monitoring 313 healthcare professionals who had contact with monkeypox patients in Colorado, U.S. from 1 May to 31 	Published 23 September 2022

		<p>July 2022, this study found that the risk of transmission in healthcare settings can be classified as ‘low’, as none of the staff had contracted the virus</p> <ul style="list-style-type: none"> • Only 23% of healthcare professionals were wearing all the recommended personal protective equipment at the time of exposure • The authors emphasized the importance of infection-prevention measures, including appropriately educating and training the workforce • A few limitations exist with the study, including the lack of generalizability as many of the included clinics were referral sites and thus had higher compliance, and the underreporting of post-exposure prophylaxis vaccination data <p>Source</p>	
	<ul style="list-style-type: none"> • Epidemiology 	<ul style="list-style-type: none"> • The primary focus of this paper was to examine the forecast of monkeypox cases by analyzing data from 10 countries at the end of August 2022 and proposing a parametric regression model for incidence indicators • The 10 countries under analysis included Brazil, Canada, France, Germany, the Netherlands, Peru, Portugal, Spain, United Kingdom, and the United States • The findings from this study found that despite outbreaks occurring across the globe, they are largely contained and under control in most countries (with the exception of the United States and Peru) <p>Source</p>	<p>Published 19 September 2022</p>
	<ul style="list-style-type: none"> • Epidemiology 	<ul style="list-style-type: none"> • The aim of this study was to estimate the global risk of monkeypox importation considering hypothetical scenarios of travel restrictions by varying passenger volumes using the airline travel network • Passenger volume data at 1,680 airports in 176 countries (and territories) as well as the time of first confirmed monkeypox case were extracted from publicly available data sources <ul style="list-style-type: none"> ○ A survival analysis technique was used to estimate the importation risk • The arrival time range was nine to 48 days since the first case was identified in the U.K. on 6 May 2022 	<p>Published 18 September 2022 (pre-print)</p>

		<ul style="list-style-type: none"> ○ Travel restrictions had a minor impact on the global airline importation risk against monkeypox ● The estimated risk of importation showed that most locations will have an intensified importation risk regardless of the geographic region by 31 December 2022 ● The authors concluded that airports should enhance local capacities to identify monkeypox cases and prepare to carry out contact tracing and isolation <p>Source</p>	
	<ul style="list-style-type: none"> ● Prevention and control 	<ul style="list-style-type: none"> ● This study examined behavioural changes in men who have sex with men (MSM) and transgender women in the U.S. ● Of the 703 individuals who completed the study survey, 55.9% reported a change in their sexual behaviours because of the monkeypox outbreak, with approximately a quarter of participants becoming abstinent or avoiding having any type of sex, asking their sexual partners if they have symptoms of monkeypox, or inspecting their sexual partners for symptoms ● Results of this study demonstrated that MSM and transgender women used a variety of exposure-mitigation strategies, including limiting the number of sexual partners they had and limiting their exposure by avoiding crowded social venues where skin-to-skin contact is likely to occur ● These findings can be applied to public-health intervention campaigns for MSM and transgender women that address monkeypox exposure <p>Source</p>	<p>Published 14 September 2022</p>
	<ul style="list-style-type: none"> ● Diagnosis 	<ul style="list-style-type: none"> ● This prospective diagnostic accuracy evaluation study recruited 50 individuals and evaluated the accuracy of patient self-collected skin lesions, pharyngeal, and rectal swabs ● The study found that the performance of self-collected and physician-collected samples was similar, suggesting that self-sampling is a reliable strategy for diagnosing monkeypox <p>Source</p>	<p>Last updated 20 September 2022 (pre-print)</p>
	<ul style="list-style-type: none"> ● Diagnosis 	<ul style="list-style-type: none"> ● This study examined epidemiological characteristics, specimen collection practices, and cycle threshold values for monkeypox virus PCR tests performed at two reference laboratories in the U.S. 	<p>Last updated 21 September 2022 (pre-print)</p>

		<ul style="list-style-type: none"> • The viral load of positive specimens was comparable between both laboratories, however, differences were explained by variations in extraction strategies and the use of dry swabs, which showed stronger viral loads than swabs in viral transport medium (VTM) • As CDC recommended collecting two swabs per patient, this study explored the utility of submitting multiple lesion swabs <ul style="list-style-type: none"> ○ When multiple specimens were collected for a single individual, the overall result concordance rate was greater than 95% ○ Skin lesions showed the highest sensitivity ○ Submitting multiple specimens in separate tubes increases the workload of the laboratory staff as well as the costs ○ Discordant positives were associated with substantially lower viral loads in comparison to the total positive cohort <p>Source</p>	
	<ul style="list-style-type: none"> • Treatment 	<ul style="list-style-type: none"> • This study described characteristics of persons treated with tecovirimat for monkeypox virus infection in the U.S. • Approximately one-half of patients with monkeypox virus infection who received tecovirimat were living with HIV infection, and time to improvement did not differ significantly with HIV infection status <ul style="list-style-type: none"> ○ Among patients with available data (n=369), 99.8% were prescribed oral tecovirimat, and 93.1% were not hospitalized ○ Adverse events were reported in 3.5% of patients, and all but one adverse event were considered non-serious ○ The median interval from initiation of tecovirimat to subjective improvement was three days; however, no control group was available for comparison • Given these findings, no conclusions could be drawn regarding the effectiveness of tecovirimat <p>Source</p>	<p>Published 16 September 2022</p>
	<ul style="list-style-type: none"> • Diagnosis 	<ul style="list-style-type: none"> • This article aimed to compare 13 pre-trained deep-learning models for monkeypox virus detection which were fine-tuned and tested on publicly available data sets based on four measures: Precision, Recall, F1 score and Accuracy 	<p>Last updated 6 October 2022</p>

		<ul style="list-style-type: none"> • Based on the results, the two best-performing fine-tuned models (Xception and DenseNet-169) were selected for an ensemble method • The proposed ensemble method had an accuracy of 87.1% and was the best performing among the 13 contenders for performance and monkeypox detection <ul style="list-style-type: none"> ○ The performance metrics of the decision fusion are 85.44% of Precision, 85.47% of Recall and 85.40% of F1-score • These results impart a higher result than both the second-best performing model Xception, and the least-performing model, VGG-16 <ul style="list-style-type: none"> ○ With a confusion matrix, the ensemble can discriminate measles and monkeypox as well as highly discriminate chickenpox <p>Source</p>	
	<ul style="list-style-type: none"> • Diagnosis 	<ul style="list-style-type: none"> • Sixteen male monkeypox patients, including five hospitalized patients and 11 outpatients, were included in this study • Five underwent serial laboratory testing or lesion and oropharyngeal swabs and blood testing; clinical information was available for a further five, and initial viral load data was available for six • Infectious virus was successfully isolated from lesion swabs but not from oropharyngeal swabs <ul style="list-style-type: none"> ○ All initial lesion swabs (performed between days three and 17 following symptom onset) were positive for monkeypox, while some oropharyngeal swabs returned negative ○ For five patients with longitudinal data available, viral load of lesion swabs remained high (consistently at or above 106 cp/ml) for two weeks and declined during the third week, while continuing to test positive ○ Oropharyngeal swabs were negative in two of five patients, and were low with a downward trend over time for the other three ○ Blood samples were positive for four of five patients and viral load declined over time • Results of the study suggests that oropharyngeal swabs and blood samples alone carry the risk of false-negative results, but 	<p>Published October 2022</p>

		<p>they may be valuable for use in pre-/asymptomatic cases or viral load monitoring, respectively</p> <ul style="list-style-type: none"> • The authors conclude that the results underscore the reliability of lesion swabs for detection of monkeypox virus, even in later stages of the disease <p>Source</p>	
	<ul style="list-style-type: none"> • Epidemiology • Clinical presentation 	<ul style="list-style-type: none"> • This observational study included 48 confirmed cases of monkeypox in Madrid, Spain • With respect to demographics: <ul style="list-style-type: none"> ○ All individuals were cisgender men, 87.5% of whom were men who have sex with men ○ 39.5% of individuals were people living with HIV and 47.9% were on daily PrEP • With respect to clinical presentation: <ul style="list-style-type: none"> ○ First symptoms included skin lesions (53.8%of individuals), fever (17.9%), and respiratory symptoms (12.8%) • 89.5% had unprotected sex in the three weeks before symptom onset, and 50% had chemsex (i.e., using drugs during sex with multiple partners) • None had travelled to or had contact with people from endemic regions • Phylogenetic analysis showed that the virus belongs to the Western African clade and is closely related to strains circulating in Europe • Seven out of 10 patients who had receptive anal sex had perianal lesions compared to one of 13 who had insertive anal sex; one out of 10 patients who had receptive anal sex had genital lesions compared to 12 out of 13 who had insertive anal sex <p>Source</p>	<p>Published online 10 July 2022</p>
	<ul style="list-style-type: none"> • Biology 	<ul style="list-style-type: none"> • The study discusses the first known monkeypox virus-encoded proteome structure, A42R, which has a similar structure to profilins <ul style="list-style-type: none"> ○ The open-reading frame encoding monkeypox A42R was amplified and cloned from monkeypox Zaire-96-I-16 strain DNA 	<p>Published 2022</p>

		<ul style="list-style-type: none"> ○ Critical analysis of A42R structure to the profilin family reveals that A42R weakly binds to actin and does not bind poly(1-proline) ● Overall, the study results suggests that the role of A42R in the replication of poxviruses may not be readily determined by comparing its structure to cellular profilins ● The study concluded that more effort on monkeypox research be directed towards developing high-resolution imaging of other monkeypox proteins <p>Source</p>	
	<ul style="list-style-type: none"> ● Epidemiology ● Clinical presentation 	<ul style="list-style-type: none"> ● This study aimed to describe and analyze the epidemiological and clinical characteristics of individuals with confirmed cases of monkeypox infection ● Using the 226 cases reported through the GeoSentinel global clinical-care-based surveillance system in 29 countries from 1 May to 1 July 2022, the following was found: <ul style="list-style-type: none"> ○ 99% of men were gay, bisexual or have sex with men ○ Of the men who had a known HIV status, 44% had HIV infection ○ 99% of cases reported sexual or close intimate contact within the 21 days before symptom onset ○ 40% of cases reported close contact with someone who had confirmed monkeypox ○ 13% were admitted to the hospital, 53% of whom had severe illness ○ Patients with HIV were more likely to experience diarrhea, perianal rash or lesions, and rash burden ● The researchers recommend that pre-exposure monkeypox vaccination guidelines should be expanded to include those at high risk of infection and who plan to engage in sexual or close intimate contact <p>Source</p>	Published 7 Oct 2022
	<ul style="list-style-type: none"> ● Epidemiology 	<ul style="list-style-type: none"> ● The aim of this study was to measure the degree of contamination in isolation rooms of patients with confirmed monkeypox in a U.K. hospital ● Surface swabs of areas in isolation rooms, personal protective equipment of healthcare workers, and air samples were used 	Published 7 Oct 2022

		<ul style="list-style-type: none"> 93% or 56 out of 60 samples were found to be positive, indicating widespread environmental contamination, especially after clinical contact and changing of bedding <p>Source</p>	
	<ul style="list-style-type: none"> Prevention and control 	<ul style="list-style-type: none"> This report identified incidence of monkeypox among vaccinated (with Jynneos vaccination) versus unvaccinated individuals in 32 U.S. jurisdictions Out of 6,471 monkeypox cases, 5,402 (83.5%) were reported among males aged 18-49 years, which coincides with prior research 85.3% of positive cases were among unvaccinated persons, and monkeypox incidence was found to be 14 times higher among unvaccinated individuals compared to those who had received their first vaccine dose ≥ 14 days earlier The authors concluded that while the extent and durability is unknown, the Jynneos vaccine in single dosage has been shown to provide some protection against monkeypox infection Furthermore, it is recommended that eligible individuals receive both doses of the vaccine to prevent ongoing spread <p>Source</p>	Published 7 Oct 2022
	<ul style="list-style-type: none"> Epidemiology Prevention and control 	<ul style="list-style-type: none"> This study observed the effects of the Modified Vaccinia Ankara-Bavarian Nordic vaccine on monkeypox-infected patients in the U.S. immediately after receiving a single dose <ul style="list-style-type: none"> 7,339 patients received the first dose of the vaccine and 90 patients tested positive for monkeypox after the first day of administering the vaccine Eight monkeypox cases occurred more than 28 days after the first dosage and two of these occurred more than 14 days after receiving the second dose Post-vaccination monkeypox occurred two weeks after administering the first dose Researchers concluded that due to the limitations of small sample size, non-uniform post-vaccination observations and recency of the vaccine distribution, larger studies are needed to measure the vaccine's effectiveness <p>Source</p>	Published 30 September 2022

	<ul style="list-style-type: none"> Epidemiology 	<ul style="list-style-type: none"> The researchers of this study collected 356 samples from 50 confirmed monkeypox-infected men (median age of 34) from multiple anatomical sites (skin, anus, blood, urine, and semen) in France The proportion of positive samples and monkeypox viral loads were compared with PCR cycle thresholds over 14 days The results revealed that on day zero monkeypox was detected more frequently on the skin, anus, and throat, and viral loads were more expressed on skin lesions and anal samples <ul style="list-style-type: none"> High monkeypox viral loads in skin and mucosa (including genital and anal sites) suggest transmission occurs through body contact rather than respiratory droplets or contact with bodily fluids At diagnosis, 83% of patients were detected with monkeypox suggesting male sexual secretion as a possible pathway for transmission Monkeypox is rare to be expressed within blood and urine in other sampled sites from weeks one to four <ul style="list-style-type: none"> Monkeypox was detected in six of seven patients' blood on day zero After 14 days, clinical samples support a viral clearance of monkeypox in bodily fluids and anatomical compartments due to a short viraemic phase The study concluded that further research is needed to understand how sexual contact may play a role in the viral transmission of the monkeypox virus <p>Source</p>	<p>Published 29 September 2022</p>
	<ul style="list-style-type: none"> Diagnosis 	<ul style="list-style-type: none"> In this study, an Android mobile application was developed to detect, classify, and preliminarily diagnose human monkeypox through skin lesions The authors created the application through a trained deep learning system using skin lesion image databases, with the best network showing an accuracy of 91.11% The application would help enable early diagnosis from the comfort of people's homes and ultimately reduce the spread of monkeypox <p>Source</p>	<p>Published 10 Oct 2022</p>

	<ul style="list-style-type: none"> • Epidemiology • Prevention and control 	<ul style="list-style-type: none"> • This study reported on four separate confirmed cases of children with monkeypox in England • The cases occurred in the following settings: <ul style="list-style-type: none"> ○ One secondary school (aged 11-16), one primary school (aged five to 11), one reception year of a primary school (aged four to five) and one nursery (aged two to five) ○ Index cases were an adult staff member in close contact • Public health action was taken immediately, which included daily incident management meetings, isolation of exposed contacts away from school for 21 days, supplemental education to parents, and vaccination • No secondary cases occurred among these incidents; there is ultimately low risk of developing monkeypox among staff and students following exposure to confirmed cases in education settings <p>Source</p>	Published 6 Oct 2022
	<ul style="list-style-type: none"> • Diagnosis 	<ul style="list-style-type: none"> • This study investigated the specificity of monkeypox virus real-time diagnostic assay primers and probes by aligning the sequences of CDC recommended assays to 1,730 genome sequences reported worldwide • Findings reported wide mismatch in forward and reverse primers at 99.08% and 97.46%, respectively • The impact of these primer mismatches resulted in ~11-fold underestimation of initial template DNA and four-fold increase in the 95% limit of detection, indicating that current monkeypox generic assays may not be optimal • The study concluded that it is important to correct for mismatches (particularly to achieve full complementarity between primers) as it could provide more sensitive detection of currently circulating monkeypox virus strains <p>Source</p>	Published 6 Oct 2022 (pre-print)
	<ul style="list-style-type: none"> • Treatment 	<ul style="list-style-type: none"> • The study overviews three clinical cases of patients with severe monkeypox infection that were treated with tecovirimat <ul style="list-style-type: none"> ○ The patients present with underlying comorbidities (ulcerative colitis, acute syphilis, and HIV infection) and a high baseline monkeypox viremia 	Published 30 September 2022

		<ul style="list-style-type: none"> • Monkeypox viremia was the prognostic marker when administering the treatment response <ul style="list-style-type: none"> ○ Tecovirimat was well tolerated with no significant side effects, however, due to monkeypox’s self-limiting nature, tecovirimat cannot be used for therapy <p>Source</p>	
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Appendix 2b: Key findings from evidence documents that address the question, organized by document type and sorted by relevance to the question and monkeypox

Type of document	Relevance to question	Key findings	Recency or status
Guidelines	<ul style="list-style-type: none"> • Prevention and control • Prognosis • Treatment 	<ul style="list-style-type: none"> • These guidelines provide a clinical management algorithm for pregnant women with suspected monkeypox virus exposure, including isolation and fetal surveillance recommendations • It is recommended that all cases of monkeypox virus in pregnancy are reported to WHO and an international registry for emerging pathogens Tecovirimat and vaccinia immune globulin can be considered for pregnant women who are severely ill Source (low-quality AGREE II rating; published in The Lancet) 	Published 2 July 2022
	<ul style="list-style-type: none"> • Prevention and control • Treatment 	<ul style="list-style-type: none"> • This is a French guideline produced to inform the management of patients with mild or moderate monkeypox infection as well as infection control • Recommendations were drafted based on a literature search and a review of the evidence by an expert panel to produce four levels of recommendations • With respect to considerations for specific treatments for patients with monkeypox infection, it is recommended that not all symptomatic cases should be treated with a drug but those at higher risk should be considered for treatment <ul style="list-style-type: none"> ○ Recommendations and optional recommendations are provided regarding the use of tecovirimat, brincidofovir, cidofovir, and anti-monkeypox immunoglobulins • General guidelines to control the spread of monkeypox infection are also presented, with a focus on the isolation of infected 	Published 1 September 2022

Type of document	Relevance to question	Key findings	Recency or status
		<p>patients, environmental control, transportation, and communication from health authorities</p> <ul style="list-style-type: none"> • Specific recommendations to control the spread of monkeypox for both infected patients and healthcare workers in charge of infected patients are presented • Specific guidelines for managing monkeypox infection in children are also presented • Finally, specific guidelines addressing the occurrence of monkeypox in a school or children’s community are presented • Source (high-quality AGREE II rating; published in The Clinical Microbiology and Infection) 	
Full systematic reviews	<ul style="list-style-type: none"> • Clinical presentation 	<ul style="list-style-type: none"> • This systematic review sought to review the evidence regarding neurological complications associated with monkeypox • Twelve cases of individuals with monkeypox presenting with neurological symptoms were identified in the literature • The following neurological complications were identified: <ul style="list-style-type: none"> ○ Low mood ○ Seizures ○ Encephalitis ○ Respiratory failure ○ Encephalopathy • Seven cases of encephalitis were identified; three of these patients died, two made a full recovery, and two did not have a reported outcome status • Only one patient underwent cerebrospinal fluid diagnostics, and there were orthopoxvirus-reactive IgM identified in this patient • Of the five reported cases of seizures, three were secondary to viral-induced encephalitis • The authors emphasize the importance of appropriately identifying monkeypox in young children given their increased susceptibility to monkeypox-associated encephalitis • Source (2/10 McMaster Health Forum AMSTAR rating) 	Literature last searched 19 June 2022
	<ul style="list-style-type: none"> • Clinical presentation 	<ul style="list-style-type: none"> • This systematic review and meta-analysis assessed the clinical features, hospitalizations, complications and deaths of monkeypox confirmed or probable cases 	Published 10 August 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • Among the 1958 patients, rashes (93%), fever (72%), pruritus (65%), and lymphadenopathy (62%) were the most prevalent symptoms; other symptoms included fatigue (60%), sore throat (57%), headache (50%), cough (47%), photophobia (32%), arthralgia (26%), difficult breathing (25%), conjunctivitis (19%), nausea/vomiting (19%), and diarrhea (4%) 35% of patients were hospitalized, and 4% of hospitalized patients had fatal outcomes The authors concluded that countries must urgently prepare human resources and infrastructure to treat patients according to the most reliable clinical information <p>Source (8/11 McMaster Health Forum AMSTAR rating)</p>	
	<ul style="list-style-type: none"> • Diagnosis 	<ul style="list-style-type: none"> • This study described a saliva-based polymerase chain reaction (PCR) assay for human monkeypox, test performance, and the clinical implementation of the PCR assay at three testing sites in Los Angeles, United States • The PCR assay was not specific to the human monkeypox genus, as it included several other orthopoxvirus subspecies such as cowpox and rabbitpox • Laboratory analysis showed 100% agreement between the saliva-based test and known positive and negative specimens • Clinical testing from the three Los Angeles testing sites identified 22 cases of human monkeypox among 132 individuals screened (16.7%) <ul style="list-style-type: none"> ○ Of those 22 patients, 16 (72.7%) reported symptoms, four (18.2%) did not have a rash at the time of testing, and one patient reported being asymptomatic • Additionally, the authors conducted a systematic rapid review of studies reporting the performance of oral pharyngeal or saliva-based tests for human monkeypox <ul style="list-style-type: none"> ○ The systematic rapid review identified six studies, in which 24 patients had tests performed on oropharyngeal or saliva specimens, and the results of the tests were positive among 100% of patients with positive lesion swabs for human monkeypox infection 	Published 9 August 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> The authors concluded that saliva-based PCR tests are potential tools for outbreak control, and performance of the tests requires further evaluation <p>Source (5/10 McMaster Health Forum AMSTAR rating)</p>	
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> This systematic review synthesized the estimates from the evidence of the effective reproduction number and incubation period for the monkeypox virus The effective reproduction number in ongoing outbreaks in six countries from May to July 2022 was also estimated A total of 11 studies were included, which provided six reproduction number estimates in five regions and seven incubation period estimates in five regions The incubation period ranged from five to 41 days for the West African clade of the monkeypox virus and from eight to 14 days for the Congo basic clade Of the six countries with increasing confirmed cases, the United States had the highest reproductive number, estimated to be 1.55, and in 70 countries with cases, the estimated reproductive number of all aggregated cases was 1.29 The study highlights that compared to earlier reproduction number estimates, transmission of the monkeypox virus may have slowed down recently due to increased awareness of the epidemic <p>Source 5/10 (McMaster forum AMSTAR rating)</p>	Last updated 26 July 2022
	<ul style="list-style-type: none"> Clinical presentation 	<ul style="list-style-type: none"> The aim of this systematic review was to investigate the neurological and psychiatric presentations of monkeypox (monkeypox) virus infection, with the range of presentation being from nonspecific neurological symptoms (e.g., myalgia and headache) to rarer but more severe neurological complications (e.g., encephalitis and seizures) Of the 19 eligible studies that were included (1,512 participants, 1,031 with confirmed infection using CDC criteria or PCR testing), most were cohort studies and case series with no controlled populations 	Published 11 July 2022 (pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • The most frequent clinical feature of neuropsychiatric presentations of monkeypox was myalgia, followed by headache, fatigue, seizure, confusion, and encephalitis • Less evidence regarding the psychiatric sequelae of monkeypox and the prevalence of anxiety and depression was found • The study concluded that its preliminary suspicion that there are monkeypox-related nervous system presentations may warrant surveillance within the current monkeypox outbreak <p>Source (8/11 AMSTAR rating)</p>	
	<ul style="list-style-type: none"> • Clinical presentation • Diagnosis • Prognosis • Treatment 	<ul style="list-style-type: none"> • This review appraised the availability, scope, quality, and inclusivity of clinical managements for monkeypox virus globally • The quality was assessed using the Appraisal of Guidelines for Research and Evaluation (AGREE) II tool • The results of the databases and grey literature search showed: <ul style="list-style-type: none"> ○ Out of the 14 included guidelines, most of the guidelines were of low-quality with a median AMSTAR score of 2 out of 7 (range of 1 to 7), lacked detail, and covered a narrow range of topics ○ Most guidelines focused on adults, five provided some advice for children, three for pregnant women, and three for people living with HIV ○ Treatment guidance was mostly limited to advice on antivirals, in which seven out of 14 guidelines advised cidofovir, four advised tecovirimat, and one advised brincidofovir ○ One guideline provided recommendations on supportive care and treatment of complications ○ All guidelines recommended vaccination as post-exposure prophylaxis (PEP) • The findings showed that most of the difference across the guidelines were recommendations for antivirals and vaccines • The findings identified a lack of guidance on the treatment and PEP, and often there was contradictory advice for different population groups such as children, pregnant women and people living with immunosuppression, which could exacerbate their vulnerability in outbreaks 	Published 14 June 2022 (pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • Most of the identified guidelines did not document the methodology used, which was reflected in the poor-quality assessments • The review highlighted the need for a rigorous framework for producing guidelines ahead of epidemics and a platform for quickly reviewing and updating guidance as new evidence emerges <p>Source (7/9 AMSTAR rating)</p>	
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • This systematic review examined peer-reviewed and grey literature on the transmission of monkeypox, including the number of confirmed, probable, and/or possible cases, geographic spread, and patient characteristics • Research on monkeypox documented a total of 48 confirmed and probable cases reported in six African countries during the 1970s, which increased over the next several decades but was not reported outside Africa until 2003 in the United States • From 2009-19 there have been almost 20,000 suspected or confirmed cases of monkeypox, and of those cases one case was in Israel in 2018, three in the U.K. in 2018 and one in 2019, and one in Singapore in 2019 • The median age at presentation has increased from four to five years old from 1970-1989 to 21 years in 2010-19, with cases outside of Africa even higher and occurring most frequently in adult males • The authors hypothesize that this increase may be due to the cessation of smallpox vaccinations, which provided some cross-protection against monkeypox <p>Source (4/11 AMSTAR rating)</p>	Literature last searched 7 September 2020
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • Monkeypox is characterized by a pustular rash indistinguishable from smallpox, and outcomes can range from severe to fatal • Remote populations in Central and West Africa are most affected by outbreaks with the recent outbreaks occurring for the first time in 20 years in Nigeria and Cameroon • There is an increase in reported outbreaks and number of cases by year in the Democratic Republic of Congo (DRC) and number of outbreak reports per year in the Central African 	Literature last searched 15 August 2018

Type of document	Relevance to question	Key findings	Recency or status
		<p>Republic, but data are insufficient to measure trends in secondary attack rates and case-fatality rates</p> <ul style="list-style-type: none"> • Outside of DRC, there has been a notable increase in number of individual monkeypox outbreak reports between 2010 and 2018, particularly in the Central African Republic, but it is noted that this does not necessarily translate to an increase in annual cases over time in these areas • In Nigeria, geographical patterns of infections suggest a possible new and widespread zoonotic reservoir • Limited and anecdotal evidence exists for the use of antibiotics for prophylaxis against secondary cutaneous infection <p>Source (AMSTAR rating 6/11)</p>	
Rapid reviews	<ul style="list-style-type: none"> • Prevention and control • Treatment • 	<ul style="list-style-type: none"> • This rapid review explored the repurposing potentials of smallpox vaccines and drugs in the monkeypox outbreaks based on their comparative benefits and risks • Based on current evidence, the review found two replication-competent (ACAM2000 and APSV) and one replication-deficient (MVA-BN) vaccinia virus vaccines were effective against orthopoxvirus, including the monkeypox virus • ACAM2000 showed immunogenic effect and efficacy against monkeypox infection, although there are adverse effects, including myocarditis/pericarditis • The efficacy and safety profile of APSV appears similar to ACAM2000, with similar concerns regarding the risk of occurring myocarditis/pericarditis <ul style="list-style-type: none"> ○ United States' Food and Drug Administration (FDA) authorized APSV for emergency use authorization on a case-by-case basis in situations in which ACAM2000 is not available • MVA-BN has been approved in the U.S. and Canada as a vaccine for the prevention of monkeypox infections <ul style="list-style-type: none"> ○ MVA-BN displays a favourable safety profile with local reactions as the most frequent side effect ○ MVA-BN's safety profile has not been established among pregnant women 	Published 23 August 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> The combined use of antiviral drugs, including cidofovir, brincidofovir, and tecovirimat, and vaccinia immune globulin (produced from the pooled blood of the vaccinated population by the smallpox vaccine) can enhance significant effectiveness in immunocompromised subjects <p>Source (1/9 AMSTAR rating)</p>	
Non-systematic reviews	<ul style="list-style-type: none"> Diagnosis 	<ul style="list-style-type: none"> This review outlines how PCR testing can be optimized to be the most effective, overcoming the challenges with PCR testing experienced in the COVID-19 pandemic It is recommended that in silico analysis of PCR assays will increase the chances the assay will perform well though it cannot replace wet laboratory assessment The most likely adverse effect of a poorly designed PCR assay will be on the limit of detection (LOD), which will lead to false-negative results and reduced analytical sensitivity; guidelines state that diagnostic PCRs should include positive controls at low (above the LOD) but easily detectable concentration To mitigate false-negative results, laboratories should evaluate published protocols by using control materials or specimens with their own reagents and instruments; one cannot follow protocols verbatim Contamination of assays should be monitored by individual laboratories with whole-process negative pathogen controls that contain human genomic DNA <p>Source</p>	Published 11 August 2022
	<ul style="list-style-type: none"> Prevention and control 	<ul style="list-style-type: none"> This review found that vaccinia viruses can be inactivated on artificially contaminated surfaces by 70% ethanol (≤ 1 minute), 0.2% peracetic acid (≤ 10 min) and 1% to 10% of a probiotic cleaner (1 h) Hydrogen peroxide (14.4%) and iodine (0.04% - 1%) were effective in suspension tests, sodium hypochlorite (0.25% - 2.5%; 1 min), 2% glutaraldehyde (10 min) and 0.55% ortho-phthalaldehyde (5 min) were effective on artificially contaminated surfaces Copper (99.9%) was equally effective against vaccinia virus and monkeypox virus in 3 minutes 	Published 28 June 2022

Type of document	Relevance to question	Key findings	Recency or status
	<ul style="list-style-type: none"> Prevention and control 	<p>Source</p> <p>The WHO released interim guidance on vaccines and immunization for monkeypox</p> <ul style="list-style-type: none"> The organization does not recommend the use of first-generation vaccines held in national reserves related to the smallpox eradication program Mass vaccination is not required or recommended at this time based on current assessment of risks and benefits, but strongly encouraged to countries to convene their national immunization advisory groups to determine relevance and context Most interim vaccination recommendations are related to off-label use (i.e., smallpox vaccines off-label for monkeypox) and vaccines approved for monkeypox such as MVA-BN, LC16, or ACAM2000 <ul style="list-style-type: none"> MVA-BN has been approved in Canada in 2019 Human-to-human spread can be controlled by other measures such as early case-finding, diagnosis and care, and contact-tracing Post-exposure prophylaxis (PEP) is recommended with an appropriate second- or third-generation vaccine, within four days of first exposure among contacts of cases <ul style="list-style-type: none"> Children, pregnant women, and immunocompromised persons (including persons living with HIV) may be considered Pre-exposure prophylaxis (PrEP) is recommended for health workers at high risk, laboratory personnel working with orthopoxviruses, clinical laboratory personnel performing diagnostic testing for monkeypox, and any outbreak response team members Vaccination program should be accompanied with strong communication and conduct of vaccine effectiveness studies <p>Source</p>	<p>Published 14 June 2022</p>
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> A rapid literature review of monkeypox transmission in healthcare settings outside of endemic regions found that although many exposures in healthcare settings have been documented, only a single transmission event has been reported 	<p>Published 9 June 2022</p>

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> Definitions of exposure varied significantly, making it difficult to properly assess the extent to which healthcare personnel were exposed to the virus Important details about exposures such as the types of interactions that took place, PPE worn and the duration of the interaction were not made available, limiting the ability to stratify risk and fully comprehend the nature of exposure in healthcare settings <p>Source</p>	
	<ul style="list-style-type: none"> Epidemiology (including transmission) Clinical Presentation 	<ul style="list-style-type: none"> A pooled analysis from clusters in Italy, Australia, Czech Republic, Portugal, and the United Kingdom including 124 cases showed that the current monkeypox epidemic differs from previous outbreak in terms of age (54.29% of individuals in their 30s), gender (most cases being males), risk factors and transmission route, with sexual transmission being highly likely Clinical presentation is also atypical, being largely characterized by anogenital lesions and rashes, with fewer on the face and extremities The most common symptom reported was fever (54.29%) followed by inguinal lymphadenopathy (45.71%) and exanthema (40%). Risk factors included being male, having sex with other men, engaging in risky behaviours and activities such as condomless sex, human immunodeficiency virus positivity, and a history of previous sexually transmitted infections <p>Source</p>	Published 8 June 2022
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> This World Health Organization (WHO) publication of disease outbreak news provides updates and short summaries of guidance, including on vaccination As of 2 June 2022, 780 laboratory confirmed cases have been notified to WHO under the International Health Regulations (IHR), or identified by WHO from official public sources in 27 non-endemic countries in four WHO regions <ul style="list-style-type: none"> Preliminary data from PCR assays indicate that the monkeypox virus strains detected in Europe and other non-endemic countries belong to the West African clade 	Published 4 June 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> ○ Clinical and public-health incident response has been activated at WHO and in many member states to coordinate comprehensive case finding, contact tracing, laboratory investigation, clinical management, isolation, and implementation of infection and prevention control measures ● Genomic sequencing of viral DNA of the monkeypox virus is being undertaken, and currently the following countries have full-length or partial genome sequences: Belgium, France, Germany, Israel, Italy, the Netherlands, Portugal, Slovenia, Spain, Switzerland, and the United States ● Interim guidance is being developed to support member States with surveillance, laboratory diagnostics and testing, case investigation and contact tracing, clinical management, vaccines and immunization, and risk communication and community engagement ● Currently, the public-health risk at the global level is assessed as moderate, however the public-health risk could become high if the virus establishes itself in non-endemic countries as a widespread human pathogen ● Human-to-human transmission occurs through close proximity or direct physical contact (e.g., face-to-face, skin-to-skin, mouth-to-mouth, mouth-to-skin contact including during sex) with skin that may have recognized or unrecognized infectious lesions or contact with contaminated materials (e.g., linens, bedding, electronics, clothing) ● Smallpox and monkeypox vaccines, where available, are being deployed in a limited number of countries to manage close contacts, and while smallpox vaccines have been shown to be protective against monkeypox, there is also one vaccine approved for prevention of monkeypox ● WHO provides the following interim advice: <ul style="list-style-type: none"> ○ All countries should be on the alert for signals related to people presenting with a rash that progresses in sequential stages that may be associated with fever, enlarged lymph nodes, back pain, and muscle ache ○ Increasing awareness among potentially affected communities, as well as healthcare providers and laboratory 	

Type of document	Relevance to question	Key findings	Recency or status
		<p>workers, is essential for identifying and preventing further cases and effective management of the current outbreak</p> <ul style="list-style-type: none"> ○ Caring for patients with suspected or confirmed monkeypox requires early recognition through screening protocols adapted to local settings; prompt isolation and rapid implementation of appropriate infection, prevention, and control measures; testing to confirm diagnosis; symptomatic management of patients with mild or uncomplicated monkeypox; and monitoring for and treatment of complications and life-threatening conditions <p>Source</p>	
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • This joint report by the World Health Organization’s Regional Office for Europe and the European Centre for Disease Prevention and Control (ECDC) provides interim advice on Risk Communication and Community Engagement (RCCE) during the monkeypox outbreak in Europe • The features of the outbreak in Europe contribute to a complex RCCE context, which includes several components: <ul style="list-style-type: none"> ○ Predominantly affected communities, which needs to be properly considered in all RCCE activities and consideration for a risk of stigmatization ○ Uncertainty, in which there are many unknown aspects of the disease in this early stage of the outbreak ○ Mass gatherings, especially as the summer months approach ○ Relaxation of COVID-19 public-health measures, in which many countries have reported general sentiment of pandemic fatigue • Risk-communication response for countries should consider the following suggestions: <ul style="list-style-type: none"> ○ Identify target groups relevant to the monkeypox outbreak in Europe (i.e., population groups at risk need to be alerted about specific risks and protective measures; broader public needs to be informed about disease and preventive measures) ○ Tailor risk communication through channels and spokespersons that target groups trust ○ Acknowledge uncertainty by labelling public-health advice as preliminary and based on current evidence, and committing 	<p>Published 2 June 2022</p>

Type of document	Relevance to question	Key findings	Recency or status
		<p>to provide further information and guidance as it becomes known</p> <ul style="list-style-type: none"> ○ Package messages and health advice relevant to specific settings and circumstances ○ Provide public-health advice specific to the monkeypox outbreak without comparing it with or leveraging other health issues ○ Use pictures of monkeypox symptoms to increase understanding but not generate fear ● Community engagement approaches should be used to support targeted risk communication messages to populations or groups more likely to be exposed to the virus, which would require that public-health authorities at national and sub-national levels identify and actively work with relevant civil-society organizations, community-based organizations and stakeholders, and leverage the trust they have to ensure that the affected communities are properly informed and empowered to protect themselves from the disease <p>Source</p>	
	<ul style="list-style-type: none"> ● Epidemiology 	<ul style="list-style-type: none"> ● Monkeypox cases have been growing across an expanding number of non-endemic countries in recent months <ul style="list-style-type: none"> ○ Future outbreaks are likely to increase in size and frequency due to the cessation of smallpox vaccine programs, which provide cross-protection ● Based on global travel trends, traveller volumes originating from flights from countries where monkeypox is endemic are greatest to Paris, London, Dubai, Johannesburg, and Brussels ● Supporting endemic countries by strengthening laboratory capacity and increasing timely access to smallpox vaccination for close contacts can help mitigate further chains of transmission <p>Source</p>	Published 31 May 2022
	<ul style="list-style-type: none"> ● Epidemiology (including transmission) ● Prevention and control 	<ul style="list-style-type: none"> ● This document from the World Health Organization provides interim guidance on surveillance, case investigation, and contact tracing for monkeypox outbreaks ● WHO expects there will be more cases of monkeypox identified as surveillance expands in non-endemic countries 	Published 22 May 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • The current immediate actions focus on informing those who may be most at risk for monkeypox virus infection with accurate information, stopping further spread, and protecting frontline workers • Clinicians should report suspected cases immediately to local public-health authorities • Probable and confirmed cases of monkeypox should be reported immediately to WHO through International Health Regulation (IHR) national focal points (NFPs) • If there is a suspect case of monkeypox virus, case investigation should consist of clinical examination of the patient with appropriate personal protective equipment (PPE), questioning the patient about possible sources of infection, and safe collection and dispatch of specimens for laboratory examination to be confirmed for monkeypox virus • As soon as a suspected case is identified, contact identification and contact tracing should be initiated, and contacts should be monitored at least daily for the onset of any signs or symptoms for a period of 21 days from last contact with a patient or contaminated materials • Quarantine or exclusion from work are not necessary during the contact tracing period if there are no symptoms present or begin to develop <p>Source</p>	
	<ul style="list-style-type: none"> • Epidemiology • Prevention and control 	<ul style="list-style-type: none"> • Cases of monkeypox acquired in the EU have been reported recently in nine EU member states (Austria, Belgium, France, Germany, Italy, Portugal, Spain, Sweden, and the Netherlands) <ul style="list-style-type: none"> ○ Monkeypox does not spread easily (usually 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) and the nature of the presenting lesions in some cases suggest transmission occurred during sexual intercourse • EU/EEA countries should focus on prompt identification, management, contract tracing and reporting of new monkeypox cases 	Published 23 May 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> ○ Countries should update their contact-tracing mechanisms and review availability of smallpox vaccines, personal protective equipment and antivirals ○ Healthcare workers should wear gloves, water-resistant gowns, and FFP2 respirator when screening suspected cases or caring for monkeypox cases ○ Proactive risk communication and multiple community-engagement activities should be implemented to provide updates and increase awareness for those at risk and the wider public <p>Source</p>	
	<ul style="list-style-type: none"> • Biology • Epidemiology (including transmission) • Prevention and control • Clinical presentation • Diagnosis • Treatment 	<ul style="list-style-type: none"> • Monkeypox is a zoonotic disease caused by the monkeypox virus which is a member of the orthopoxvirus genus • The two possible means of monkeypox virus transmission are animals-to-human transmission and human-to-human transmission, and respiratory droplets and contact with body fluids, contaminated patient’s environment or items, skin lesion of an infected person associated with inter-human transmission <ul style="list-style-type: none"> ○ Animal-to-human transmission occurs through direct contact with the above viral hosts or by direct contact with blood ○ Human-to-animal transmission has not been reported • Monkeypox symptoms present in three phases including an incubation period of four to 21 days, followed by a prodromal illness with signs including lymph node enlargement, headache, fever, back pain, myalgia, intense asthenia, pharyngitis, sweating and malaise, followed by an exanthema phase that includes vesiculopustular rashes that appear within one to 10 days spread over the body • Vaccination against smallpox provides cross-protection against other OPV species including monkeypox and many patients were born after the cessation of smallpox eradication program • Diagnosis of monkeypox can occur through genetic methods (i.e., PCR or RT-PCR), phenotypic methods based on clinical diagnosis, immunological methods including IgG and IgM antibody detection and immunohistochemistry for viral antigen detection, and electron microscopy 	<p>Published 12 November 2020</p>

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • Antivirals such as Tecovirimat, Cidofovir and Brincidofovir have shown efficacy in in vitro and animal studies, but their effectiveness in humans is unknown <ul style="list-style-type: none"> ○ Brincidofovir may have an improved safety profile compared to Cidofovir ○ Cidofovir and Brincidofovir may be considered in severe cases of monkeypox ○ Human clinical trials of Tecovirimat suggested that the drug was safe and tolerable with only minor side effects <p>Source</p>	
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Prevention and control • Clinical presentation • Diagnosis • Prognosis • Treatment 	<ul style="list-style-type: none"> • The frequency and geographic distribution of human monkeypox cases across West and Central Africa have increased in recent years <ul style="list-style-type: none"> ○ Monkeypox is largely found in rodents and has been detected in squirrels, rats, mice, and monkeys ○ Indirect or direct contact with live or dead animals is assumed to be the main source of human monkeypox infections ○ Secondary human-to-human transmission is considered common and presumably occurs through respiratory droplets or indirect or direct contact with body fluids, lesion material and contaminated surfaces or other material • The clinical presentation of monkeypox is similar to smallpox but generally less severe <ul style="list-style-type: none"> ○ Incubation period is estimated at five to 21 days, and symptoms and signs at two to five weeks ○ The illness begins with non-specific symptoms and signs including fever, chills, headaches, lethargy, asthenia, lymph node swelling, back pain, and myalgia, followed by rashes of varying size that appear first on the face then across the body, hands, legs, and feet ○ Complications can include secondary bacterial infections, respiratory distress, broncho-pneumonia, encephalitis, corneal infection with vision loss, gastrointestinal involvement, vomiting, and diarrhea with dehydration ○ Case fatality rates have varied from 1% to 10% and occur mostly among young adults and children, especially those with immunosuppression 	Published December 2019

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • Most confirmed monkeypox cases are younger than 40 years old, a population born after the discontinuation of the smallpox vaccination campaign, possibly reflecting a lack of cross-protective immunity <ul style="list-style-type: none"> ○ Prevention measures for animal-to-human transmission include avoiding contact with rodents and primates, limiting direct exposure to blood and inadequately cooked meat, and using personal protective equipment when handling potential animal reservoir species ○ Prevention measures for human-to-human transmission include avoiding close contact with anyone infected and healthcare providers using personal protective equipment when treating infected patients • For diagnosis, optimal clinical specimens for laboratory analyses include those from skin lesions, exudate, or crusts stored in a dry, sterile tube (without viral transport media) and kept cold <ul style="list-style-type: none"> ○ Analysis should be carried out using electron microscopy through polymerase chain reaction • Monkeypox is treated through supportive care, symptomatic management, and treatment of secondary bacterial infections <p>Source</p>	
	<ul style="list-style-type: none"> • Biology • Epidemiology (including transmission) • Prevention and control • Clinical presentation • Diagnosis • Prognosis • Treatment 	<ul style="list-style-type: none"> • This review looked at the monkeypox infection in Nigeria, its most recent biology, virus-host interaction, epidemiology, diagnosis, chemotherapy, prevention, and control strategies • The monkeypox virus falls into two distinct strains, based on genetic, geographic, and phenotypic variation, these being the West African and the Congo Basin groups, with defined epidemiological and clinical differences • Transmission to humans is primarily by exposure to animal reservoirs (primary zoonotic transmission), such as squirrels • The most recent outbreak in Nigeria started in September 2017 and currently, this is the largest outbreak caused by the West African strain, and further investigation measures are in place to improve the existing knowledge to ensure effective prevention and control strategies 	Published April 2019

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • The clinical presentation of the monkeypox virus largely resembles that of smallpox, with an incubation period of seven to 17 days, and includes fever, muscle aches, backache, lymphadenopathy, followed by lesions and rashes all over the body • The recent development and license of Tecovirimat as an antipoxvirus cure is an achievement in antiviral therapy • Public health measures, such as case isolation, contact tracing, avoiding contact with animals or materials suspected of being infected, use of personal protective equipment and good hand-hygiene practices, remain the best measures for preventing and controlling human monkeypox <p>Source</p>	
	<ul style="list-style-type: none"> • Biology • Epidemiology (including transmission) • Clinical presentation 	<ul style="list-style-type: none"> • This review looked at the history and evolution of monkeypox outbreaks in Africa and the United Kingdom, the changing clinical presentations, and the possible factors underlying the increasing numbers being detected • Clinical presentations of the monkeypox virus include symptoms with skin and mucosal lesions which are difficult to distinguish from smallpox, and the infection starts with fever, headache, back pain, myalgia and asthenia followed by eruption of skin and mucosal lesions starting with the face • The exact mode of transmission of the monkeypox virus to humans remains unknown <ul style="list-style-type: none"> ○ It is assumed that animal-to-human infection occurs through direct or indirect contact with monkeypox-infected animal bodily fluids through handling, bites or scratches • Current evidence suggests that the outbreak is caused by multiple source emergence into the human population, and not sustained by human-to-human transmission • Most of the currently available data on monkeypox comes from individual cases or outbreak reports which do not provide an overall accurate picture • There are current knowledge gaps in the epidemiology, host reservoir, emergence, transmission, pathogenesis, and prevention of monkeypox 	Published January 2019

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> The authors noted that there is a need to build public health and surveillance capacities across Africa Source	
	<ul style="list-style-type: none"> Clinical presentation 	<ul style="list-style-type: none"> The review describes neurological presentations of monkeypox, such as fever, pharyngitis, anorexia, weakness, headache, adenopathy, and a vesiculopapular rash Differential diagnostic tests and treatments are discussed by the authors The authors conclude that emerging pathogens that cause human disease will continue to grow due to changes in ecology and climate, and increased risk of diseases-transmitting vectors for humans Source	Published September 2022
	<ul style="list-style-type: none"> Diagnosis 	<ul style="list-style-type: none"> The study focuses on portable nucleic acid tests for rapid detection of the monkeypox virus The assays used a loop-mediated isothermal amplification (LAMP) to amplify the distinct clades and sequences of the genome The authors used the GeneTiger and the miniPCR and were able to detect single copies of monkeypox virus within 30 minutes Source	Last updated 10 August 2022 (pre-print)
	<ul style="list-style-type: none"> Diagnosis 	<ul style="list-style-type: none"> This study describes the various testing methods used for confirmed diagnosis of the monkeypox virus The World Health Organization (WHO) recommends real-time quantitative polymerase chain reaction (RT-qPCR) alone or in combination with sequencing, with various targets in the viral genome Different methods utilize different targets in the viral genome, which in turn will result in different sensitivities and their limit of detection will differ based on the varying strains of the monkeypox virus RT-qPCR have been used to monitor monkeypox virus infection in several countries, which combined with next-generation sequencing technology can provide accurate detective results and information on the genome sequencing 	Published 10 August 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> Monitoring of the monkeypox virus in animal reservoir may reveal more viral clades, which will further broaden the diversity of the monkeypox virus Different testing methods and their suitability should be considered due to the genetic diversity of the virus and the context in which the virus presents itself The authors further emphasize that reducing the cost of testing, increasing the sensitivity and specificity, and developing rapid tests for point-of-care for rural areas will help increase the monitoring of monkeypox infections Source	
	<ul style="list-style-type: none"> Biology 	<ul style="list-style-type: none"> The following study uses the APOBEC3 molecular clock to estimate the date of emergence of monkeypox virus Source	Last updated 6 August 2022
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> This non-systematic review summarized what can be learned from the top 100 highly cited articles in monkeypox research. Of the 100 most cited articles, USA had the largest number at 77 documents, of which vaccine studies are the most concerned topic in this field, and 15 studies analyzed the protection efficacy and immunogenicity of different vaccines. In the Democratic Republic of Congo, it was suggested that there has been a 20-fold increase in human monkeypox incidence after 30 years of cessation of the smallpox vaccination campaign. The authors advise that public health organizations must increase vigilance to monkeypox through enhancing surveillance systems, building detection capacity, and informing human behaviour to reduce transmission. Source	Literature last searched 22 May 2022
	<ul style="list-style-type: none"> Prevention and Control 	<ul style="list-style-type: none"> In many parts of Africa, frontline healthcare workers are at risk of contracting and transmitting monkeypox, and so vulnerable clinical settings must work to strengthen infection prevention and control protocols including the use of personal protective equipment The smallpox vaccine can offer a secondary prevention strategy to prevent infection of monkeypox in healthcare workers Source	Published February 2019

Type of document	Relevance to question	Key findings	Recency or status
	<ul style="list-style-type: none"> • Biology • Clinical presentation • Diagnosis • Treatment 	<ul style="list-style-type: none"> • Human monkeypox - After 40 years, an unintended consequence of smallpox eradication Source 	Published 14 July 2020
Protocols for reviews that are already underway	<ul style="list-style-type: none"> • Biology • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • Monkey pox virus – Zoonotic characteristics living evidence Source 	Anticipated completion date 30 September 2022
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • Transmission dynamics of the human monkeypox: A systematic review Source 	Anticipated completion date 30 November 2022
	<ul style="list-style-type: none"> • Clinical presentation 	<ul style="list-style-type: none"> • Clinical characteristics of monkeypox: a systematic review and meta-analysis Source 	Anticipated completion date 30 September 2022
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • Monkeypox virus and pregnancy: systematic review Source 	Anticipated completion date 30 September 2022
	<ul style="list-style-type: none"> • Treatment 	<ul style="list-style-type: none"> • A systematic review of use of antivirals in human monkeypox outbreak Source 	Anticipated completion date 31 December 2022
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • Ophthalmic manifestations of monkeypox virus infection: A systematic review and meta-analysis of prevalence Source 	Anticipated completion date 18 September 2022
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • Systematic review: Imported monkeypox Source 	Anticipated completion date 4 September 2022
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • Monkeypox vaccine effectiveness: A systematic review and meta-analysis Source 	Anticipated completion date 25 August 2022
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • Monkeypox as a sexually transmitted disease: a systematic review Source 	Anticipated completion date 23 December 2022
<ul style="list-style-type: none"> • Clinical presentation 	<ul style="list-style-type: none"> • The prevalence and spectrum of neurological and psychiatric presentations in infections with monkeypox: a systematic review Source 	Anticipated completion 8 July 2022	

Type of document	Relevance to question	Key findings	Recency or status
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> The epidemiology of monkeypox disease Source 	Anticipated completion 8 July 2022
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> Epidemiology of monkeypox in Africa: A systematic review Source 	Anticipated completion 10 July 2022
	<ul style="list-style-type: none"> Clinical presentation 	<ul style="list-style-type: none"> The human monkeypox virus and the neurologist: A systematic review Source 	Anticipated completion 31 July 2022
	<ul style="list-style-type: none"> Clinical presentation 	<ul style="list-style-type: none"> Prevalence of clinical manifestations and complications in monkeypox patients: A systematic review and meta-analysis Source 	Anticipated completion 31 July 2022
	<ul style="list-style-type: none"> Epidemiology (including transmission) Clinical presentation 	<ul style="list-style-type: none"> Epidemiology, clinical manifestations, and outcomes of monkeypox infection in humans: a systematic review and meta-analysis Source 	Anticipated completion 30 August 2022
	<ul style="list-style-type: none"> Epidemiology (including transmission) Prevention and control 	<ul style="list-style-type: none"> A systematic review on the global burden of human monkeypox after COVID-19 vaccination: epidemiology and implications for outbreaks Source 	Anticipated completion 1 November 2022
	<ul style="list-style-type: none"> Clinical presentation 	<ul style="list-style-type: none"> The prevalence and spectrum of neurological and psychiatric presentations in infections with monkeypox: A systematic review Source 	Anticipated completion 1 July 2022
	<ul style="list-style-type: none"> Clinical presentation Prevention and control 	<ul style="list-style-type: none"> Maternal, congenital, and paediatric monkeypox infection – consequences and prevention – A living systematic review Source 	Anticipated completion 31 August 2022
	<ul style="list-style-type: none"> Epidemiology 	<ul style="list-style-type: none"> A systematic review on the global burden of human monkeypox after COVID-19 vaccination: Epidemiology and implications for outbreaks Source 	Anticipated completion 1 November 2022
	<ul style="list-style-type: none"> Epidemiology 	<ul style="list-style-type: none"> Prevalence of monkeypox transmission by sexual contact transmission: Systematic review Source 	Anticipated completion 30 July 2022
	<ul style="list-style-type: none"> Epidemiology 	<ul style="list-style-type: none"> The epidemiology of monkeypox disease Source 	Anticipated completion 8 July 2022

Type of document	Relevance to question	Key findings	Recency or status
	<ul style="list-style-type: none"> Epidemiology Clinical presentation 	<ul style="list-style-type: none"> Global epidemiological and clinical characteristics of monkeypox cases: A Systematic review, 1970–2022 Source 	Anticipated completion 16 July 2022
Titles and questions for reviews being planned	None identified		
Single studies	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> This study examined monkeypox, HIV, and sexually transmitted infections (STI) surveillance data from eight jurisdictions of the United States (U.S.) to determine HIV and STI diagnoses among persons with monkeypox infections and assess differences in the monkeypox infection’s clinical features according to the HIV infection status 1,969 persons with monkeypox infections during the period of 17 May to 22 July 2022 were examined <ul style="list-style-type: none"> HIV prevalence was 38%, and 41% had received a diagnosis of one or more other reportable STIs in the previous year (2021) A higher proportion of persons with HIV infection that had a confirmed monkeypox infection were hospitalized compared with persons without HIV infection (8% versus 3%) The authors concluded that persons with HIV infection or STIs are disproportionately represented among persons with monkeypox, and that consideration should be given to prioritizing persons with HIV infection and STIs for monkeypox vaccination plans Source 	Published 9 September 2022
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> This study presented the results from studies that evaluated the presence of monkeypox DNA in diagnosed patients during the 2022 outbreak Included studies must have evaluated at least two biological samples, and the outcomes of interest were the PCR positivity and cycle threshold (Ct) values The meta-analysis found a PCR positivity rate that was very close to 100% in samples from skin lesions as well as increasing differences in Ct values in samples with lower positivity rates 	Published 7 September 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • These results indicate a high risk of infection with monkeypox from close contact with skin lesions, and that skin lesions swabs are most effective at detecting monkeypox DNA using PCR testing Source	
	<ul style="list-style-type: none"> • Clinical presentation 	<ul style="list-style-type: none"> • A chart review to evaluate clinical characteristics, comorbidities, including HIV infection and sexually transmitted infections (STIs) was conducted using confirmed monkeypox cases in 42 health centres and clinics from 17 German cities during a period of 19 May 2022 to 30 June 2022 • By 30 June 2022, 546 monkeypox infections were reported <ul style="list-style-type: none"> ○ All patients identified as men who have sex with men (MSM) ○ 256 of 546 (46.9%) were living with HIV infection ○ Most frequent localizations of monkeypox virus infections were genital (49.9%) and anal (47.9%) ○ Most frequent general symptoms were with fever (53.2%) and lymphadenopathy (42.6%) • The authors concluded that the clinical picture revealed no apparent differences between MSM with or without HIV infection Source	Published 4 September 2022
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • The cross-sectional observational study focused on public awareness of monkeypox in Bangladesh • Among 1,711 respondents, more than half were aware of monkeypox but had insufficient understanding of the transmission pathways, vaccination, and symptoms of monkeypox Source	Last updated 1 September 2022
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • The authors measure antibodies among historically smallpox-vaccinated, monkeypox PCR-positive and recently vaccinated individuals with Jynneos • They found that the immunization series in non-primed individuals yielded relatively low levels of monkeypox neutralizing antibodies, however, a third vaccination further boosted the antibody responses Source	Last updated 1 September 2022

Type of document	Relevance to question	Key findings	Recency or status
	<ul style="list-style-type: none"> Epidemiology 	<ul style="list-style-type: none"> Transmission of the monkeypox virus has been associated with close contact, primarily sexual behaviour, between men The CDC adapted previously developed models of sexual infection transmission to investigate the spread of monkeypox among men who have sex with men <ul style="list-style-type: none"> Survey data indicates that men who have sex with men have taken steps to protect themselves and their partners, including reducing one-time sexual partnerships This study uses a model of the natural history of monkeypox and behaviours among men who have sex with men This model demonstrates a 40% decrease in one-time partnerships yielded a 20-31% reduction in the percentage of men who have sex with men infected and a delay in the spread of the outbreak <ul style="list-style-type: none"> The findings from this study show that changes already being reported by men who have sex with men can have important implications for the trajectory of the monkeypox outbreak <p>Source</p>	Published 2 September 2022
	<ul style="list-style-type: none"> Epidemiology Prevention and control 	<ul style="list-style-type: none"> This study investigated the sexual behaviours among gay, bisexual and other men who have sex with men seeking to reduce their chances of acquiring monkeypox in response to public health messaging <ul style="list-style-type: none"> A follow-up survey was completed by a sample of 824 men who have sex with men who have responded to the annual American Men's Internet Survey 48% of survey respondents reported reducing their number of sex partners, 50% reported reducing one-time sexual encounters, and 50% reported reducing sex with partners met on dating apps or at sex venues since learning about the monkeypox outbreak Survey results indicate that the receipt of the vaccine was more common among respondents reporting two or more partners during the preceding 14 days (30.1%) than among those reporting no partners or one partner (13.9%) and among those reporting engaging in group sex with male partners during the preceding 3 months (31.5%) than among those not engaging in group sex during that time (12.8%) 	Published 2 September 2022

Type of document	Relevance to question	Key findings	Recency or status
		<p>Survey data suggests racial, ethnic and geographic differences in vaccination, partially attributed to issues surrounding equitable access</p> <ul style="list-style-type: none"> • A limitation to this study is that the survey did not ask whether respondents had seen harm reduction messaging, thus changes cannot be ascribed directly to messaging efforts • Expanding vaccine availability and coverage, and encouraging men who have sex with men to take actions to protect their sexual health are recommended <p>Source</p>	
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • This study uses Natural Language Processing techniques, a type of advanced machine learning, to understand the attitudes of the common public towards the monkeypox virus • Tweets posted on Twitter between 1 June and 25 June 2022 containing the word “monkeypox” were collected • This study used sentiment analysis to understand the perception of the public towards the monkeypox virus, and Latent Dirichlet Allocation topic modelling to understand significant aspects of the monkeypox virus discussed online • The results of the sentiment analysis indicate that the ratio of people posting positively about the monkeypox virus is higher than that of people posting negatively <ul style="list-style-type: none"> ○ This indicates that the general public has not yet panicked to much extent about the virus • The results of the topic modeling indicate that among tweets about monkeypox having negative sentiments, the public discussed deaths, the severity of the virus, lesions, whether the virus is airborne, vaccines, and how the virus would affect daily and travel activities • The techniques used in this study can help researchers and policymakers understand the issues that concern the public about the monkeypox virus so effective awareness programs to address the concerns of the general public can be implemented <p>Source</p>	<p>Published September 2022</p>

Type of document	Relevance to question	Key findings	Recency or status
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> This study aimed to estimate the true number of monkeypox infections, including detected and undetected, in most affected countries The study used a capture-recapture method in 10 of the most affected countries: Brazil, Canada, France, Germany, Italy, Netherlands, Portugal, Spain, the U.K., and the U.S. There is heterogeneity across countries on the impact of missed cases on the total number of cases: <ul style="list-style-type: none"> Brazil, France, Spain, and the U.K. showed that the number of infections could reasonably be more than three times the observed number Canada, Germany and Italy show that estimated numbers of cases are above two times the observed ones Portugal shows an estimated ratio below two The study concludes that there is a need for a robust data-driven approach for epidemiologic analyses <p>Source</p>	Published 27 August 2022
	<ul style="list-style-type: none"> Treatment 	<ul style="list-style-type: none"> Adverse events and clinical resolution of systemic symptoms and lesions in an uncontrolled cohort study of patients with monkeypox who were treated with tecovirimat were assessed 25 patients with confirmed monkeypox infections and who had completed a course of tecovirimat therapy were identified through the U.S. Sacramento County Department of Public Health between 3 June and 13 August 2022 All patients were self-reported male, with a median age of 40.7 years At the time of treatment, systemic symptoms, lesions or both were present for a mean of 12 days Tecovirimat therapy was generally well tolerated with no patient discontinuing therapy, with the most reported adverse effects including fatigue, headache, nausea, itching, and diarrhea However, limitations include the inability to differentiate adverse effects from symptoms related to the infection and the lack of a control group <p>Source</p>	Published 22 August 2022

Type of document	Relevance to question	Key findings	Recency or status
	<ul style="list-style-type: none"> • Biology 	<ul style="list-style-type: none"> • This study analyzed the monkeypox viral sequences during the 2022 pandemic to assess whether the virus is undergoing adaptation for better survival and transmission among the human population • The authors analyzed tandem repeats and linkage disequilibrium from 415 monkeypox viral sequences of the 2022 worldwide pandemic that belong to the B.1 clade from the period of 1 January to 20 July 2022 • The analysis shows that the 2022 monkeypox viral population has diverged into four lineages and 11 subgroups based on the tandem repeats • Additionally, 11 new recombinants were identified: six from Slovenia, one from Australia, one from Italy, two from Germany, and one from Spain • The study concluded that the monkeypox genome is evolving and expanding rapidly, and that a combination of tools, including genomic surveillance, tandem repeats, and linkage disequilibrium analyses, are needed to monitor and track phylogenetic dynamics of the monkeypox virus <p>Source</p>	Last updated 18 August 2022 (pre-print)
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Clinical presentation 	<ul style="list-style-type: none"> • This observational study described the clinical characteristics and complications of patients with a monkeypox infection in Bichat Claude Bernard university hospital in Paris, France • 264 patients diagnosed with monkeypox infection between 21 May and 5 July 2022 underwent a standard medical examination and had at least one and up to three samples collected (throat swab, skin swab, EDTA blood sample) • 245 were men who have sex with men (MSM) and 90 practised chemsex in the last three months <ul style="list-style-type: none"> ○ 112 patients had a contact with a confirmed monkeypox case, and the contact was of a sexual nature for 95% of the contacts (86/91) • The majority of patients had fever (68%) and adenopathy (69%), and skin lesions mostly affected the genital (54%) and perianal (40%) areas 	Last updated 23 August 2022 (pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> Overall, 17 patients were hospitalized and none of them were immunocompromised Source	
	<ul style="list-style-type: none"> Prevention and control 	<ul style="list-style-type: none"> This study examined the awareness and response to the monkeypox outbreak in the most affected communities in the U.K. using a cross-sectional survey Of the 1,932 respondents that completed the survey between 15 June and 27 July 2022, 34% reported a limited understanding of public-health information on monkeypox, 52% considered themselves at risk, 61% agreed people infected with monkeypox should isolate for 21 days, 49% reported they would first attend a sexual health clinic if infected, 86% reported they would accept a vaccine, and 59% believed monkeypox originated from animals The respondents differed by gender and sexual identity in terms of trust in healthcare providers, perception of risk of monkeypox, and willingness to be vaccinated The group of respondents was made up largely of white, employed men who have sex with men with university education The sources of information trusted most by respondents were healthcare professionals (37%), official health agencies (29%), and mainstream media (12%) The study concluded that further research is needed to establish awareness, risk perception, healthcare engagement, and improve vaccine acceptability, especially among more diverse and vulnerable populations Source	Last updated 25 August 2022 (pre-print)
	<ul style="list-style-type: none"> Prevention and control 	<ul style="list-style-type: none"> A monkeypox clinical decision support system (CDSS) tool was developed and implemented into the electronic health record of a large integrated healthcare system in Massachusetts and New Hampshire Over the first six weeks, the tool was used 55 times to evaluate monkeypox infection and allowed for rapid and frequent iterations with input of subject-matter experts based on evolving epidemiological risk factors and testing strategies 	Last updated 17 August 2022 (pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> The CDSS tool also identified areas to improve the efficiency of diagnostic evaluation and to alert clinicians of the monkeypox work-up in progress and infection control protocols in real-time <p>Source</p>	
	<ul style="list-style-type: none"> Prevention and control 	<ul style="list-style-type: none"> In this study, the monkeypox epidemic within the U.K. population was assessed by simulating control options over a 12-week projection period using a discrete population transmission model The study found that the monkeypox virus may have already infected a significant portion of men-who-have-sex-with-men (MSM) with the highest sexual activity It was also found that immunity through vaccination among targeted groups, coupled with a behavioural-driven decrease in the transmission rate of infected individuals, is leading to the case incidence flattening followed by a decline over the 12-week projection period <p>Source</p>	Last updated 17 August 2022 (pre-print)
	<ul style="list-style-type: none"> Prevention and control 	<ul style="list-style-type: none"> In this study, optimal vaccine allocation was explored using a deterministic compartmental model to reflect two representative gay, bisexual, and other men who have sex with men (GBMSM) networks in Ontario cities In the model, a simulated rollout of 5,000 vaccines over 15 days, starting 60 days after an epidemic seeding of 10 imported cases, was used The researchers varied the city sizes, epidemic potentials (R_0), mixing between cities, and distribution of imported cases between cities in their modelling to determine the “optimal” allocation of doses between cities The modelling revealed that a fixed number of vaccine doses can avert more infections over the short term when they are prioritized to a network with more initial infections, a larger transmission network, and a network with greater epidemic potential <ul style="list-style-type: none"> The results also suggested that proximity-based and risk-based vaccine prioritization can help to minimize transmission 	Last updated 19 August 2022 (pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • Prioritization of vaccine allocation should be grounded in an understanding of context-specific risk factors and the connectedness of multiple transmission networks Source	
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • The intentions of healthcare workers (HCWs) in France and Belgium to get vaccinated against monkeypox were explored in this study, as well as the factors that were associated with this attitude • The researchers conducted an anonymous online survey from 15 June to 8 August 2022, and of the 690 respondents, 397 were HCWs • 55.4% of the HCWs who responded said that they would probably get the monkeypox vaccine, while 79% said that they would accept the vaccine if it was recommended for the general public • Those who had a favourable attitude towards monkeypox vaccination in HCWs were more likely to have COVID-19 vaccine eagerness and concerns about monkeypox epidemics Source	Last updated 25 August 2022 (pre-print)
	<ul style="list-style-type: none"> • Treatment 	<ul style="list-style-type: none"> • Tecovirimat was administered to patients with confirmed monkeypox as part of an expanded access program (EAP) to contribute to the evidence base on use of the drug as treatment for monkeypox • Tecovirimat is an antiviral drug that has been approved by the FDA for the treatment of smallpox and by the European Medicine Agency for the treatment of orthopoxvirus diseases • Data on clinical signs and symptoms, treatment, disease progression, and outcomes were recorded daily for 14 patients from December 2021 to February 2022 • The rate of appearance of active lesions decreased gradually throughout treatment, with the median time for new lesions being five days following the start of treatment Source	Last updated 26 August 2022 (pre-print)
	<ul style="list-style-type: none"> • Biology 	<ul style="list-style-type: none"> • The study describes the first evidence of recombination of the monkeypox genome in natural transmission, where the authors 	Last updated 13 August 2022 (pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		<p>identified eight new recombinants and concluded that the monkeypox genome is evolving and expanding quickly</p> <ul style="list-style-type: none"> The authors also concluded that tandem repeats analysis and genomic surveillance are useful tools to monitor and track phylogenetic dynamics <p>Source</p>	
	<ul style="list-style-type: none"> Clinical presentation 	<ul style="list-style-type: none"> This study characterized the German cases of monkeypox using an anonymous questionnaire that was sent to the mailing lists of the German AIDS Society and the German Association for Outpatient Physicians for Infectious Diseases and HIV Medicine 301 cases were studied; all of the cases were gbMSM, including 141 with HIV infection and 135 with pre-exposure prophylaxis Most skin lesions were in the anal and genital areas, and the most common symptoms included fever, headache, limb pain, and painfully swollen lymph nodes 5% of patients were hospitalized and there were no deaths Only 41% of patients had not been given a diagnosis of an STI in the six months before their monkeypox infection <p>Source</p>	<p>Published 12 August 2022</p>
	<ul style="list-style-type: none"> Epidemiology (including transmission) Prevention and control 	<ul style="list-style-type: none"> This study involved retrospectively screening 224 samples collected for gonorrhea and chlamydia testing at a sexual health clinic in Belgium in May 2022 using a monkeypox PCR assay to assess the extent of undiagnosed infections Of the 224 samples, four leftover DNA extracts from four different men came back positive for monkeypox Only one of the men had symptoms of monkeypox (a painful vesicular perianal rash) at the time of sample collection; this case was classified as an unrecognized symptomatic case Three of the men reported no symptoms of monkeypox at any time between two months prior to sampling and being recalled to clinic following the retrospective analysis <ul style="list-style-type: none"> Basic laboratory investigations of renal and liver function as well as C-reaction proteins conducted at the time of sampling were within normal limits for these three men The three men with no symptoms all reported having condomless sexual intercourse with at least one male partner in 	<p>Published 12 August 2022</p>

Type of document	Relevance to question	Key findings	Recency or status
		<p>the month prior to sampling as well as sexual intercourse with at least one partner following sampling</p> <p>Source</p>	
	<ul style="list-style-type: none"> • Diagnosis 	<ul style="list-style-type: none"> • The researchers in this study evaluated the CDC recommended monkeypox generic real-time PCR assay as well as the specificity of seven other real-time PCR assays for monkeypox and orthopoxvirus detection • Primer sequences were aligned against 683 reported monkeypox genomes as of 5 August 2022 • Wide variations in the primer and probe sequences were identified in the analysis compared to the genome of currently circulating monkeypox strains • The study concluded that it is critical to develop updated assays for the detection of monkeypox so that accurate and specific data is used to inform public-health risk mitigation strategies <p>Source</p>	<p>Last updated 11 August 2022</p>
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • In this study, a stochastic model was developed to quantify the number of monkeypox infections, contacts made by the infectors, and duration from the arrival of the primary case (the person who brings the disease to a community) to the detection of the index case (the first patient to be identified by health authorities with the disease) in a non-endemic country (Korea) • Using the model, the researchers set up eight scenarios and ran 10,000 simulations for each scenario: <ul style="list-style-type: none"> ○ If the primary case did not self-report, the average number of infections could range from 30 to 67 and the number of contacts made by infectors could range from 221 to 498 ○ If the primary case did self-report, the average number of infections and contacts could range from five to seven and 40 to 52, respectively ○ On average, the duration from primary case arrival until the first index case detection ranged from eight to 10 days if the case does not self-report, compared to approximately three days if the primary case self-reports • The study found that the number and duration of monkeypox infections were strongly affected by self-reporting behaviour of 	<p>Last updated 11 August 2022</p>

Type of document	Relevance to question	Key findings	Recency or status
		<p>the primary case and how delayed the detection of the index case was</p> <ul style="list-style-type: none"> • In Korea, if the monkeypox primary case had not self-reported right after symptom onset, hundreds of contacts and dozens of infections could have occurred in the local community once the index case was found, and more efforts would have been needed to control the disease <p>Source</p>	
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • An environmental sampling was conducted in Dallas, Texas, United States, at the residence of a person who had travel-associated human West Africa monkeypox virus • A targeted swab sampling was collected 15 days after the person who had monkeypox left their household • The results showed that: <ul style="list-style-type: none"> ○ There was extensive DNA contamination, and viable virus from seven samples was isolated in a cell culture ○ There was no statistical difference between PCR positivity of porous versus nonporous surfaces, however there was a statistical difference detected for viable virus in cultures of porous versus nonporous surfaces after at least 15 days <p>Source</p>	<p>Published 11 August 2022</p>
	<ul style="list-style-type: none"> • Clinical presentation 	<ul style="list-style-type: none"> • This study investigated the clinical and virological characteristics of cases of human monkeypox in Spain by analyzing laboratory-confirmed cases in three sexual health clinics in Madrid and Barcelona • The results showed: <ul style="list-style-type: none"> ○ 181 participants had a confirmed monkeypox diagnosis and enrolled in the study, with 166 (92%) identifying as gay, bisexual men, or men-who-have-sex-with-men (gbMSM) and 15 (8%) identifying as heterosexual men or women ○ All participants presented with skin lesions ○ 70 participants (39%) had complications that required treatment, including proctitis, tonsillitis, penile oedema, abscess, and exanthem ○ Median incubation was 7.0 days ○ Viral load was higher in lesion swabs than in pharyngeal specimens 	<p>Published 8 August 2022</p>

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> The authors recommended that due to the variability of the clinical presentations, physicians should have a low threshold for suspicion of monkeypox <p>Source</p>	
	<ul style="list-style-type: none"> Epidemiology (including transmission) Prevention and control 	<ul style="list-style-type: none"> The aim of this study was to describe the outcomes of vaccinating high-risk contacts receiving Imvanex smallpox vaccine as an early post-exposure ring vaccination The study also evaluated tolerance and potential breakthrough infections after the first dose For the observational analysis, 276 individuals received one dose of vaccine with a median delay of 11 days after being exposed to a confirmed monkeypox patient Among the vaccinated individuals, 12 (4%) had a confirmed monkeypox breakthrough infection that was not severe – 10 of these individuals developed a monkeypox infection five days following vaccination and two had a breakthrough infection at 22 and 25 days <ul style="list-style-type: none"> The researchers were not surprised by the 10 breakthrough infections five days after vaccination, but they were surprised by the two other breakthrough infections and hypothesized that these two patients, who were the only patients in this group with pets, may have been persistently exposed to the virus through their domestic pets acting as carriers The study concluded that the Imvanex vaccine was effective and well-tolerated against monkeypox even though it did not completely prevent breakthrough infections <p>Source</p>	Last updated 4 August 2022
	<ul style="list-style-type: none"> Epidemiology (including transmission) Prevention and control 	<ul style="list-style-type: none"> The willingness and determinants of sexual behaviour change in men-who-have-sex-with-men (gbMSM) to potentially reduce further monkeypox transmissions was explored through an online survey 394 gbMSM were recruited as participants and asked whether they would be willing to reduce the number of sexual partners and the number of sexual encounters in the context of the monkeypox epidemic 	Published 3 August 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> ○ Socio-demographic, behavioural, and psycho-social information was also collected, such as age, relationship status, education, migration status, HIV status ● The survey findings showed that: <ul style="list-style-type: none"> ○ The overall intentions to reduce the number of sexual partners and sexual activity was high, however only a minority had developed definite intentions ○ Dating and open relationship status was a positive predictor for sexual behaviour changes ○ Vaccination intentions did not predict sexual behaviour changes ○ Those participants that are not on pre-exposure prophylaxis (PrEP) were more likely to change their sexual behaviour ○ Monkeypox infection concerns were negatively related to weaker intentions and only predicted definite intentions for sexual behaviour changes <p>Source</p>	
	<ul style="list-style-type: none"> ● Epidemiology (including transmission) ● Clinical presentation 	<ul style="list-style-type: none"> ● This cross-sectional study describes the monkeypox cases in Spain ● Of the 185 patients, most cases started with localized homogenous papules, not pustules, in the area of inoculation, which could be cutaneous or mucous; small pustules appeared later in some cases and heterogenous lesions occurred during this generalized phase; less common lesions included mucosal ulcers and monkeypox whitlows <ul style="list-style-type: none"> ○ All patients had systemic symptoms ○ Four patients were hospitalized and there were no deaths ● Smallpox vaccination and well-controlled HIV disease were not associated with markers of severity ● Contact during sex was the most likely mechanism of transmission; 76% of patients had other sexually transmitted diseases upon screening <p>Source</p>	Published 2 August 2022
	<ul style="list-style-type: none"> ● Prevention and control 	<ul style="list-style-type: none"> ● The levels of community testing, contact tracing, and vaccination required to reduce the effective reproduction number (Rt) of the monkeypox virus below one for high-risk men-who-have-sex-with-men (gbMSM) 	Published 2 August 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • A deterministic branching model was utilized with infectious individuals being identified with a probability that varies based on community detection rate and whether their source case had undergone contact tracing • The authors found that the critical threshold to vaccinate depends on the basic reproduction number of the monkeypox virus and on other public-health measures <p>Source</p>	
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • The population-based cohort study aimed to identify the risk factors for monkeypox virus infection and define who are considered at the highest risk, with an endpoint of a confirmed case of monkeypox • The authors defined their highest-risk population as those who have used HIV-PrEP or erectile dysfunction therapy or were diagnosed with STIs by rectal PCR • The subjects in the highest-risk group have a 20-fold risk for monkeypox virus infection and conclude that these findings may assist in prioritizing risk groups <p>Source</p>	Literature last published 25 July 2022 (pre-print)
	<ul style="list-style-type: none"> • Biology 	<ul style="list-style-type: none"> • The study described the phylogenomics, host-pathogen interactome, and mutational cascade of monkeypox • The authors reported a clustering of strain Israel 2018 from Clade 1 with four isolates reported from the recent outbreak • A large number of mutations within the current outbreak clade indicates the need for a fast response with genomic analysis of the newly detected strains to develop better prevention and treatment methods <p>Source</p>	Last updated 25 July 2022 (pre-print)
	<ul style="list-style-type: none"> • Clinical presentation 	<ul style="list-style-type: none"> • This study reports the clinical features, longitudinal virological findings, and response to off-label antivirals in seven patients with monkeypox who were diagnosed from 2018 to 2020 (four men and three women) • Three acquired monkeypox in the UK; one was a healthcare worker, one acquired it abroad and transmitted it to an adult and child in their household 	Published August 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • Symptoms include viraemia and reactive low mood; five patients spent more than three weeks in isolation due to prolonged PCR positivity • Three patients were treated with brincidofovir (200 mg once a week orally), all of whom developed elevated liver enzymes resulting in therapy cessation; one patient was treated with tecovirimat (600 mg twice daily for two weeks orally) and they experienced no adverse effects, had a shorter duration of viral shedding and illness (10 days of hospitalization) compared with the other patients; one patient had a mild relapse six weeks after hospital discharge <p>Source</p>	
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Prevention and control 	<ul style="list-style-type: none"> • This study uses a network model to simulate a monkeypox epidemic among men who have sex with men (gbMSM) • This model follows a separable temporal exponential family random graph model of a Belgian population of gbMSM <ul style="list-style-type: none"> ○ Additionally, a population of men who have sex with men with high rates of partner change (HR-gbMSM) was included in this model ○ The model was refined to include main and casual partnerships among low-risk and HR-gbMSM in terms of number of partners and frequencies of sexual encounters • This study indicates that unrecognized infections have an important impact on the epidemic • The findings suggest that contact tracing helps to reduce epidemic size even if only 10% of contacts effectively ceased sexual activity • This study suggests that the vaccination of individuals at the highest risk of infection reduces epidemic size more than post-exposure vaccination of sexual partners <ul style="list-style-type: none"> ○ This is particularly the case if only a small proportion of partners can be traced • Limitations to this study include the absence of accurate estimates of key parameters such as the proportion with unrecognized infection and the per-encounter transmission 	Last updated 31 July 2022 (Pre-print)

Type of document	Relevance to question	Key findings	Recency or status
	<ul style="list-style-type: none"> • Prevention and control • Diagnosis 	<p>probability and how this varies according to the type of sexual contact</p> <ul style="list-style-type: none"> • Additionally, the model did not capture superspreading events <p>Source</p> <ul style="list-style-type: none"> • This study investigated the ability to self-diagnose a potential monkeypox infection, and determinants of vaccination intention and self-isolation intention after exposure among gbMSM in the Netherlands • A cohort of 394 men who have sex with men (gbMSM) were recruited through an online survey and online dating app • Participants were provided with four images and asked to indicate the conditions depicted in each of the images <ul style="list-style-type: none"> ○ This study found that about half were able to self-diagnose monkeypox, however, a high false positive rate was also found where syphilis stage-2 was most frequently misdiagnosed as monkeypox • This study found that 72% had a high intention to get vaccinated <ul style="list-style-type: none"> ○ Among socio-demographic determinants, gbMSM who were single but dating, who had a polyamorous relationship and who were retired were most likely to have high vaccination intentions ○ No behavioral determinants were found to be statistically associated with vaccination intentions ○ Among psycho-social determinants, knowing someone who has/had monkeypox and being worried about a monkeypox infection was associated with high vaccination intention • This study found that 44% had high intention to self-isolate after monkeypox exposure <ul style="list-style-type: none"> ○ Those who were retired, first-generation and second-generation migrants showed higher intentions to self-isolate ○ gbMSM who perceived more problematic consequences due to a monkeypox infection were also more likely to self-isolate ○ Those who had bachelor and master's degrees were less likely to self-isolate ○ No behavioral determinants were found to be associated with high self-isolation intentions 	<p>Last updated 31 July 2022 (Pre-print)</p>

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> The study suggests that efforts to increase vaccination, intentions to isolate and ability to self-diagnose should be aimed at gbMSM at the highest risk, especially those with little concern about monkeypox and those with a high level of education without a non-Western migration background <p>Source</p>	
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> The single study (pre-print) described the global spatial landscape of orthopoxviruses (including monkeypox), and found significant spatial heterogeneity with population susceptibility from 57% to 96% based on the strength and longevity of the smallpox vaccination campaign in addition to demographic changes and waning of cross-protective immunity within a nation The authors reported that demographic changes since eradication of smallpox leads to susceptibility and less so by historical smallpox vaccination efforts The authors indicated that lowest levels of susceptibility included parts of Finland, Bulgaria, Monaco, Japan, and Sweden, whereas the most susceptible countries were Australia, Yemen, Colombia, Guinea-Bissau, and Ethiopia <ul style="list-style-type: none"> The authors noted that large countries such as India, China, Brazil, the U.S., and central and western Africa were notable areas for susceptibility <p>Source</p>	Last updated 30 July 2022 (Pre-print)
	<ul style="list-style-type: none"> Biology 	<ul style="list-style-type: none"> The study found that the monkeypox virus strain isolated in 2018 is the same lineage as the current 2022 virus strains However, 46 new mutations were observed in the monkeypox virus-2022 strains The authors also reported that ten proteins in the monkeypox virus are prone to novel mutations <p>Source</p>	Published 29 July 2022
	<ul style="list-style-type: none"> Prevention and control 	<ul style="list-style-type: none"> A retrospective study evaluated the humoral and cellular immune responses for up to six months after vaccination with COH04S1 two-dose vaccine in a subgroup of 20 volunteers in a phase one clinical trial 	Last updated 29 July 2022 (Pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • A detectable humoral and cellular response for up to six months post vaccination was found at all tested dose levels (e.g., 28 vs. 56 days apart) • Increased timing between vaccinations marginally increased the magnitude of the long-term response compared to volunteers with a shorter vaccination interval • The authors concluded that the COH04S1 vaccine induces a robust and durable immunity and could be tested in non-inferiority clinical trials <p>Source</p>	
	<ul style="list-style-type: none"> • Prevention and control • Diagnosis 	<ul style="list-style-type: none"> • This study adapted two published quantitative PCRs to use as a dual-target monkeypox test • Clinical performance against a commercial orthopoxvirus research-use only PCR kit • The assay showed a 100% positive (n=11) and 100% negative (n=56) agreement • Timely and scalable PCR tests are necessary to curb the spread of monkeypox <p>Source</p>	Published 29 July 2022
	<ul style="list-style-type: none"> • Clinical presentation 	<ul style="list-style-type: none"> • This study characterizes the clinical features of monkeypox in humans in a regional high consequences infectious disease centre with primary and secondary care referrals and affiliated sexual health centres in south London from May to July 2022 • 197 participants had a mean age of 38 years, all being men, with 196 identifying as gay, bisexual, or other men who have sex with men • All presented with mucocutaneous lesions, mostly on genitals or in the perianal area • 170 participants reported systemic illness, with the most common symptoms being fever, lymphadenopathy, and myalgia • 71 reported rectal pain, 33 reported sore throats, 31 penile oedema, 27 oral lesions and 9 tonsillar signs • 70 had a concomitant HIV infection • 20 patients were admitted to hospital for the management of symptoms, most commonly rectal pain and penile swelling <p>Source</p>	Published 28 July 2022

Type of document	Relevance to question	Key findings	Recency or status
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Prevention and control 	<ul style="list-style-type: none"> • To determine whether monkeypox viral DNA can be detected and monitored in wastewater, this study deployed digital PCR assays that target genomic monkeypox (monkeypox virus) DNA in the routine wastewater surveillance program in the Greater Bay Area in California • Wastewater samples were taken daily from 19 June to 20 July 2022, and researchers found that monkeypox virus DNA was consistently detected in samples across the majority of test sites (8/9), with increasing concentrations of DNA over time • To provide a second line of evidence for monkeypox DNA detection, a second monkeypox assay specific to the West African clade of monkeypox virus was used on a subset of samples <ul style="list-style-type: none"> ○ There was no significant difference between results of the two assays, proving that monkeypox virus DNA detections using the first assay were true positives • Robust surveillance of monkeypox virus using wastewater testing can provide data for targeting public health resources and raise awareness among healthcare professionals so that they can better recognize and manage monkeypox cases <p>Source</p>	Last updated 26 July 2022 (Pre-print)
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Prevention and control 	<ul style="list-style-type: none"> • This study investigated environmental contamination with monkeypox virus from infected patients admitted to isolation rooms in the UK to inform infection prevention and control measures • Environmental swabbing was done in four positive pressure isolation rooms, four negative pressure ensuite bathrooms, four positive pressure ventilated anterooms, and three anterooms for PPVL respiratory isolation rooms where monkey pox cases had been isolating <ul style="list-style-type: none"> ○ PPE from doffing areas in addition to air sampling pre and post bedding changes were taken ○ Samples were analyzed by qPCR ○ Virus isolation was done for four samples by taking samples every 48-72 hours from a tissue culture flask to measure cytopathic effects (CPE) 	Last updated 21 July 2022 (Pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • This study identified widespread surface contamination in occupied patient rooms, on healthcare worker personal protective equipment after use, and in doffing areas <ul style="list-style-type: none"> ○ 93% (56/60) of surface swab taken from patients rooms and bathrooms had detectable monkey pox DNA ○ 89% (8/9) samples taken from the ante rooms were positive and half (2/4) the samples from the ward corridor were positive ○ The majority of air samples taken from anterooms and corridors pre and during doffing were negative (25%, 5/20) • The samples taken in this study from doffing procedures indicated that gloves, gowns, and the anteroom floor had detectable monkeypox virus DNA (7/12) <ul style="list-style-type: none"> ○ Visors (3 samples) had no detectable DNA ○ One air samples was positive in a corridor pre-doffing but samples taken from the pre-doffing from anterooms and from anterooms and corridors during doffing were all negative • The results of this study indicated significant contamination in isolation facilities and the potential for aerosolization of monkeypox virus during specific activities • The variability in the frequency of detection and the Ct values observed from different patient rooms may be due to individual patient factors, the point during patient infection that sampling was performed, staff or patient behavior, and the frequency of cleaning <p>Source</p>	
	<ul style="list-style-type: none"> • Clinical presentation 	<ul style="list-style-type: none"> • An international group of clinicians contributed to an international case series to describe the presentation, clinical course, and outcomes of PCR-confirmed monkeypox • 528 infections were studied from 27 April to 24 June 2022, at 43 sites in 16 countries • 98% were gay or bisexual men, 75% were White, and 41% had human immunodeficiency virus infection • 95% presented with a rash, 73% had anogenital lesions, and 41% had mucosal lesions 	Published 21 July 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> Systemic symptoms before the rash included fever, lethargy, myalgia, headache, lymphadenopathy Virus DNA was detected in 29/32 of persons in whom seminal fluid was analyzed Antiviral treatment was given to 5% of people; 13% were hospitalized <p>Source</p>	
	<ul style="list-style-type: none"> Prevention and control 	<ul style="list-style-type: none"> The primary objective of this study was to examine the susceptibility of four population samples (France, Bolivia, Laos, and Mali) to the monkeypox virus This study analyzed blood samples of approximately 6,500 subjects to detect antibodies that neutralize the vaccinia and cowpox viruses Given the finding of a low seroprevalence of orthopoxvirus in those under analysis, individuals from the four regions, (and to a larger extent, Europe, Africa, Asia, and South America) are very likely to be susceptible to monkeypox infections <p>Source</p>	Published 17 July 2022 (pre-print)
	<ul style="list-style-type: none"> Diagnosis 	<ul style="list-style-type: none"> This study reports on the laboratory testing methods of the Laboratory Response Network (LRN) in the US to detect Orthopoxvirus A non-variola Orthopoxvirus real-time PCR Primer and Probe Set (non-variola Orthopoxvirus [NVO] assay) was being used from 17 May to 30 June 2022 This study reports that 2,009 samples were received and of those samples, 36.6% (n=395 individuals) were non-variola Orthopoxvirus positive <ul style="list-style-type: none"> 159 of these cases were confirmed as monkeypox by the CDC, and confirmatory testing is pending for 236 persons One case was determined to be from the West African clade by the CDC A rapid turnaround time for test results is critical to quickly initiate public health action to control the spread of monkeypox Although the capacity for LRN NVO testing is high, challenges include acquiring public health approvals for testing and challenges navigating public health testing procedures 	Published 15 July 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> The expansion to five commercial laboratories starting the week of 15 July 2022 is anticipated to make testing more accessible, increase convenience for providers and patients, and further augment national capacity <p>Source</p>	
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> An analysis was conducted to identify monkeypox virus genomes in multiple domestic locations from an imported case of monkeypox in a traveler that had returned from Nigeria to the United Kingdom Positive samples of the genome were identified using vacuum and surface sampling techniques, which allows for an analysis of both porous and non-porous contaminated surfaces The analysis confirms that there is a potential for the monkeypox virus to be recovered in environmental settings associated with known positive cases There is a necessity for rapid environmental assessment to reduce potential exposure to close contacts of a suspected or confirmed case <p>Source</p>	Published 15 July 2022 (pre-print)
	<ul style="list-style-type: none"> Biology Epidemiology (including transmission) 	<ul style="list-style-type: none"> monkeypox virus is genetically structured in two major clades: clades 1 and 2/3 This study explored the population transmission of Monkeypox virus (monkeypox virus) in West Africa (WA) (clade 2/3), and the Congo Basin (CB) (clade 1) Complete monkeypox virus genomes (n = 90; no current outbreak genomes) were downloaded from the National Center for Biotechnology Information (NCBI) in order to conduct population structure analysis, recombination analysis, and time estimate phylogenetic reconstruction Genetic diversity and nucleotide diversity was higher in clade WA (clade 2/3) than clade CB (clade 1), with geographic clusters around Nigerian sequences (clade 2) and West African sequences (clade 3) The CB (clade 1) sequences had a low frequency polymorphism possibly related to a population expansion after a bottleneck event 	Published 14 July 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • Structural analysis indicated virtually no mixing between the WA and CB clade, and according to linkage modelling, clade WA (clade 2/3) diverged less from an ancestral population than clade CB (clade 1) • Overall, phylogenetic evidence suggests that the WA clade is the origin of all monkeypox strains, with clade CB splitting off 560-860 years ago, depending on which model was used <ul style="list-style-type: none"> ◦ The split of clades 2 and 3 (Clade WA) was dated to 1785 CE with the time to the most common ancestor of 140-180 years ago • The results of this study provide a better understanding of monkeypox epidemiology in the endemic region to gain insight into the events that originated and are sustaining the current multi-country outbreak <p>Source</p>	
	<ul style="list-style-type: none"> • Biology 	<ul style="list-style-type: none"> • Genomic surveillance is an essential resource to monitor and track the evolution of pathogens, and this study conducted a phylogenomic analysis of available Monkeypox virus genomes to determine their evolution and diversity • The analysis showed that all monkeypox virus genomes were grouped into three clades: two previously characterized clades and a newly emerging clade that has genomes from the ongoing 2022 multi-country outbreak • The broader geographical expansion suggests multifactorial factors as drivers of the current outbreak • Integrating epidemiological data with genomic surveillance should help generate real-time data to develop adequate preventive and control measures <p>Source</p>	Published 12 July 2022
	<ul style="list-style-type: none"> • Prevention and control • Diagnosis 	<ul style="list-style-type: none"> • This study reported on the rapid development and implementation of mobile responsive survey solutions for healthcare personnel (HCP) at an academic health center in Boston, Massachusetts to identify possible exposure to monkeypox, perform exposure risk assessment and stratification, and conduct symptom monitoring during the exposure window 	Published 11 July 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • Research Electronic Data Capture (REDCap) tools that were modernized to support contact tracing and exposure investigations for monkeypox were deployed within 24 hours of identification of a suspected patient, with the full suite of response solutions being employed within four days of confirmation of the monkeypox diagnosis • Clinical follow-up of suspected patients was integrated into the design, and real-time updates allowed for improvements in HCP symptom monitoring compliance and enhanced tracking • The study highlighted that the modernized nature of the REDCap tool that was used, efficient communications from the teams involved, and the experience of the response tool's development team prior to and during the COVID-19 pandemic made it possible for the mobile response tools for identifying and monitoring monkeypox cases to be implemented quickly <p>Source</p>	
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • This observational study reported on confirmed cases of monkeypox diagnosed at an STI clinic in Madrid • Various genetic analyses were performed from 18 May to the beginning of June 2022 using swabs of vesicular lesions from 48 patients, all of whom were cisgender men <ul style="list-style-type: none"> ◦ The median age of the patients was 35 • The study found that 89.5% of the patients had unprotected sex in the three weeks before the onset of the symptoms • The first symptom was skin lesions in 53.8%(21) of patients, followed by 17.9%(7) who had fever first, 12.8%(5) who had respiratory symptoms, 5.1%(2) who had headache, 5.1%(2) who had rash, 2.6%(1) who had asthenia, and 2.6%(1) who had proctitis • The most prevalent symptoms were the presence of vesicular-umbilicated and pseudo-pustular skin lesions (93.8%), asthenia (66.6%), and fever (52.1%) • The location of the lesions suggests that transmission occurred during sexual intercourse, with a statistical relation between the location of the lesions and the role of the patients regarding sexual practices 	Published 10 July 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> This study indicated that “chemsex,” or the consumption of drugs during sex with multiple partners for several hours or days, was linked to a greater prevalence of monkeypox, COVID-19 and other STIs Sequencing analysis indicated the virus circulating in Spain belongs to the western African clade, which were known to be direct descendants of viruses previously detected in Nigeria, the UK, Singapore, and Israel in 2017-2018 <p>Source</p>	
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> This study reported on reproductive number (Ro) estimates for monkeypox in England, Spain and Portugal as of 18 June 2022 There were 2,551 confirmed cases from 56 populations as of 18 June 2022, with England (n=550), Spain (n= 497), and Portugal (n=276) having the highest cumulative number of confirmed cases Ro estimates for England, Spain, and Portugal study populations from 18 May and 18 June 2022 were statistically greater than one (the condition that an epidemic outbreak occurs), with the estimate for Spain being statistically higher than those for England and Portugal Serial interval was found to be positively correlated with the Ro estimation, with lower Ro estimates if a shorter interval of 6.8 days was assumed Limitations of the Ro estimates include possible skewing due to any super-spreading individual or event, a possible lack of generalizability of results due to homogenous social mixing assumption, and the use of estimates from an earlier outbreak report of a similar virus strain <p>Source</p>	Published 8 July 2022 (pre-print)
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> This study presented crowdsourced predictions using Metaculus – a forecasting technology platform – of global projections for confirmed monkeypox cases and deaths 686 unique predictions were collected between 19 May and 24 May 2022 on Metaculus, and provided the following results: 	Published 7 July 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> ○ The crowdsourced platform estimated probability of global infections placed on 1,000 to 10,000 was 0.51, with a 0.46 probability on 10,000 or more infections ○ The estimated probability of 100 to 1000 deaths was 0.59, with a 0.23 probability on 1000 or more deaths ○ Probabilities for 10 to 100 cases by 1 July 2022 was 0.56 and 0.51 for USA and Canada, respectively ○ The probability for 30 to 100 countries reporting one or more infections by 31 July 2022 was 0.75, with fewer estimating that there would be 100 or more countries with reported infections (0.09) ● The study concluded that a human judgment forecasting platform may be able to quickly generate probabilistic predictions that may be especially important when data are sparse or when historical data has been collected in different locations, limiting the accuracy of mechanistic models <p data-bbox="953 719 1031 743">Source</p>	
	<ul style="list-style-type: none"> ● Epidemiology (including transmission) 	<ul style="list-style-type: none"> ● This study aimed to investigate the asymptomatic transmission of monkeypox from a sample of male sexual health clinic attendees in Belgium ● Of the 224 male attendees who were sampled, three positive monkeypox-specific polymerase chain reaction (PCR) tests were identified; none of the positive cases reported symptoms (pre- and post-sampling) or contact with confirmed cases ● All three positive cases did report engaging in sexual activity with at least one male partner within a few days to one month prior to sampling ● The findings from this study provide evidence for the potential asymptomatic transmission of monkeypox between close contacts and suggest that further action may be required to contain an outbreak <p data-bbox="953 1230 1031 1255">Source</p>	Published 5 July 2022 (pre-print)
	<ul style="list-style-type: none"> ● Epidemiology (including transmission) ● Clinical presentation 	<ul style="list-style-type: none"> ● This observational study described the demographic and clinical characteristics of patients diagnosed with confirmed monkeypox virus that attended open access sexual health clinics in London, UK between 14 May and 25 May 2022 	Published 1 July 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • The study identified the following demographic characteristics of the 54 confirmed cases: <ul style="list-style-type: none"> ○ All patients identified as men who have sex with other men (gbMSM) ○ A median age of 41 years ○ 38 of 54 individuals were White and born in the UK ○ 13 of 54 individuals were living with HIV • The clinical characteristics included: <ul style="list-style-type: none"> ○ 36 of 54 individuals reported fatigue ○ 31 individuals reported fever ○ 10 individuals had no prodromal symptoms ○ All patients presented with skin lesions ○ No fatal outcomes were reported • The study identified frequent anogenital symptoms, which suggests that transmissibility occurred through local inoculation during close skin-to-skin or mucosal contact <p>Source</p>	
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Clinical presentation 	<ul style="list-style-type: none"> • In this study focused on enhanced surveillance of monkeypox cases in Bas-Uélé, Democratic Republic of Congo, 106 households with at least one suspected monkeypox case were visited and whenever possible, skin lesions were screened by PCR for the monkeypox virus, as well as by the varicella-zoster virus when negative for the former <ul style="list-style-type: none"> ○ A suspected monkeypox case was defined as “any person with an active generalized vesicularpustular rash” ○ Contact and clinical history information was also collected from all household members • Of the 77 suspected cases that were tested, 27.3% were positive for monkeypox, 58.4% for chickenpox, and 14.3% negative for both • Confirmed monkeypox cases presented more often with monomorphic skin lesions on the palms of hands and soles of feet, but no combination of symptoms had a strong confirming power for decisive diagnosis • The authors concluded that intensified surveillance of monkeypox in Africa is critical considering the current outbreak 	Published 6 July 2022 (pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		<p>outside of Africa, and that rapid field diagnostics are needed to optimize worldwide early detection and surveillance of monkeypox</p> <p>Source</p>	
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> This study documented the creation of an open-access database to track the occurrence of cases in different countries, as well as information on age, gender, dates of symptom onset and laboratory confirmation symptoms, locations, travel history, and additional metadata During early stages of outbreaks, it was found that retrieving reliable data on the characteristics of cases at a global scale is challenging Working with the WHO Hub for Pandemic and Epidemic Intelligence, the team is defining a contact data schema allowing countries and researchers to estimate key epidemiological parameters such as incubation period and serial interval across various settings <p>Source</p>	<p>Published 1 July 2022</p>
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> This study documented the creation of an open-access database to track the occurrence of cases in different countries, as well as information on age, gender, dates of symptom onset and laboratory confirmation symptoms, locations, travel history, and additional metadata During early stages of outbreaks, it was found that retrieving reliable data on the characteristics of cases at a global scale is challenging Working with the WHO Hub for Pandemic and Epidemic Intelligence, the team is defining a contact data schema allowing countries and researchers to estimate key epidemiological parameters such as incubation period and serial interval across various settings <p>Source</p>	<p>Published 1 July 2022</p>
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> This study built dynamic models to mimic the spread of the monkeypox virus (monkeypox) as an emerging zoonosis in a hypothetical metropolitan area, including high- and low-risk transmission among humans and animals to humans 	<p>Published 29 June 2022</p>

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • The model followed the SEIR framework to include 1) Infectious (prodromal phase); 2) Infectious (rash phase); 3) Isolated (infectious); and 4) Isolated (susceptible) subpopulations • Transmission in the human population was modelled using a transmission risk parameter and a contact matrix that describes contacts between and within-population subgroups • Additionally, the authors modelled the spread of the monkeypox virus in humans considering animal hosts like rodents (e.g., rats, mice, squirrels, chipmunks, etc.) and emphasize their role and transmission of the virus in a high-risk group, including men-who-have-sex-with-men • The results showed that the monkeypox virus may spill over from high-risk groups (e.g., men-who-have-sex-with-men) to broader populations if efficiency of transmission increases in the higher-risk group • The risk of outbreak can be greatly reduced if at least 65% of symptomatic cases can be isolated and their contacts traced and quarantined <p>Source</p>	
	<ul style="list-style-type: none"> • Biology 	<ul style="list-style-type: none"> • This study found that the monkeypox virus outbreak described so far in non-endemic countries belongs to clade 3 and most likely has a single origin <p>A mutational analysis shows signs of potential monkeypox human adaptation in ongoing microevolution</p> <p>Source</p>	Published 24 June 2022
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • This study conducted an online survey of the United States' (US) general public about their knowledge and attitudes, their trusted sources of information, and to test whether COVID-19 vaccination status was associated with monkeypox vaccination attitudes or intentions to receive one if it was recommended • The survey included 856 participants, of which 51% was female, 41% had a college degree or higher and 38% was 55 years or older, which was similar to the US population • Sources of information deemed most reliable to convey information about the outbreak were healthcare professionals, health officials (e.g., Centers for Disease Control and 	Published 23 June 2022

Type of document	Relevance to question	Key findings	Recency or status
		<p>Prevention), and social media accounts of healthcare professionals and researchers</p> <ul style="list-style-type: none"> • Almost half the respondents (47%) feel that their knowledge level about Monkeypox is poor or very poor • Current COVID-19 vaccination status was a strong predictor of positive intentions of receiving a monkeypox vaccination if recommended • The low levels of knowledge about monkeypox indicate the need for more clear communication about the outbreak <p>Source</p>	
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • Using a modelling framework, the authors modelled a monkeypox outbreak in a simulated population of 50 million people with socioeconomic and demographic characteristics of a high-income European country • The baseline scenarios projected that with no public health emergency interventions, monkeypox could lead to small national outbreaks of moderate duration, but they would all subside in 23 to 37 weeks, depending on the number of cases introduced • Contact tracing with isolation of symptomatic cases would reduce the number of secondary cases by 72.2% following the introduction of 3 cases, 66.1% after 30 cases, and 68.9% after 300 cases • Adding ring vaccination to contact tracing would reduce the number of secondary cases by 77.8% following the introduction of 3 cases, 78.7% after 30 cases, and 86.1% after 300 cases <p>Source</p>	<p>Published 23 June 2022</p>
	<ul style="list-style-type: none"> • Diagnosis 	<ul style="list-style-type: none"> • The study developed a real-time PCR assay • Five of the 10 clinical samples tested positive within the detectable range • The authors concluded that their real-time qPCR assay could be utilized in the multi-country outbreak <p>Source</p>	<p>Last updated 23 June 2022 (Pre-print)</p>
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • This study estimated the incubation period of the monkeypox virus (monkeypox) using United States data from 22 probable and confirmed patient cases reported from 17 May 2022 to 6 June 2022 	<p>Published 21 June 2022</p>

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • The incubation period was estimated from exposure to first symptom onset • All 22 monkeypox patients included in the analysis were male, with a median age of 37 years • Commonly reported symptoms included lesions in the anal and genital areas, swollen lymph nodes, rectal pain, headache, and fatigue • The mean incubation period from exposure to first symptom onset was 7.6 days and the 95th percentile was 17.1 days • The results align with the current Centers for Disease Control and Prevention’s recommendations for monitoring close contacts of people with monkeypox for 21 days after their last exposure <p>Source</p>	
	<ul style="list-style-type: none"> • Prevention and control • Clinical presentation 	<ul style="list-style-type: none"> • This study aimed to report on the rapid development and implementation of mobile responsive survey solutions for notification of possible exposure, exposure risk assessment and stratification, and symptom monitoring of healthcare personnel after exposure to the monkeypox virus (monkeypox) • A suite of tools using REDCap ((Research Electronic Data Capture) were used to develop the following three tools, building on prior use of REDCap technology as part of patient monitoring at Massachusetts General Hospital’s special pathogens unit and treatment facilities: <ol style="list-style-type: none"> 1) notification of possible exposure 2) exposure risk assessment and stratification 3) symptom check • All healthcare personnel on a trace list received a notification of possible exposure survey tool to identify healthcare personnel who could have been exposed to the index patient and to exclude healthcare personnel with no possible exposure • Once HCP had been identified as meeting a preliminary definition of monkeypox exposure, the next step was to conduct risk assessment and classification <ul style="list-style-type: none"> ○ Healthcare personnel were presented with a series of exposure scenarios and asked to identify which ones applied to their interactions with the index patient 	Published 16 June 2022 (pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> ○ Based on responses, each healthcare personnel were categorized as high, intermediate, or low/uncertain risk ● Healthcare personnel identified in high, intermediate, and low/uncertain risk classifications required symptom monitoring for 21 days from their last exposure per public health guidance and completed a symptom check survey ● For those that answered yes to symptom questions including fever, chills, new lymphadenopathy and new skin rash, they would be provided with instructions to self-isolate and contact occupational health services immediately ● These tools were deployed within 24 hours of identification of a patient with suspected monkeypox, with the full suite in production within 4 days of confirmation of the diagnosis of monkeypox <p>Source</p>	
	<ul style="list-style-type: none"> ● Clinical presentation 	<ul style="list-style-type: none"> ● This single study focused on monkeypox cases with exclusive genital lesions and the need to note such presentations as authentic sexually transmitted disease presentations ● Two patient cases are presented in which rashes and lesions were concentrated in the genital area ● The authors argue that the high prevalence of genital lesions may mean the virus is particularly well transmitted sexually and clinicians should be cognizant of exclusive genital lesions to offer timely ring vaccination <p>Source</p>	Published 14 June 2022
	<ul style="list-style-type: none"> ● Epidemiology (including transmission) 	<ul style="list-style-type: none"> ● This study aimed to estimate the incubation period for monkeypox using the reported time of exposure and symptom onset for confirmed monkeypox cases detected in the Netherlands up to 31 May 2022 ● The study fitted parametric distributions to the observed incubation periods among 18 cases with symptom onset and exposure histories for monkeypox, using a likelihood-based approach, allowing for exposure to be a single time point or a time interval (due to number of consecutive dates of potential exposure) 	Published 13 June 2022 (pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> ○ The 18 cases used for data collection were all men that identified themselves as men who have sex with men (gbMSM) ● Using a best-fitted distribution, the mean incubation period was estimated to be 8.5 days (95% confidence intervals of 6.6–10.9 days), with a range of 4.2 to 17.3 days for the 5th to 95th percentiles, respectively ● The estimated 95th percentile of 17.3 days supports the use of 21 days for monitoring or quarantining close contacts of cases to limit further spread of the infection <p>Source</p>	
	<ul style="list-style-type: none"> ● Epidemiology (including transmission) 	<ul style="list-style-type: none"> ● The authors used a branching process transmission model fitted to empirical sexual partnership data in the UK to show that a small fraction of individuals with disproportionately large number of partners can explain the growth of monkeypox cases among the gbMSM population (despite the absence of such patterns in past outbreaks) ● It is plausible that monkeypox had a large transmission potential in the gbMSM sexual contact network in the past, but due to the small number of imported cases in non-endemic settings, it had not reached high degree members of this network yet ● The study also suggests that the basic reproduction number (R0) for monkeypox over the gbMSM sexual contact network may be substantially larger than 1 ● It was inferred that the non-sexually associated R0 for monkeypox would be substantially lower than the R0 for the gbMSM sexual network if the proportion of non-sexually associated cases remained low in the future; however, the authors warned that the R0 may still be >1 if the R0 for the gbMSM sexual network is high ● It was recommended that ongoing support and public health messaging facilitates prevention and early detection among gbMSM with a large number of partners <p>Source</p>	Last updated 13 June 2022 (pre-print)
	<ul style="list-style-type: none"> ● Epidemiology 	<ul style="list-style-type: none"> ● The Lancet correspondence describes the case of two white British men with reported monkeypox 	Published 31 May 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> The case report describes that one man developed perioral white spots and painful perianal blistering lesions 24 hours after kissing an unrelated individual with a crusted oral lesion The second man reported perioral papules (blistered and ulcerated) and papules on the mons pubis and penile shaft 48 hours after The report indicates that skin lesions at the point of sexual contact were likely the location of infection, which was followed by lymphadenopathy, fever, headache, and diarrhea The authors concluded that healthcare workers should use appropriate PPE and receive education on clinical pathways to manage possible monkeypox cases, and encouraged collaborative efforts with clinicians and patients to ensure sensitive community engagement/education to avoid stigmatization <p>Source</p>	
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> This study assessed the effect of an enhanced surveillance approach to detect monkeypox virus (monkeypox) cases and measure the cumulative incidence of monkeypox in priority states in Nigeria Three priority states and their local government areas (LGAs) were identified based on previous disease incidence: Rivers, Delta, and Bayelsa Out of the three states, 30 hotspots of the LGAs out of the 56 total LGAs (54%) were engaged for enhanced surveillance and community volunteers were trained to conduct active case searches and follow-up with their LGA surveillance facilitators weekly and monthly over a period of three months Overall, 25 suspected cases and three confirmed cases of monkeypox were identified The study showed that enhanced surveillance improved reporting of monkeypox in hotspots of LGAs across the priority states <p>Source</p>	Published 25 May 2022
	<ul style="list-style-type: none"> Clinical Presentation Diagnosis Prognosis Treatment 	<ul style="list-style-type: none"> This study retrospectively examined the longitudinal clinical course of monkeypox in the U.K., viral dynamics, and the adverse events of novel antiviral therapies in seven patients who were diagnosed from 2018-2021 	Published 24 May 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • four patients were men and three were women • three acquired monkeypox in the U.K.: one was a healthcare worker, and one was a patient who acquired it abroad and transmitted it to an adult and child in their household • Viraemia, prolonged virus DNA detection in upper respiratory tract swabs, low mood, and PCR-positive deep tissue abscess were some of the disease features • five patients remained in isolation for more than three weeks due to PCR positivity • three patients were treated with brincidofovir (200 mg once a week orally), all developing elevated liver enzymes, which resulted in the stopping of therapy • one patient received Tecovirimat (600 mg twice daily for two weeks orally) and experienced no adverse effects with a shorter duration of viral shedding and illness (10 days of hospitalization) • one patient experienced a mild relapse six weeks after discharge <p>Source</p>	
	<ul style="list-style-type: none"> • Clinical presentation 	<ul style="list-style-type: none"> • A prospective observational study in the Democratic Republic of Congo reported 216 patients who were positive for monkeypox virus <ul style="list-style-type: none"> ○ The study reported three deaths, in addition to fetal death occurring in four of five patients who were pregnant at admission ○ Patients with fatal disease had higher viral DNA in blood, maximum lesion count, and on day of admission ○ Patients with hypoalbuminemia had a high risk of severe disease • The most common complaints were rash (96.8%), malaise (85.2%), sore throat (78.2%), and lymphadenopathy/adenopathy (57.4%) • The most common physical exam findings included monkeypox rash (99.5%), and lymphadenopathy (98.6%) <ul style="list-style-type: none"> ○ Patients under five years of age had the highest lesion count, and primary household cases tended to have higher lesion counts than secondary or later household cases <p>Source</p>	<p>Last updated May 29 2022 (Pre-print)</p>

Type of document	Relevance to question	Key findings	Recency or status
	<ul style="list-style-type: none"> • Epidemiology • Prevention and control 	<ul style="list-style-type: none"> • Among monkeypox cases examined in this study, contact with a person with generalized skin eruption within the past three weeks was reported in 70% of cases <ul style="list-style-type: none"> ○ Recent bushmeat consumption (giant pouched rat, primates, squirrels) was very common (more than 80% of cases) • Enhanced surveillance of monkeypox in Bas-Uélé province in the Democratic Republic of Congo confirmed only 27% of suspected cases as identified through an adapted community case definition, with most cases finally diagnosed as chickenpox <ul style="list-style-type: none"> ○ Rapid field diagnostics should be adopted to optimize worldwide early detection and surveillance of monkeypox <p>Source</p>	Last updated 5 June 2022 (Pre-print)
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Prevention and Control • Clinical Presentation 	<ul style="list-style-type: none"> • The study describes an imported case of monkeypox from Nigeria to the United Kingdom, whereby secondary transmissions occurred within the family to an adult and toddler • After arriving to the U.K., Case 1 developed a vesicular lesion <ul style="list-style-type: none"> ○ By day 19, Case 1 was afebrile, lesions had crusted, and they tested negative for monkeypox by PCR in urine, blood, lesion fluid, and nose/throat swab ○ 19 days after Case 1 symptoms' onset, their 18-month-old child developed lesions ○ 33 days after Case 1 symptoms' onset, an adult member of the family developed a vesicular rash, and had confirmed monkeypox • Contacts of Case 1 included household contacts, healthcare workers, hospital laundry workers, and members of the public <ul style="list-style-type: none"> ○ 30 contacts in Wales were identified for active surveillance as they had direct exposure of broken skin or mucous membranes to a symptomatic patient, and they were contacted daily for 21 days by Public Health Wales to check for symptoms; eight were identified for passive surveillance <p>Source</p>	Published 21 August 2021
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Clinical presentation • Diagnosis 	<ul style="list-style-type: none"> • A suspected monkeypox case was defined as an individual with a vesicular or pustular rash with deep-seated, firm pustules, and ≥ 1 of the following symptoms: fever preceding the eruption, lymphadenopathy (inguinal, axillary, or cervical), or pustules or crusts on the palms of the hands or soles of the feet 	Published 4 June 2021

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • A confirmed monkeypox case requires detection of Orthopoxvirus or monkeypox virus DNA with real-time polymerase chain reaction (PCR) or isolation of monkeypox virus in culture from ≥ 1 specimen • Swab eluates, crust homogenates, or blood from suspected cases were used to test monkeypox infection • Based on data obtained from monkeypox surveillance from 2011–15 in Tshuapa Province, DRC, the study evaluated differences in cumulative incidence, exposure histories, and clinical presentation of laboratory-confirmed monkeypox cases by sex and age groups • The following findings were reported for the period 2011-15: <ul style="list-style-type: none"> ○ The average annual incidence was 14.1 per 100,000 ○ The incidence was higher in male patients except among those 20-29 years old, but females aged 20-29 years also reported a high frequency of exposure (26.2%) to people with monkeypox-like symptoms ○ The highest incidence was among 10-to-19-year-old males, the cohort reporting the highest proportion of animal exposures (37.5%) ○ The incidence was lower among those presumed to have received smallpox vaccination than among those presumed unvaccinated ○ No differences were observed by age group in lesion count or lesion severity score ○ Monkeypox incidence was twice that reported during 1980-85 • In conclusion, the increase in the incidence of monkeypox might be linked to declining immunity provided by smallpox vaccination • The high proportion of cases attributed to human exposures suggests changing exposure patterns <p data-bbox="953 1230 1033 1260">Source</p>	
	<ul style="list-style-type: none"> • Clinical presentation • Prognosis 	<ul style="list-style-type: none"> • This study describes the clinical course and management of 40 hospitalized monkeypox cases during the 2017-18 human monkeypox outbreak in Nigeria using retrospective records 	Published 15 October 2020

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • The most common clinical features observed (in order) included skin rash, fever, lymphadenopathy, genital ulcers, body aches, headache, sore throat, pruritus, and conjunctivitis and photophobia • The most common first symptoms were rash and fever • Twenty-one (52.5%) of 40 cases developed one or more complications including (in order of frequency) secondary bacterial infection, gastroenteritis, sepsis, bronchopneumonia, encephalitis, keratitis, and premature rupture of membrane at 16 weeks' gestation and resultant intrauterine fetal death • Patients with HIV type 1 co-infection were significantly more likely to have larger skin rashes, genital ulcers, secondary bacterial infection, and longer duration of illness • Five (12.5%) of the 40 cases died • Sequelae observed amongst 18 patients discharged from hospital and seen at follow-up included hyperpigmented atrophic scars, patchy alopecia, hypertrophic skin scarring, and contracture/deformity of facial muscles; three of the 18 patients showed complete healing after eight weeks of follow-up <p data-bbox="951 837 1035 862">Source</p>	
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • This study uses historical data from the Democratic Republic of the Congo to estimate the reproduction number (R) and basic reproduction number (R0) of smallpox and monkeypox in a population with imperfect immunity • In the early 1980s, when smallpox vaccination had nearly 100% coverage in the country and the vaccination campaign ended, it was estimated monkeypox had an R value of 0.32 (uncertainty interval (UI): 0.22-0.40) and an R0 value of 2.13 (UI: 1.46-2.67) • With data from 2011-12 that indicate a 60% population immunity against orthopoxvirus species, the R value for monkeypox was calculated to be 0.85 (UI: 0.51-1.25) • The authors propose two theories for how monkeypox could become endemic in the Democratic Republic of the Congo: <ul style="list-style-type: none"> ○ Frequent outbreaks with $R < 1$ may occur due to involuntary human contact with animal reservoirs 	Published 8 July 2020

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> ○ Monkeypox may undergo sustained human-to-human transmission ($R > 1$) ○ In either case, the authors note that repeated circulation in humans favours pathogen evolution and the emergence of human-adapted pathogens ● The authors note that their estimates rely on data for the Democratic Republic of the Congo and may differ for areas with virus clades, societal structures, population densities, and residual orthopoxvirus immunity <p>Source</p>	
	<ul style="list-style-type: none"> ● Epidemiology (including transmission) 	<ul style="list-style-type: none"> ● This study described the transmission of monkeypox virus from an investigation that Public Health England (PHE) conducted of two unrelated cases of monkeypox that affected travellers returning from Nigeria ● A clinical diagnosis of suspected monkeypox was made for the second of these patient cases, and infection prevention and control measures for an infectious disease were implemented, including enhanced personal protective equipment (PPE) consisting of disposable gown, disposable gloves, filtering facepiece of the respirator, and face shield or goggles ● The patient was transferred to an airborne infectious disease treatment centre, and monkeypox was confirmed by PHE ● Transmission may occur through close contact with skin lesions of an infected person, via fomites, or by exposure to large respiratory droplets during face- to-face contact ● Transmission of monkeypox occurred between the second patient to a healthcare worker, and most likely the only exposure risk identified during assessment of the infected healthcare worker was the changing of potentially contaminated bedding, when patient 2 had multiple skin lesions but before a diagnosis of monkeypox had been considered ● It was deemed that the risk to the public is very low as the effective human to human transmission requires close contact with an infected individual or virus-contaminated materials, however, monkeypox is considered a high-consequence infectious disease in England 	Published April 2020

Type of document	Relevance to question	Key findings	Recency or status
	<ul style="list-style-type: none"> • Clinical presentation • Prognosis 	<p>Source</p> <ul style="list-style-type: none"> • This study uses a cross-sectional sample of 223 confirmed cases from a monkeypox surveillance program in the Democratic Republic of the Congo to investigate the association between exposure to rodents and non-human primates with rash severity amongst confirmed cases • Rash severity was classified as either mild (5-100 lesions) or severe (>100 lesions) • Those with confirmed monkeypox tended to be younger, male, and live in forested areas • Hunting of non-human primates was associated with rash severity in both unadjusted and adjusted models (OR= 2.78 (95% CI: 1.18, 6.58)), while exposure to non-human primates was associated with rash severity only in an unadjusted model • There was no association found between rodent exposure and monkeypox rash severity <p>Source</p>	Published 24 December 2019
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Clinical presentation 	<ul style="list-style-type: none"> • This cross-sectional study was conducted in Mfou district, Cameroon one year after a monkeypox outbreak involving captive chimpanzees • The goals of the study were to describe the seroprevalence of orthopoxviruses and explore factors associated with exposure to bushmeat amongst employees of a primate sanctuary and residents of nearby villages • A total of 125 participants were recruited • Forty-three participants (34.4%) were IgG positive for anti-orthopoxvirus antibodies; however, amongst those born after the era of routine smallpox vaccination only four (6.3%) were positive for anti-orthopoxvirus antibodies • These four individuals did not report histories of smallpox-like disease or have contact with sick chimpanzees during the outbreak • The presence of anti-orthopoxvirus antibodies in individuals born after the era of smallpox vaccination suggests the possibility of asymptomatic circulation of an orthopoxvirus (which was most likely monkeypox) in human populations 	Published 25 November 2019

Type of document	Relevance to question	Key findings	Recency or status
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Clinical presentation 	<p>Source</p> <ul style="list-style-type: none"> • This study aimed to describe the clinical and epidemiological features of the 2017 to 2018 human monkeypox outbreak in Nigeria, the largest documented human outbreak of the west African strain of the monkeypox virus • Data was collected with a standardized case investigation form based on a case definition of human monkeypox from previously established guidelines • Diagnosis of the human monkeypox virus infection was confirmed by viral identification with real-time PCR and detection of antibodies • The results showed that 122 confirmed or probable cases of human monkeypox were recorded in 17 states of Nigeria, infecting individuals from the ages of two to 50 years • All patients had rashes on all parts of the body, fever, headaches, and lymphadenopathy • The results suggest endemicity of monkeypox virus in Nigeria, with some evidence of human-to-human transmission <p>Source</p>	Published August 2019
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Prevention and control 	<ul style="list-style-type: none"> • A cross-sectional study was conducted between 25 September and 31 December 2017 to review clinical and laboratory characteristics of all suspected and confirmed cases of human monkeypox identified at Niger Delta University Teaching Hospital, and to appraise its plans, activities and challenges in responding to the outbreak • To respond to the outbreak, the hospital established a make-shift isolation ward for case management by a monkeypox response team and provided infection and control resources • Challenges identified included: some healthcare workers being reluctant to participate in the outbreak with some avoiding suspected patients; stigma and discrimination experienced by patients and their family members; and refusal of isolation • Continued training was offered, and using a collaborative approach among all involved stakeholders addressed some of these challenges and eventually led to successful containment of the outbreak 	Published 17 April 2019

Type of document	Relevance to question	Key findings	Recency or status
	<ul style="list-style-type: none"> • Biology • Epidemiology (including transmission) 	<p>Source</p> <ul style="list-style-type: none"> • The study consisted of an outbreak investigation involving human monkeypox cases from four districts (Impfondo, Betou, Dongou, and Enyelle) in the Likouala department of the Republic of the Congo • Active and retrospective cases were identified and reported by health facilities, patients, and family and community members • Confirmed and suspected monkeypox cases were investigated and data was collected using the Ministry of Health's standardized case report form • The authors of the study investigated 43 suspected human monkeypox cases during the period of 22 March and 5 April in 2017 by interviewing suspected case patients and collecting dried blood strips and vesicular and crust specimens from active lesions, and narrowed the number down to 22 confirmed, probable, and possible cases • The results showed that there were no epidemiologic links between cases from different districts, and all hypothesized human to human transmission events appeared to have been contained within the individual districts • There was no evidence suggesting that the virus was introduced from neighbouring countries • The authors noted some challenges associated with the remote regions of the districts, such as limited health and transportation infrastructure, absence of specimen collection supplies, and a well-functioning cold chain, that would have resulted in inconsistent and incomplete reporting <p>Source</p>	Published February 2019
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Prevention and control 	<ul style="list-style-type: none"> • Three different thresholds to trigger a public-health response to monkeypox were evaluated using surveillance data from Tshuapa Province in the Democratic Republic of Congo from 2011-13 • Three different statistical thresholds were used: Cullen, c-sum, and a World Health Organization (WHO) method based on monthly incidence 	Published 20 December 2018

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • The study concluded that using signals detected by a single method may be inefficient and overly simplistic for triggering public-action for monkeypox • Instead, a response algorithm is proposed which integrates the WHO method as an objective threshold with contextual information about epidemiological and spatiotemporal links between suspected cases • This approach can be used to determine whether routine surveillance, alert status, or outbreak status are needed and can be modified for use in different countries <p>Source</p>	
	<ul style="list-style-type: none"> • Treatment 	<ul style="list-style-type: none"> • While smallpox was eradicated in 1980, the variola virus (VARV) causing smallpox, still exists <ul style="list-style-type: none"> ◦ Tecovirimat is currently developed as an oral smallpox therapy • This study evaluated the efficacy of Tecovirimat in non-human primate (monkeypox) and rabbit (rabbitpox) models, along with a safety trial involving 449 human adults • The minimum dose of Tecovirimat required to achieve >90% survival in the monkeypox model was 10 mg per kilogram of body weight for 14 days, and 40 mg per kilogram in the rabbitpox model • The monkeypox model was more effective in estimating required drug exposure in humans • A dose of 600 mg twice daily for 14 days was used to test in humans, and no troubling adverse events were observed <p>Source</p>	Published 5 July 2018
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Prevention and Control 	<ul style="list-style-type: none"> • The majority of monkeypox cases occurred in the Democratic Republic of the Congo (DRC); however, in the last decade, the number of cases in other African countries have been increasing • Nigeria is currently experiencing the largest outbreak of human monkeypox with 80 confirmed cases • The closer contact between animals and humans through deforestation, climate change, hunting, and population movement might be a factor in the increasing recent cases 	Published 16 March 2018

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • Robust disease surveillance systems with initial and long-term financial and human resource investment are required to stop the further spread of monkeypox <ul style="list-style-type: none"> ○ Currently, no mandatory reporting is required through the Integrated Disease Surveillance and Response system across Africa, but it is recommended ○ Coordination of interventions and routine sharing of information between human and wildlife sectors is necessary because monkeypox is a zoonotic disease 	
	<ul style="list-style-type: none"> • Diagnosis • Prevention and Control • Prognosis • Treatment 	<p>Source</p> <ul style="list-style-type: none"> • This observational study reported on fetal outcomes for one of four pregnant women who participated in an observational study at the General Hospital of Kole (Sankuru Province in the Democratic Republic of Congo), where 222 symptomatic subjects were followed from 2007 to 2011 • Diagnosis: <ul style="list-style-type: none"> ○ Patients meeting the WHO case definition of monkeypox virus infection, which uses clinical findings and history, were enrolled in the study ○ Laboratory confirmation of infection was conducted by polymerase chain reaction (PCR) analysis of blood specimens or samples of other bodily fluids ○ Staff used the WHO clinical severity score based on the number of skin lesions to classify cases of human monkeypox • Prevention, control and Treatment: <ul style="list-style-type: none"> ○ During hospitalization, pregnant women received antibiotics (amoxicillin, chloramphenicol via eye drops, and erythromycin, as well as gentamycin, if necessary) for prevention or control of bacterial superinfection, paracetamol and papaverine were given as analgesics, metronidazole and mebendazole were administered for giardiasis and other intestinal parasitic infections, and quinine as given for malaria • Prognosis: • Three of 4 pregnant women identified as having monkeypox virus Findings of this study confirm that maternal monkeypox virus infection may have adverse consequences for the fetus without apparent correlation with severity of maternal disease 	Published 17 October 2017

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> ○ Further infection experienced fetal demise ● studies should focus on the relatively high risk of fetal demise among pregnant women with monkeypox virus <p>Source</p>	
	<ul style="list-style-type: none"> ● Clinical presentation ● Diagnosis 	<ul style="list-style-type: none"> ● This study used cohort data from 2009 to 2014 from Democratic Republic of Congo to evaluate two surveillance case definitions for monkeypox and clinical characteristics associated with confirmed cases ● The cohort included 333 laboratory confirmed cases of monkeypox, 383 laboratory confirmed varicella zoster virus cases, and 36 cases that were confirmed not to be either of these viruses ● It was found that monkeypox and varicella zoster viruses presented with several of the same signs and symptoms, including key rash characteristics, and identified 12 specific signs/symptoms that are important to look for when investigating monkeypox cases ● The analysis used 12 signs and symptoms that were identified as having high sensitivity and/or specificity values, and found that monkeypox cases with fever before a rash in addition to seven or eight of the other signs and symptoms had a more balanced performance between sensitivity and specificity ● However, a surveillance case definition with more specificity was identified as being needed to be able to document and detect endemic human monkeypox cases, and that laboratory-confirmed diagnosis is needed in the absence of such a definition <p>Source</p>	Published 11 September 2017
	<ul style="list-style-type: none"> ● Biology ● Clinical presentation ● Diagnosis 	<ul style="list-style-type: none"> ● This study used in vivo bioluminescent imaging (BI) to study monkeypox virus infection from Central Africa in laboratory and wild-caught animals by experimentally infecting African wild-caught rope squirrels via intranasal and intradermal exposure ● After infection, the study researchers monitored viral replication and shedding of the monkeypox virus via in vivo BI, viral cultures, and real-time PCR ● The results showed that monkeypox virus infection in African rope squirrels caused mortality and moderate to severe 	Published 21 August 2017

Type of document	Relevance to question	Key findings	Recency or status
		<p>morbidity, with clinical signs including pox lesions in the skin, eyes, mouth and nose</p> <ul style="list-style-type: none"> • Intranasal and intradermal exposures induced high levels of viremia, fast systemic spread, and long periods of viral shedding, in which viral shedding was still detectable after 15 days post-infection • The study shows that rope squirrels shed large quantities of the virus and for long periods, supporting the hypothesis that they play a potential role in monkeypox virus transmission to humans and other animals in the Central African region <p>Source</p>	
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • In this study, a stochastic dynamic transmission model was developed to simulate the potential spread of monkeypox and evaluate containment strategies on a university campus • Results of the model found that detection and isolation of monkeypox cases was key to containment of an outbreak, leading to 33%-85% of secondary infections being averted (depending on the detection rate) • While quarantine of known contacts was found to have little benefit when 50% of cases were detected and isolated, vaccination was found to be a useful strategy when combined with detection and isolation <p>Source</p>	<p>Last updated 9 September 2022 (pre-print)</p>
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • This study describes a method for qualitatively assessing the presence of monkeypox virus DNA in wastewater that was developed in the Netherlands • This study involved taking wastewater samples from five city districts of Amsterdam, two wastewater treatment plants in Amsterdam, and from Amsterdam Schiphol International Airport • Samples were processed and DNA extracted, and the presence of monkeypox DNA was tested for using a real-time PCR assay for generic monkeypox detection as well as an assay specific to the West-African clade <ul style="list-style-type: none"> ○ Samples were deemed monkeypox-positive when both assays yielded a signal resulting in a cycle threshold value 	<p>Published 3 September 2022</p>

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • A total of 108 wastewater sample were collected between 16 May and 3 July 2022 for this study <ul style="list-style-type: none"> ○ Monkeypox DNA was detected in 45 (42%) of these sample ○ The cycle threshold values indicated a relatively low concentration of DNA in the positive samples • Samples from 28 February to 6 March were also tested as negative controls, and no monkeypox DNA could be detected in these samples, confirming the absence of monkeypox in the Netherlands at that time • The authors conclude that this study provides proof of principle that wastewater monitoring can aid with disease surveillance for monkeypox <p>Source</p>	
	<ul style="list-style-type: none"> • Diagnosis 	<ul style="list-style-type: none"> • This study investigates the use of digital monitoring for COVID-19 using commercial wearable devices <ul style="list-style-type: none"> ○ The use of this technology can be extended to monitoring for other infectious diseases for which there are diagnostic test shortages, such as monkeypox ○ Allocating diagnostic tests to individuals identified as being the most likely to test positive allow fewer tests to be used to capture the same number of positive cases • Data from the Covidentify study and the MyPHD study were used, including smartwatch data from 2887 individuals A diagnostic testing decision support model was designed to intelligently allocate diagnostic tests in a surveillance population where there are insufficient tests <ul style="list-style-type: none"> ○ This model used resting heart rate and the number of steps taken as predictors for COVID-19 before the onset of symptoms • This study indicated that resting heart rate features distinguished between COVID-19-positive and -negative cases earlier in the course of the infection than steps features <ul style="list-style-type: none"> ○ Using both these parameters together increases the area under the receiver operating characteristic curve, indicating a greater diagnostic ability 	Published 1 September 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> The predictive value of these parameters varied based on the device type and resolution of the data collected <p>The results of this study suggest that, if deployed on a large scale and without needing self-reported symptoms, the ITA method could improve the allocation of diagnostic testing resources</p> <p>Source</p>	
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> The correlation between monkeypox DNA in infected patients and virus infectivity were evaluated in this study which included 43 specimens from 32 male patients in Israel The study found a strong negative correlation between the sample DNA and virus infectivity, and also that most patients appeared to present higher viral loads in dermal lesion samples than in oropharynx samples <p>Source</p>	Published 1 September 2022
	<ul style="list-style-type: none"> Prevention and control 	<ul style="list-style-type: none"> This study developed a mathematical model to capture the transmission dynamics of the monkeypox outbreak in the U.S., and also to project the impact of urgent diagnostic and vaccination interventions Monkeypox transmission dynamics were retrospectively (prior to 15 July) simulated across six representative states, and notable gaps were found between the estimated and confirmed numbers of cases in these states Modeling also found that the implementation of ring vaccination had a clear coverage-dependent impact on curbing the spread of monkeypox <p>Source</p>	Published 1 September 2022
	<ul style="list-style-type: none"> Biology 	<ul style="list-style-type: none"> The study focused on two monkeypox-infected <i>in vitro</i> models, and found highly expressed genes that play important roles in the progression of monkeypox infection The study contributes to understanding the specific mechanisms to pathophysiology and modes of transmissions <p>Source</p>	Published September 2022
	<ul style="list-style-type: none"> Biology 	<ul style="list-style-type: none"> The study revealed that the B.1 lineage emerged in Europe potentially from surge of cases and the broader transmission globally 	Published September 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> Epidemiological information with genomic surveillance will be important to generate real-time data to implement control measures Source	
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> The study focuses on the presence of monkeypox in anal and urethral swabs of patients in a sexual clinic in Milan The study concludes that this is the first study to find viable monkeypox in these regions among symptomatic and asymptomatic cases, and the possibility of an unconfirmed sexual route of monkeypox virus transmission Source	Published September 2022
	<ul style="list-style-type: none"> Biology 	<ul style="list-style-type: none"> This study investigated the spatio-temporal associations between physical, socio-economic, and socio-cultural risk factors, and annual monkeypox incidence at the health-zone level in the Democratic Republic of Congo Data on monkeypox infections was collected weekly at the health zone from January 2000 to December 2015, in which it underwent data correction to reduce the risk of overestimating monkeypox cases at the health-zone level The study collected the following types of data: population; and environmental, including information on land cover, deforestation, altitude, climate, road network, active bush/forest fire The results show that primary forest, economic well-being, and temperature were positively associated with annual monkeypox virus incidence It was found that physical environmental risk factors alone could not explain the emergence of monkeypox outbreaks in the Democratic Republic of Congo Source	Published 27 August 2022
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> This study investigated 225 polymerase chain reaction (PCR)-confirmed cases of monkeypox in Italy in the monkeypox outbreak of 2022 Estimates indicate that: <ul style="list-style-type: none"> Incubation period of the virus is 9.1 days, with a 95% confidence interval of 6.5 to 10.9 days 	Published 22 August 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> ○ Mean generation time is 12.5 days, with a 95% confidence interval of 7.5 to 17.3 days ○ Reproduction number (Rt) among men who have sex with other men (MSM) of 2.43, with 95% confidence interval of 1.82 to 3.26 	
	<ul style="list-style-type: none"> • Biology • Diagnosis 	<ul style="list-style-type: none"> • This research report demonstrated that monkeypox convalescent donors produced both antibodies and B cells against monkeypox antigens A35R and H3L • Recombinant soluble truncated forms of A35R and H3L can be used in enzyme-linked immunosorbent assay (ELISA) as diagnostic tools for the detection of recently infected monkeypox patients 	Last updated 24 August 2022 (pre-print)
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Prevention and control 	<ul style="list-style-type: none"> • The study aimed to detect monkeypox DNA in the wastewater of an airport in Rome, Italy • Of 20 samples collected, three samples tested positive via real-time PCR and/or by nested PCR, confirming the presence of the virus in the wastewater • This study also shows the feasibility of using wastewater surveillance to efficiently track the introduction and diffusion of the monkeypox virus to improve early warning detection systems 	Last updated 19 August 2022 (pre-print)
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • The weekly growth incidence and the effective reproductive number (Rt) during the introduction of the monkeypox virus in Brazil was calculated using Brazil's case distribution and incidence trend, and Rt, in four states with the highest case reports: Sao Paulo, Rio de Janeiro, Minas Gerais and Goias, which include the Federal District of Brasilia • As of 22 August 2022, 3,896 monkeypox cases were confirmed in Brazil, with weekly incidence increases estimated to be between 37.5% and 82.1% • Reproductive number (Rt) estimates were statistically higher than one in all four states analyzed, with authors hypothesizing that the prolonged infectious period could explain higher Rt values 	Last updated 25 August 2022 (pre-print)

Type of document	Relevance to question	Key findings	Recency or status
	<ul style="list-style-type: none"> Prevention and control 	<ul style="list-style-type: none"> The transmission of monkeypox virus was simulated using Susceptible-Exposed-Infectious-Recovered (SEIR) modelling to assess how effective a vaccination strategy in combination with other public-health measures was in mitigating outbreaks The study found that outbreaks can be controlled well by isolating confirmed cases and vaccinating their close contacts Additionally, post-exposure prophylaxis was found to be more effective for containment amidst summer gatherings compared to a broad vaccination campaign, and restricting attendance through vaccination requirements can help to better secure mass-gathering events <p>Source</p>	Last updated 16 August 2022 (pre-print)
	<ul style="list-style-type: none"> Prevention and control 	<ul style="list-style-type: none"> This study used the findings from a cross-sectional survey to assess and compare perceptions about monkeypox and COVID-19 in Saudi Arabia Of the 1,546 participants, 62.6% reported being more concerned about COVID-19 than monkeypox Approximately half of all participants perceive of monkeypox as a dangerous disease that warrants respiratory and contact precautions With respect to specific concerns regarding monkeypox, 60.4% of participants worried about the progression into a global pandemic, 57.8% worried about infection in themselves or a family member, 23.8% were concerned about a national lockdown, and 15.8% worried about international flight shutdowns Half (50.6%) of all participants were generally in favour of vaccination against monkeypox, but vaccination for certain specific groups (such as immunocompromised individuals and the elderly) was more accepted The following characteristics were associated with higher odds of acceptance of monkeypox vaccination: <ul style="list-style-type: none"> Age younger than 45 Perceiving of monkeypox as dangerous and virulent Having an educational level less than a university degree 	Published 10 August 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> ○ Being worried about themselves or family members contracting monkeypox ○ Being more worried about monkeypox compared to COVID-19 <p>Source</p>	
	<ul style="list-style-type: none"> ● Prevention and control 	<ul style="list-style-type: none"> ● The single study focused on the perceptions of healthcare workers about monkeypox in Saudi Arabia ● In a cross-sectional survey of 1,130 healthcare workers, most people were more worried about COVID-19 than monkeypox, and more than half of the respondents worried about the likelihood of another pandemic ● Most healthcare workers agreed that tighter infection prevention measures should be implemented <p>Source</p>	Last updated 3 August 2022 (pre-print)
	<ul style="list-style-type: none"> ● Biology 	<ul style="list-style-type: none"> ● The study focuses on monkeypox DNA correlations with virus infectivity in clinical samples <p>Source</p>	Last updated 3 August 2022 (pre-print)
	<ul style="list-style-type: none"> ● Biology 	<ul style="list-style-type: none"> ● The study reports that a distinct phylogenetic cluster of monkeypox genomes suggests an early and cryptic spread of the virus <p>Source</p>	Last updated 3 August 2022 (pre-print)
	<ul style="list-style-type: none"> ● Treatment 	<ul style="list-style-type: none"> ● The study describes the potential anti-monkeypox virus activity of atovaquone, mefloquine, and molnupiravir, and their potential use as treatments <p>Source</p>	Last updated 2 August 2022 (pre-print)
	<ul style="list-style-type: none"> ● Biology 	<ul style="list-style-type: none"> ● The study describes genetic variability, including gene duplication and deletion, in early sequences from the 2022 European monkeypox outbreak <p>Source</p>	Last updated 25 July 2022 (pre-print)
	<ul style="list-style-type: none"> ● Biology 	<ul style="list-style-type: none"> ● In this study, a new metagenomic sequencing approach for extraction and enrichment of monkeypox (monkeypox virus) DNA was evaluated ● Results of the study showed a very significant improvement in efficiency of sequencing, number of reads, depth of coverage, and the trustworthiness of consensus sequencing 	Last updated 31 July 2022 (Pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • Specifically, when comparing the original read counts with the final quality controlled read counts, the monkeypox virus DNA metagenomic enrichment approach kept around 50% of the reads, while the non-enrichment method kept 2-7 % • These results show that using the new sequencing approach allows for more samples to be processed and reduces time and costs to diagnosis <p>Source</p>	
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Clinical presentation 	<ul style="list-style-type: none"> • This study uses the Zeno SWATH MS to study the plasma proteome of a group of monkeypox patients with a similar infection history and clinical severity • The study population includes five patients with PCR-confirmed monkeypox virus infection <ul style="list-style-type: none"> ○ All patients identified as men having sex with men and had practiced receptive anal sexual intercourse within 14 days prior to hospitalization ○ Additionally, all patients had attended the same social event 10-14 days before developing symptoms, three of whom considered it most likely to have been infected on that occasion • Proteomic measurements were performed on days one to three after admission to the hospital <ul style="list-style-type: none"> ○ The proteomes of monkeypox patients were compared to those of healthy volunteers and COVID-19 patients • This study found a correlation between plasma protein markers and disease severity, approximated by the degree of skin manifestation <ul style="list-style-type: none"> ○ All monkeypox patients exhibited mild to moderate symptoms ○ The data collected in this study showed increased levels of specific acute phase proteins and overall lower nutritional response proteins compared to healthy controls ○ This study found a range of similarities and differences between the host response in monkeypox and COVID-19 infection 	Last updated 29 July 2022 (Pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> This study demonstrates the utility of proteomics in analyzing rare diseases This study indicated that the partial overlap between monkeypox and COVID-19 host response proteins could allow the repurposing of a clinically applicable COVID-19 biomarker panel assay, resulting in the successful classification of monkeypox patients <p>Source</p>	
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> This study quantified the population of men who have sex with men (gbMSM) in North Carolina where 20 cases of monkeypox had been identified as of 19 July 2022 The study also estimated the proportion of those with more than one sexual partners per year Data from the 2015-16 National Health and Nutrition Examination Survey (NHANES) was used to determine that 1.9% of the US male population identify as gbMSM and an estimated 65,100 men in North Carolina identify as gbMSM Of those men, the study estimated that 15,700 had more than one sexual partner in the last year These findings suggest that vaccines should be offered to, at a minimum, 15,700 sexually active gbMSM in North Carolina to reduce the risk of monkeypox infection <p>Source</p>	Last updated 21 July 2022 (Pre-print)
	<ul style="list-style-type: none"> Biology 	<ul style="list-style-type: none"> This study evaluates the performance and added value of the MinION real-time TGS sequencing device for sequencing the complete genome of a monkeypox virus strain, obtained from a pustular lesion in a remote area of Central Africa MinION sequencing has been used to study other epidemics and it has helped link congenital malformations to the Zika virus A total of 146,920 raw reads were obtained with sizes ranging from 66 bp to 68 kb for a median of 1946 bp It was concluded that the data obtained from directly sequencing DNA extracted from a lesion is sufficient to complete the genome of the virus <p>Source</p>	Published 24 June 2022

Type of document	Relevance to question	Key findings	Recency or status
	<ul style="list-style-type: none"> Epidemiology (including transmission) Prevention and control 	<ul style="list-style-type: none"> This study used a mathematical modelling framework that has been applied to investigate the transmission of measles, Ebola, and SARS-CoV-2 to model the monkeypox virus outbreak in a simulated population of 50 million people with socio-economic and demographic characteristics typical of a high-income European country The study's findings align with the World Health Organization's current assessment that the overall public-health risk at a global level for the monkeypox virus is "moderate" <p>Source</p>	Last updated 31 May 2022 (pre-print)
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> This study aims to explain the research gaps on the virus epidemiology in endemic countries and present hypotheses for the recent increase of outbreaks in West Africa, and other non-endemic regions such as Europe, America, and Australia <p>Source</p>	Published 28 May 2022
	<ul style="list-style-type: none"> Epidemiology (including transmission) Prevention and control Treatment 	<ul style="list-style-type: none"> Imported monkeypox from international traveller, Maryland, U.S., 2021 <p>Source</p>	Published May 2022
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> Exportation of monkeypox virus from the African continent <p>Source</p>	Published 19 April 2022
	<ul style="list-style-type: none"> Biology Epidemiology (including transmission) Prevention and control 	<ul style="list-style-type: none"> Monkeypox in a traveller returning from Nigeria - Dallas, Texas, July 2021 <p>Source</p>	Published 8 April 2022
	<ul style="list-style-type: none"> Treatment 	<ul style="list-style-type: none"> New methylene blue derivatives suggest novel anti-orthopoxviral strategies <p>Source</p>	Published July 2021
	<ul style="list-style-type: none"> Biology 	<ul style="list-style-type: none"> Genomic history of human monkey pox infections in the Central African Republic from 2001 to 2018 <p>Source</p>	Published 22 June 2021
	<ul style="list-style-type: none"> Epidemiology (including transmission) 	<ul style="list-style-type: none"> Re-emergence of human monkeypox and declining population immunity in the context of urbanization, Nigeria, 2017-20 <p>Source</p>	Published April 2021
	<ul style="list-style-type: none"> Epidemiology (including transmission) Clinical presentation Diagnosis 	<ul style="list-style-type: none"> Human monkeypox virus infection in plateau state, north central Nigeria: a report of two cases <p>Source</p>	Published 30 December 2021

Type of document	Relevance to question	Key findings	Recency or status
	<ul style="list-style-type: none"> • Prognosis • Treatment 		
	<ul style="list-style-type: none"> • Diagnosis 	<ul style="list-style-type: none"> • CRISPR/Cas9 as an antiviral against orthopoxviruses using an AAV vector Source	Published 9 November 2020
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • Imported monkeypox, Singapore Source	Published August 2020
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • Assessment of media reportage of monkeypox in southern Nigeria Source	Published January 2020
	<ul style="list-style-type: none"> • Biology • Epidemiology (including transmission) • Clinical presentation 	<ul style="list-style-type: none"> • Monkeypox virus emergence in wild chimpanzees reveals distinct clinical outcomes and viral diversity Source	Published July 2020
	<ul style="list-style-type: none"> • Biology 	<ul style="list-style-type: none"> • Comparison of multiplexed immunofluorescence imaging to chromogenic immunohistochemistry of skin biomarkers in response to monkeypox virus infection 	Published 23 July 2020
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • Confidence in managing human monkeypox cases in Asia: A cross-sectional survey among general practitioners in Indonesia Source	Published June 2020
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • Knowledge of human monkeypox viral infection among general practitioners: a cross-sectional study in Indonesia Source	Published March 2020
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • Use of surveillance outbreak response management and analysis system for human monkeypox outbreak, Nigeria, 2017-19 Source	Published February 2020
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • Co-administration of Tecovirimat and ACAM2000™ in non-human primates: Effect of Tecovirimat treatment on ACAM2000 immunogenicity and efficacy versus lethal monkeypox virus challenge Source	Published 16 January 2020
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • Do monkeypox exposures vary by ethnicity? Comparison of Aka and Bantu suspected monkeypox cases Source	Published January 2020
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • Temporal and spatial dynamics of monkeypox in democratic republic of Congo, 2000-2015 	Published September 2019

Type of document	Relevance to question	Key findings	Recency or status
		Source	
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Clinical presentation • Diagnosis 	<ul style="list-style-type: none"> • Human monkeypox in Sierra Leone after 44-year absence of reported cases Source	Published May 2019
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Treatment 	<ul style="list-style-type: none"> • Intrafamily transmission of monkeypox virus, Central African Republic, 2018 Source	Published August 2019
	<ul style="list-style-type: none"> • Diagnosis 	<ul style="list-style-type: none"> • Recombinase polymerase amplification assay for rapid detection of Monkeypox virus Source	Published September 2019
	<ul style="list-style-type: none"> • Biology • Diagnosis 	<ul style="list-style-type: none"> • Molecular evidence of human monkeypox virus infection, Sierra Leone Source	Published June 2019
	<ul style="list-style-type: none"> • Biology • Epidemiology (including transmission) • Clinical presentation 	<ul style="list-style-type: none"> • Diagnosis of imported monkeypox, Israel, 2018 Source	Published May 2019
	<ul style="list-style-type: none"> • Diagnosis 	<ul style="list-style-type: none"> • Preliminary screening and in vitro confirmation of orthopoxvirus antivirals Source	Published 2019
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Prevention and control 	<ul style="list-style-type: none"> • Two cases of monkeypox imported to the United Kingdom, September 2018 Source	Published September 2018
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • Investigation of an outbreak of monkeypox in an area occupied by armed groups, Central African Republic Source	Published June 2018
	<ul style="list-style-type: none"> • Diagnosis 	<ul style="list-style-type: none"> • Intranasal monkeypox marmoset model: Prophylactic antibody treatment provides benefit against severe monkeypox virus disease Source	Published 21 June 2018
	<ul style="list-style-type: none"> • Biology • 	<ul style="list-style-type: none"> • Genomic characterization of human monkeypox virus in Nigeria Source	Published March 2018
	<ul style="list-style-type: none"> • Clinical presentation 	<ul style="list-style-type: none"> • Improving the care and treatment of monkeypox patients in low-resource settings: applying evidence from contemporary biomedical and smallpox biodefense research Source	Published 12 December 2017

Type of document	Relevance to question	Key findings	Recency or status
	<ul style="list-style-type: none"> • Diagnosis 	<ul style="list-style-type: none"> • Validation of a pan-orthopox real-time PCR assay for the detection and quantification of viral genomes from non-human primate blood <p>Source</p>	Published 3 November 2017
	<ul style="list-style-type: none"> • Biology • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • Assessing monkeypox virus prevalence in small mammals at the human-animal interface in the Democratic Republic of the Congo <p>Source</p>	Published 3 October 2017
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • Varicella co-infection in patients with active monkeypox in the Democratic Republic of the Congo <p>Source</p>	Published September 2017
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • A single vaccination of non-human primates with highly attenuated smallpox vaccine, lc16m8, provides long-term protection against monkeypox <p>Source</p>	Published 24 July 2017
	<ul style="list-style-type: none"> • Biology 	<ul style="list-style-type: none"> • Monkeypox virus host factor screen using haploid cells identifies essential role of GARP complex in extracellular virus formation <p>Source</p>	Published 12 May 2017
	<ul style="list-style-type: none"> • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • Presumptive risk factors for monkeypox in rural communities in the Democratic Republic of the Congo <p>Source</p>	Published 13 February 2017
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • Awareness and preparedness of human monkeypox outbreak among university student: Time to worry or one to ignore? <p>Source</p>	Published September 2022
	<ul style="list-style-type: none"> • Diagnostics 	<ul style="list-style-type: none"> • Rapid and reliable inactivation protocols for the diagnostics of emerging viruses: The example of SARS-CoV-2 and monkeypox virus <p>Source</p>	Published 11 September 2022
	<ul style="list-style-type: none"> • Biology 	<ul style="list-style-type: none"> • Just saiyen: Tail-trimming human monkeypox virus assemblies emphasizes resolvable regions in inverted terminal repeats to improve the resolution of reference and production genomes for genomic surveillance <p>Source</p>	Last updated 9 September 2022 (Pre-Print)
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Prevention and control 	<ul style="list-style-type: none"> • This study describes six cases of patients diagnosed with monkeypox and had a history of vaccination against smallpox before the current global outbreak 	Published 22 Aug 2022

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> • All patients were men aged 44 to 64, four of which were either asymptomatic or had very mild symptoms, one of which complained about a fever and had a single pustule, and another with fatigue, malaise, headache, diarrhea, fever, and asynchronous itching pustular-annular lesions in the genital and perianal areas that spread to arms, back and mouth • All patients recovered without further complications and the authors state that their case descriptions add to data evaluating the potential efficacy of smallpox vaccination, suggesting that it may reduce symptom severity, result in more localized manifestations, and result in a milder clinical course <p>Source</p>	
	<ul style="list-style-type: none"> • Biology • Epidemiology (including transmission) 	<ul style="list-style-type: none"> • This study investigated the presence of monkeypox virus genome in the sewer sheds in Paris, France, and to date the emergence of the virus • 16 sewer sheds in Paris receive weekly sampling for the past two years, in which the first detection of the monkeypox virus genome occurred in the wastewater on 23 May 2022 in three different sewer sheds • This timeline correlated temporally with the identification of the first case of infection in Paris, France • Genome detection in sewer sheds covering other areas through the following weeks could suggest that other cases might have existed and not been diagnosed yet when first human cases were identified <p>Source</p>	Last updated 19 August 2022 (pre-print)
	<ul style="list-style-type: none"> • Treatment 	<ul style="list-style-type: none"> • Virtual screening and molecular dynamics were utilized to explore the potential of repurposing multiple drugs against monkeypox that have been previously approved by U.S. Food and Drug Administration (FDA) or other jurisdictions for other applications • High protein similarity was observed throughout poxvirus targets for bindings sites in general: <ul style="list-style-type: none"> ○ NMCT and rutaecarpine ○ Nilotinib ○ Simeprevir 	Last updated 18 August 2022 (pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		<ul style="list-style-type: none"> ○ Hypericin and Naldemedine ○ Fosdagrocorat and Lixivaptan Source	
	<ul style="list-style-type: none"> • Biology 	<ul style="list-style-type: none"> • A pair formation model was used to describe scenarios under which the monkeypox virus can spread, and estimate the reproduction number of human monkeypox to be approximately 2.3 using global and Canadian data Source	Last updated 18 August 2022 (pre-print)
	<ul style="list-style-type: none"> • Clinical presentation 	<ul style="list-style-type: none"> • The study describes the characteristics of hospitalization for monkeypox in Milan, Italy Source	Published 4 August 2022
	<ul style="list-style-type: none"> • Treatment 	<ul style="list-style-type: none"> • Pharmacokinetics and efficacy of a potential smallpox therapeutic, Brincidofovir, in a lethal monkeypox virus animal model Source	Published 3 February 2021
	<ul style="list-style-type: none"> • Epidemiology (including transmission) • Clinical presentation 	<ul style="list-style-type: none"> • A tale of two viruses: co-infections of monkeypox and varicella zoster virus in the Democratic Republic of Congo Source	Published 7 December 2020
	<ul style="list-style-type: none"> • Prevention and control 	<ul style="list-style-type: none"> • Acceptance and willingness to pay for a hypothetical vaccine against monkeypox viral infection among frontline physicians: A cross-sectional study in Indonesia Source	Published 7 October 2020
	<ul style="list-style-type: none"> • Biology 	<ul style="list-style-type: none"> • Analgesia during monkeypox virus experimental challenge studies in prairie dogs (<i>Cynomys ludovicianus</i>) Source	Published 1 July 2019
	<ul style="list-style-type: none"> • Biology 	<ul style="list-style-type: none"> • Characterization of monkeypox virus dissemination in the black-tailed prairie dog (<i>Cynomys ludovicianus</i>) through in vivo bioluminescent imaging Source	Published 26 September 2019
	<ul style="list-style-type: none"> • Biology 	<ul style="list-style-type: none"> • Monkeypox virus phylogenetic similarities between a human case detected in Cameroon in 2018 and the 2017-18 outbreak in Nigeria Source	Published April 2019
	<ul style="list-style-type: none"> • Treatment 	<ul style="list-style-type: none"> • Effects of treatment delay on efficacy of Tecovirimat following lethal aerosol monkeypox virus challenge in cynomolgus macaques 	Published 22 September 2022

Type of document	Relevance to question	Key findings	Recency or status
		Source	
	<ul style="list-style-type: none"> • Diagnosis 	<ul style="list-style-type: none"> • Evaluation of the GeneXpert for human monkeypox diagnosis Source	Published 8 February 2017
	<ul style="list-style-type: none"> • Treatment 	<ul style="list-style-type: none"> • Using the ground squirrel (marmota bobak) as an animal model to assess monkeypox drug efficacy Source	Published February 2017

Appendix 3: Documents excluded at the final stages of reviewing

Type of document	Hyperlinked title
Guidelines	
Full systematic reviews	The virology of human monkeypox virus (hMPXV): A brief overview Human monkeypox: A review of the literature Neurologic complications of smallpox and monkeypox: A review Diagnosis and management of monkeypox: A review for the emergency clinician Diagnosis of monkeypox virus – An overview
Rapid reviews	
Non-systematic reviews	
Protocols for reviews that are already underway	
Titles and questions for reviews being planned	
Single studies	The clinical spectrum of human monkeypox: An Italian single-center case series Reemergence of monkeypox: Prevention and management Orthopox viruses and the safety margins of solvent-detergent treated plasma-derived medicinal products Sexually-transmitted monkeypox: Report of two cases Global online public interest in monkeypox compared with COVID-19: Google trends in 2022 Is there any evidence for milder courses of monkeypox virus infections with childhood smallpox vaccination? Monkeypox virus transmission to healthcare worker through needlestick injury, Brazil Proposal of the French HIV Society on the CD4 threshold below which patients living with HIV who wish to be vaccinated against Monkeypox should receive a 3-dose regimen Atypical oral presentation of monkeypox virus: A report of two cases from Florence, Italy

[Monkeypox in patient immunized with ACAM2000 smallpox vaccine during 2022 outbreak](#)

[Atypical presentation of sexually-transmitted monkeypox lesions](#)

[Coinfection of syphilis and monkeypox in HIV positive man in Prague, Czech Republic](#)

[Concern over monkeypox outbreak: What can we learn from the top 100 highly cited articles in monkeypox research?](#)

[Dynamics of SARS-CoV-2 seroassay sensitivity: A systematic review and modelling study](#)

[Efficacy of biocidal agents and disinfectants against the monkeypox virus and other orthopoxviruses](#)

[Efficacy of heat against the vaccinia virus, variola virus and monkeypox virus](#)

[Endoscopic and histologic assessment of monkey pox-associated proctitis](#)

[Enhanced surveillance of monkeypox in Bas-Uélé, Democratic Republic of Congo: The limitations of symptom-based case definitions](#)

[First report of monkeypox in a patient living with HIV from Romania](#)

[Human monkeypox virus infection in an immunocompromised man: Trial with tecovirimat](#)

[Infectious proctitis due to human monkeypox](#)

[Infectious proctitis due to human monkeypox](#)

[Monkeypox and the safety of the blood supply](#)

[Monkeypox infection and bacterial cellulitis: A complication to look for](#)

[Monkeypox infection during pregnancy: European registry to quantify maternal and fetal risks](#)

[Monkeypox virus: A novel sexually transmitted disease? A case report from France](#)

[Monkeypox, severe hepatitis a, and syphilis in an HIV returning traveler from Spain to Romania](#)

[New challenges in human monkeypox outside Africa: A review and case report from Italy](#)

	<p><u>Projected burden and duration of the 2022 monkeypox outbreaks in non-endemic countries</u></p> <p><u>Recently spreading human monkeypox virus infection and its transmission during COVID-19 pandemic period: A travelers' prospective</u></p> <p><u>Severe disseminated clinical presentation of monkeypox virus infection in an immunosuppressed patient: First death report in Brazil</u></p> <p><u>Syphilis and monkeypox co-infection: Coincidence, synergy or asymptomatic carriage?</u></p> <p><u>The roles of unrecognized monkeypox cases, contact isolation and vaccination in determining epidemic size in Belgium. A modelling study</u></p> <p><u>Unilesional monkeypox: A report of two cases from Italy</u></p> <p><u>Vaccination for monkeypox prevention in persons with high-risk sexual behaviours to control on-going outbreak of monkeypox virus clade 3</u></p>
Other types of documents	

Appendix 4: Experiences in other countries related to available evidence about monkeypox [yellow highlights = newly added or revised content in this version of the living evidence profile]

Country	Summary of experiences
Australia	<p>Biology</p> <ul style="list-style-type: none"> The government of Australia characterizes monkeypox as a viral zoonotic self-limited disease with symptoms lasting two to four weeks <p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> As of 11 October 2022, the government of Australia has reported 138 confirmed and probable cases of monkeypox, including 68 in Victoria, 53 in New South Wales, seven in Western Australia, five in Queensland, three in the Australian Capital Territory, and two in South Australia The government of Australia indicates that human-to-human transmission can occur through close contact with large lesions on the skin typically around the head and neck, body fluids (including respiratory droplets), and contaminated materials <ul style="list-style-type: none"> The government of Australia noted that transmission can likely occur between sexual partners due to intimate contact with infectious skin lesions The government of Australia indicates that the virus can also pass to the fetus via the placenta during pregnancy <p>Prevention and control</p> <ul style="list-style-type: none"> Two vaccines are available in Australia for the prevention of monkeypox, which are the 3rd generation JYNNEOS and the 2nd generation ACAM2000 <ul style="list-style-type: none"> Limited supplies of the 3rd generation Jynneos have been secured by the Commonwealth and some States and Territories Jynneos is administered in a 2-dose schedule by subcutaneous injection with a minimum dose interval between doses of 28 days Jynneos is associated with fewer potential adverse events and is safe to use in people with immunocompromise or atopic dermatitis Jynneos has not been studied in pregnant or breastfeeding women, however, there are no expected safety concerns Jynneos is considered safe for people living with HIV, however, a lower immune response is expected Common side effects include local injection site reactions, muscle aches, headache, fatigue, nausea and chills Jynneos is the preferred vaccine for both pre-exposure prophylaxis and post-exposure prophylaxis Key risk groups recommended by the Australian Technical Advisory Group on Immunization to receive vaccination are: those who have had a high risk of monkeypox contact in the past 14 days; gay, bisexual and other men who have sex with men; those living with HIV; those with a recent history of multiple sexual partners, participating in group sex, or attending sex on premises venues; sex workers; those in risk categories planning to travel to a country experiencing a significant outbreak; and immunization providers who are administering the ACAM2000 smallpox vaccine On 26 July 2022, Australia’s Chief Medical Officer, Professor Paul Kelly, declared the monkeypox (MPX) situation a Communicable Disease Incident of National Significance The government of Australia indicated that they have a vaccine available (in addition to treatments) and provided clinical guidance <ul style="list-style-type: none"> ACAM2000TM (smallpox vaccine) is available to be used for PEP (e.g., healthcare workers, household contacts, or contacts in other settings) and PrEP (e.g., healthcare workers, laboratory worker), but cannot be used in individuals with severely immunocompromised conditions, people who are pregnant, people with active eczema or other active skin conditions, people with allergies, and children under 12 months

- Individuals who have received a smallpox vaccine in the past are not recommended to be revaccinated with ACAM2000
 - The effectiveness of smallpox vaccine against monkeypox (PrEP) is 80.7% with limited available evidence on duration of protection and effectiveness of the vaccine used as PEP
 - ACAM2000™ is associated with a risk of myopericarditis, with other reported serious adverse events such as eczema vaccinatum, generalized vaccinia, progressive vaccinia, fetal vaccinia, neurological adverse events
 - ACAM2000 cannot be used for those living with HIV, or those who are pregnant or breastfeeding
 - ACAM2000 is not suitable for severely immunocompromised people, people who are pregnant or breastfeeding, people with cardiac disease or cardiac risk factors, people with active eczema, or infants below 12 months of age
 - Vaccination side effects include a small bump at the vaccination site, possible permanent scar around the vaccination site, and the need for wound care around the vaccination site
 - Following vaccination, people who receive ACAM2000 should avoid contact with other people at risk of serious adverse events, avoid blood and organ donation for at least 30 days, and avoid getting pregnant for 28 days
 - The [government of Australia](#) recommends medical advice for those who have recently traveled overseas or in contact with a case in Australia
 - The [New South Wales government](#) expects to receive up to 30,000 vaccine doses at the end of September and 70,000 doses in early 2023
 - The [New South Wales government](#) recommends the following prevention measures: 1) self-isolation until rash is fully resolved; 2) proper hand hygiene; 3) use of PPE around people infected with monkeypox; and 4) avoid contact with materials from a person infected with monkeypox (e.g., bedding)
 - People who have recently returned from overseas and have attended large parties or sex on premises venues are advised to monitor themselves for symptoms.
 - Health care professionals are to notify the local public health unit immediately of any suspected cases. Public health units will initiate a public health investigation, contact tracing, and control measures
 - On 1 June 2022, monkeypox became a [nationally notifiable disease](#) for six months
 - The government of Australia has convened national expert groups to develop treatment and vaccine guidelines
 - On 3 June 2022, the [government of Australia](#) released a public video to answer top three questions about monkeypox
 - [Health Direct Australia](#) recommends vaccinations within 4 days of having close contacts with a person infected with monkeypox. Vaccination is indicated to be 85% effective in preventing monkeypox.
 - Practicing good hand hygiene, self isolating, refraining from sexual activity, and using condoms for 8-12 weeks after recovery are suggested
 - The [New South Wales government](#) began vaccinating people at highest risk from monkeypox from 8 August 2022 using the Jynneos vaccine
 - 30,000 further doses of the Jynneos vaccine are expected at the end of September and 70,000 doses are expected in early 2023
- Clinical presentation**
- A recent [Eurosurveillance case report](#) described a case of MPX infection in an individual returning from Europe
 - The individual reported a genital rash, followed by a fever and lymphadenopathy, which then led to diffuse rash with few lesions present on the face and extremities

	<ul style="list-style-type: none"> ○ The individual was admitted to the hospital and managed with contact and airborne precautions in a single room with negative pressure ventilation ○ The case report concluded that normal CD4+ T-cell count and suppressed HIV viral load on antiretroviral therapy were potential important factors in preventing more severe outcomes ● The government of Australia indicates that the incubation period is between six to 13 days <ul style="list-style-type: none"> ○ Symptoms during one to five days include fever, rash, and swelling of lymph nodes ○ A rash usually occurs within one to three days around the face, arms, and legs in appearance of a fever ● The New South Wales government indicates that symptoms usually begin 7-14 days after exposure and can last between 5 to 21 days ● Health Direct Australia indicates that complications can include secondary infections, pneumonia, sepsis, encephalitis and eye infection <p>Diagnosis</p> <ul style="list-style-type: none"> ● The government of Australia indicates that monkeypox is confirmed with laboratory testing and clinical assessment <p>Treatment</p> <ul style="list-style-type: none"> ● The New South Wales government described that the disease is mild, but some patients may need pain medication, intravenous fluids, and viral medications for severe cases ● The government of Australia indicates that there are two therapeutic options for monkeypox: tecovirimat and vaccinia immunoglobulin <ul style="list-style-type: none"> ○ Tecovirimat has been shown to be well tolerated and active in vitro against orthopoxviruses, however, its use has not been approved for the treatment of monkeypox ○ Vaccinia immunoglobulin can be used alone or in combination with antivirals for the treatment of vaccinia-related complications
Belgium	<p>Biology</p> <ul style="list-style-type: none"> ● Monkeypox is zoonotic disease caused by an orthopoxvirus <p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> ● As of 12 October 2022, Belgium has reported a total of 779 monkeypox cases and one death within the country ● An individual may be infected with monkeypox if they come into contact with bodily fluids, mucous membranes, saliva droplets, and contaminated surfaces (e.g., bedding, towels, linen) of an infected individual ● Transmission of monkeypox can also occur from infected animals through direct contact with blood or a bite ● Researchers at the University of Antwerp and Institute of Tropical Medicine (ITM) reported nearly a full genome of a Belgium male who tested positive for monkeypox and found that this case was linked to the monkeypox outbreak in Portugal ● ITM is conducting a study to investigate “asymptomatic shedding” and the risk of monkeypox infection <p>Prevention and control</p> <ul style="list-style-type: none"> ● Belgium was the first country to announce a mandatory 21-day quarantine period for individuals infected with monkeypox ● Imvanex and Jynneos vaccines are currently the only ones to have received regulatory approval for monkeypox <ul style="list-style-type: none"> ○ A initial dose of the Jynneos vaccine is the primary vaccination method being used for the public; a second dose for those previously vaccinated will be scheduled towards the end of the calendar year (i.e., postponed for up to eight months based on the recommendation from the Superior Health Council) ● On 1 September 2022, ITM announced that moving forward, they will be administering monkeypox vaccines intradermally through a micro-dosing technique; this economical process will enable 2.5x more vaccines to be given to those at risk

	<ul style="list-style-type: none"> ○ Intradermal administration will be carried out in a two-dose regimen, with the second dose administered 28 days after the first ○ Immunocompromised individuals will continue to receive subcutaneous administrations of the monkeypox vaccine at a 28-day interval ○ ITM is planning on conducting a study to examine the effectiveness of the intradermal administration of the monkeypox vaccine ● Given the limited supply and availability of monkeypox vaccines, the first phase of the vaccination campaign is focused solely on vaccinating those on an invitational basis (e.g., male and transgender sex workers; men who have sex with men and are HIV positive or are taking pre-exposure prophylaxis and have had at least two sexually transmitted infections in the last year; at-risk individuals, including those with immune disorders or those at high-risk contact and increased risk of infection) or through referrals from their specialist <ul style="list-style-type: none"> ○ The second phase of the campaign, which focuses on prevention, has commenced, and allows individuals with two sexually transmitted infections in the last year, laboratory staff treating virus samples, and women who take pre-exposure prophylaxis to all be eligible for vaccinations ○ As of 23 September 2022, the vaccine eligibility criteria have expanded and now permit individuals without a STI diagnosis in the last 12 months to be eligible for monkeypox vaccination ● Future stages of the vaccination campaign (i.e., eligibility criteria expansion and second dose delivery) are expected to occur once there is an increase in vaccine delivery to Belgium (an estimated 30,000 doses), which is expected to take place by November 2022 ● On 8 September 2022, researchers at ITM released four recommendations to help slow the spread of the monkeypox outbreak, which include: <ul style="list-style-type: none"> ○ Recognizing that certain individuals with monkeypox may be asymptomatic; ○ Having widespread and accessible treatment for at-risk individuals; ○ More robust and intensive contact tracing processes; and ○ Increased vaccinations for the public <p>Clinical presentation</p> <ul style="list-style-type: none"> ● The most common symptoms that appear after infection are fever, muscle aches, and a headache, which are usually followed by skin lesions (blisters and lumps) appearing over the entire body ● Rashes on the palms of the hands and soles of the feet are a characteristic of the disease ● ITM researchers identified three positive samples of monkeypox within asymptomatic patients who were initially testing for sexually transmitted infections (e.g., gonorrhea and chlamydia) <p>Diagnosis</p> <ul style="list-style-type: none"> ● ITM, which is located in Antwerp, Belgium, has been permitted to conduct polymerase chain reaction (PCR) tests to detect monkeypox, and to use samples of the vesicles and scabs on the skin for analysis <p>Prognosis</p> <ul style="list-style-type: none"> ● The incubation period is typically between six and 13 days but it can range anywhere from five to 21 days ● The disease is usually mild, with the illness lasting two to four weeks in length <p>Treatment</p> <ul style="list-style-type: none"> ● Currently, there are no approved treatments for monkeypox, however, individuals typically recover on their own after a few weeks
France	<p>Biology</p> <ul style="list-style-type: none"> ● Monkeypox is a rare viral infectious disease caused by an orthopoxvirus <p>Epidemiology (including transmission)</p>

- As of **12 October 2022**, there have been **4,064 confirmed cases** of monkeypox in France; **91 of these cases have since required hospitalization**
- Among the new cases reported on **8 September 2022**, 73 monkeypox cases were detected in females and nine were reported in children
- The primary [mode of disease transmission](#) is from rodent-to-human, however, it can also be transmitted from human-to-human through direct contact with skin lesions, mucous membranes, respiratory droplets (which require prolonged face-to-face contact), and contaminated surface environments (e.g., bedding, clothes, dishes, and linen) of infected individuals

Prevention and control

- Currently, it is recommended that infected individuals complete a [full isolation period of three weeks](#) until the disappearance of all the scabs
- The infected individual is [contagious](#) upon the appearance of their first symptom(s)
- On 24 May 2022, the French National Authority for Health released a [recommendation](#) to launch their targeted vaccination strategy to help reduce the transmission of the monkeypox virus
 - This will include vaccinations for at-risk adults (e.g., exposed healthcare professionals) who have been in contact with infected individuals
 - Vaccinations should occur within the first two weeks of exposure (ideally within the first four days), using a two-dose regimen that are given 28 days apart from each other
 - The vaccine regimen is to be increased to three doses for immunocompromised individuals
- The French National Authority for Health published a [press release](#) outlining their vaccine strategy for two population groups: 1) those who have been vaccinated against smallpox in their childhood; and 2) children.
 - The recommendation involves a single vaccine dose for at-risk contacts who have been vaccinated against smallpox prior to 1980, and stated that vaccination of minors is to be considered on a case-by-case basis by a specialist who will do a robust assessment of the benefits and risks
- On 8 July 2022, the [High Authority of Health](#) expanded their existing vaccination [eligibility criteria](#), allowing the following groups to receive the monkeypox vaccine:
 - professionals working in places of sexual consumption
 - sex workers
 - men who have sex with men, and have multiple sex partners
 - transgender people with multiple sex partners
- On 25 July 2022, a digital campaign on [preventive vaccinations](#) began, with a recommendation that vaccines first be offered to the most exposed
 - As of **11 October 2022**, **168,000+ doses** have been delivered by the agency to the territories
 - As of **10 October 2022**, **120,128 doses** have been administered to those at risk across the country
 - [Vaccination centers](#) have started operating at the regional level through Regional Health Agencies, with more to open in the coming weeks
- **On 11 October 2022**, the High Authority of Health finalized the last of its recommendations regarding monkeypox vaccines:
 - The previous recommendation that both doses be administered within a 28–35-day interval is still in effect; however, they now **acknowledge that the second dose can be postponed should shortages in supply arise**

	<ul style="list-style-type: none"> ○ If an individual contracts monkeypox after administration of the first dose, the administration of a second dose is not necessary given the natural immunity conferred by infection ○ A recommendation has been put forth to include women who are occasional partners of, or live with at-risk men for pre-exposure vaccinations ○ Intradermal administration is only recommended for the second dose, and specifically in adults who received their first dose subcutaneously and had little to no side effects; it is not recommended for immunocompromised individuals, pregnant women, children, and those with a history of keloid scars <ul style="list-style-type: none"> ● Pre-exposure vaccination is completed through the third generation MVA-BN (Imvanex and Jynneos) vaccines, which the High Authority of Health has listed as being interchangeable ● A digital campaign that has been launched on the “sexosafe.fr” site has received 958,700+ clicks and 884,000+ visits; this site provides guidance on what to do if monkeypox symptoms appear as well as additional information regarding preventive measures <ul style="list-style-type: none"> ○ The campaign has been further supplemented with broadcasting efforts on community radios and the distribution of 2,842 posters and 94,500 flyers ● On 13 July, Public Health France and SIS-Association have launched a free information service to answer monkeypox-related inquiries <ul style="list-style-type: none"> ○ This service is available seven days a week from 8:00am to 11:00pm on an anonymous, confidential telephone line ○ It will provide prevention messages and responses to questions surrounding symptoms, treatment, and vaccinations ○ Since its inception, 7,986 interviews have been conducted through this platform; they are currently experiencing a decrease in the call volume to this service <p>Clinical presentation</p> <ul style="list-style-type: none"> ● An infection caused by the monkeypox virus initially presents with a fever, headaches, body aches, and asthenia, which is followed by the appearance of fluid-filled blistering rashes that eventually dry out over time and leave behind a scab and scar ● The blistering rashes typically appear on the face, hands (palms), and feet (soles), while the mouth, genital area, and lymph nodes can all be affected too ● Of the cases investigated in the country, the most commonly reported symptoms are a genito-anal rash, eruption on another part of the body, fever, and lymphadenopathy <p>Prognosis</p> <ul style="list-style-type: none"> ● The incubation period of the disease can range from five to 21 days, with the initial fever lasting anywhere from one to three days ● The disease is reportedly more severe in children and immunocompromised individuals, as there is the possibility of superinfections of skin lesions or further complications arising from existing respiratory, digestive, ophthalmological, or neurological disorders <p>Treatment</p> <ul style="list-style-type: none"> ● It is reported that this disease tends to spontaneously heal on its own, with the majority of individuals recovering within two to four weeks
Germany	<p>Biology</p> <ul style="list-style-type: none"> ● Monkeypox is an infectious disease caused by the monkeypox virus Orthopoxvirus simiae <p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> ● As of 11 October 2022, there have been 3,651 confirmed cases of monkeypox across all 16 federal states in Germany; 18 female, three adolescent, and two children have been reported to have contracted monkeypox

- The primary mode of transmission of monkeypox to humans is from [rodents](#), however it can also be transmitted through close contact with an infected individual or contaminated surface(s)
- On [19 May 2022](#), the first confirmed case of monkeypox was reported in Germany

Prevention and control

- In conjunction with the Robert Koch Institute (RKI), the Ministry of Health (BMG) has put forth a [recommendation](#) to help assist federal states in responding to the monkeypox outbreak, and a key feature of this recommendation includes ordering an isolation period of at least 21 days for infected individuals
- On [30 May 2022](#), RKI released a recommendation on hygiene measures for the treatment and care of patients diagnosed with monkeypox in health care facilities
 - This includes the use of hand disinfectant, disposable medical gloves, personal protective equipment and providing spatial accommodation (i.e., single rooms for infected patients)
- As a preventative measure, Germany has ordered [40,000 smallpox vaccine doses](#), with an additional [200,000](#) more set to follow afterwards
- The Standing Committee on Vaccination (STIKO) has put forth a [recommendation](#) to vaccinate individuals against the monkeypox virus with Imvanex/Jynneos
 - This includes vaccinations for certain [population groups](#), including 1) post-exposure prophylaxis upon monkeypox exposure in asymptomatic individuals aged 18 years and older (e.g., those who have had close physical contact with individuals with monkeypox); 2) individuals with an increased risk of exposure and infection during a potential outbreak (e.g., men aged 18 years and older with same-sex sexual contacts or multiple partners); and 3) immunocompromised individuals
 - For those who have not previously been vaccinated against smallpox, immunization with Imvanex is a two-dose regimen separated 28 days apart, while a single dose is sufficient for those with a previous smallpox vaccine (barring immunocompromised individuals who would still receive two doses in either case)
- A total of 40,000 [Jynneos vaccine doses](#) are available for use in Germany, with another 200,000 scheduled to arrive in the third quarter of 2022
 - 5,300 monkeypox doses were delivered to the federal states in July 2022 and another 19,500 were delivered during the week of 29 August 2022
 - Given the current limited supply of these vaccine doses, STIKO [recommends](#) that an initial dose be provided to those at risk, while postponing the administration of the second dose until there is sufficient supply
- RKI published a [recommendation](#) for the management of close contacts of monkeypox cases, which includes quarantining of individuals with a high risk of transmission, such as household members
- On 12 July, RKI published a [fact sheet](#) on the current available evidence surrounding the manifestation of the monkeypox virus
- On 2 September 2022, the World Health Organization published a [news release](#) regarding the management of the Berlin Pride by health authorities in Germany amidst the monkeypox outbreak
 - In conjunction with RKI, a team of researchers developed a communications campaign leading up to the event to relay information about the risks of monkeypox to those seeking to attend
 - The '[monkeypox resource toolkit](#)' was utilized by the team in their efforts to convey information in an appropriate manner; educational material and applications were shared by the event organizers

	<ul style="list-style-type: none"> • On 19 September 2022, RKI updated their recommendations regarding the close contact management of monkeypox cases, which states that a quarantine mandate is no longer in place for contact persons <ul style="list-style-type: none"> ◦ Furthermore, housemates that have had no intimate contact with positive individuals or infectious material in the home have now been reclassified as category two contacts • Upon evaluating the data on intradermal application of monkeypox vaccinations, STIKO continues to recommend the subcutaneous administration of the Jynneos/Imvanex vaccine as opposed to delivering them intradermally <p>Clinical presentation</p> <ul style="list-style-type: none"> • The symptoms include a fever, swollen lymph nodes, skin rashes, pain, and itching in the genital area <p>Diagnosis</p> <ul style="list-style-type: none"> • The virus can be detected using polymerase chain reaction (PCR) and the particles can further be detected through an electron microscope <p>Prognosis</p> <ul style="list-style-type: none"> • The incubation period is normally between six and 13 days but it can range anywhere from five to 21 days <ul style="list-style-type: none"> ◦ On 9 September 2022, RKI pre-published an article that investigated the current incubation period of monkeypox during the ongoing outbreak in Germany; nearly 20% of the cases had an incubation period of one to three days • Monkeypox cases are usually mild and people recover within the span of a few weeks, though there may be instances of severe cases that arise within the population <p>Treatment</p> <ul style="list-style-type: none"> • Tecovirimat was recently approved in the European Union to help treat monkeypox infections (however its availability is currently limited)
Italy	<p>Biology</p> <ul style="list-style-type: none"> • Human monkeypox virus is a double-stranded DNA virus <ul style="list-style-type: none"> ◦ Two genetic clades have been characterized: West African and Central African <p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> • As of 12 October 2022, Italy has reported 856 monkeypox cases • Over the past five decades, monkeypox outbreaks have been reported in 10 African countries and four countries outside of Africa, and to date, 118 cases of monkeypox have been reported in non-endemic countries <ul style="list-style-type: none"> ◦ The phylogenetic characteristics of the virus supports the hypothesis of a introduction of the West African clade into non-endemic countries • A rapid communications report dated 26 May 2022 reported four cases in Italy from 17 and 22 May 2022 <ul style="list-style-type: none"> ◦ All patients had travelled in the first two weeks of May, three participated in a mass gathering event, and one travelled for sex work, having condomless sexual intercourse with different male partners ◦ All patients had a history of sexually transmitted infections • A letter to the editor dated 9 June 2022 reported a total of 29 PCR-confirmed cases <ul style="list-style-type: none"> ◦ 23/29 travelled abroad and most of them (13/23) had vacationed on the Canary Islands ◦ There was transmission of two generations of locally acquired cases related to an index case returning to Italy from Ghana

- A [rapid communication](#) reported 33 PCR-confirmed cases of monkeypox infection from patients attending a sexual health clinic in Milan, Italy, between 15 May and 7 July 2022
 - All 33 patients were self-identified men who have sex with other men (MSM), with a median age of 38 years
 - For 32 cases, at least one analyzed anal swab was available, whereas all cases had at least one analyzed urethral swab

Prevention and control

- The four monkeypox patients in the [rapid communications report](#) dated 26 May 2022 were taken to hospitals with combined droplet and contact isolation measures; they were also given filter face piece-2 (FFP2) for care management
- [The Italian Ministry of Health](#) issued a variety of recommendations: case notification, protective measures for healthcare workers, contact tracing, possibly implementing quarantine measures, as well as providing non-stigmatizing information to at-risk populations
- Italy started its [monkeypox vaccination campaign on 8 August 2022](#), with the first doses of Jynneos (MVA-BN) vaccine being administered at the Spallanzani hospital in Rome, and vaccinations in Milan began on 11 August 2022

Clinical presentation

- In the [rapid communications report](#) dated 26 May 2022, lesions of the four patients appeared between one and three days after systemic symptoms, clustered or isolated, beginning as raised itchy papules secreting serous with central umbilication, and over days, the umbilication widened until the lesion opened and the scab formed two weeks after symptom onset
- Patient one, a male in his 30s had been treated with oral ciprofloxacin and acyclovir, and one single dose of benzylpenicillin for skin lesions during his travels in mid-May
 - At admission, multiple asynchronous deep-seated and well-circumscribed lesions with central umbilication were present on his genital area, with inguinal lymphadenopathy
 - A single lesion was present on the anterior and posterior thorax and on the left calf
- Patient one, a male in his 30s, had been taking daily-PreP, and was admitted for fever and asthenia starting in mid-May
 - Three days later, perianal lesions appeared and presented as raised, itchy papules secreting serous, with concomitant painful inguinal lymphadenopathy
 - Multiple anal lesions appeared over the next three days, followed with lesions on the back, legs, and sole of one foot
- Patient three, a male in his 30s was admitted for a two-day fever and clustered itchy popular lesions in the anal region and single lesions on head, thorax, legs, arms, hand and penis
 - He reported getting a smallpox vaccination during childhood
- Patient four, a male in his 30s was taking event-driven PreP, and was admitted for a two-day history of myalgia
 - Vesicular-papular genital lesions appeared, followed by further skin lesions that appeared six days later in the suprapubic area and chest
- In all patients, skin lesions had an asynchronous evolution
- A [letter to the editor](#) dated 9 June 2022 reported a total of 29 PCR-confirmed cases
 - 28/29 cases were males, and 16/18 reported having sex with other men
 - The median age of patients was 36 years
 - All presented with a rash, and in 18/21 cases, the rash was localized in the genital/perianal area
 - Fever was reported in 12/22 cases for whom information was available

Diagnosis

	<ul style="list-style-type: none"> • In the rapid communications report dated 26 May 2022, the four patients were positive for monkeypox DNA in real-time PCR using samples from skin, genital and anal lesions, serum, plasma, seminal fluid, feces, and the nasopharynx <ul style="list-style-type: none"> ○ Viral DNA was extracted by Qiamp Viral RNA mini kit (Qiagen) and two real-time PCRs using a Real-Star Orthopoxvirus PCR kit and a G2R_G assay which was used as a confirmatory PCR ○ Sanger sequencing was used to identify which of the two clades the virus belonged to <p>Prognosis</p> <ul style="list-style-type: none"> • An Italian man was diagnosed with COVID-19, monkeypox, and HIV at the same time in July 2022, according to a case report <ul style="list-style-type: none"> ○ The man presented with COVID-19 symptoms nine days after he returned from a five-day trip to Spain, and after testing positive for COVID-19 on 2 July 2022, he noticed a rash on his left arm which became more painful and spread across his body over the next few days ○ The man admitted that he had unprotected sex with other men while in Spain, and subsequently tested positive for monkeypox and HIV on 6 July 2022 ○ On 13 July 2022, he no longer tested positive for COVID-19 and the monkeypox rash was mostly healed; he also began standard HIV treatment <p>Treatment</p> <ul style="list-style-type: none"> • In the rapid communications report dated 26 May 2022, only patient two used anti-inflammatory and antihistaminic drugs for perianal pain and general itch <ul style="list-style-type: none"> ○ The other patients recovered spontaneously, without antiviral therapy
Netherlands	<p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> • As of 6 October, 2022, there have been 1,221 cases of monkeypox in the country • Monkeypox occurs mostly in West and Central Africa, mainly infecting rodents <ul style="list-style-type: none"> ○ Monkeypox is described as a zoonosis (a disease that can be transmitted from animals to humans) ○ The virus can enter through mucous membranes (mouth, nose, eyes) and open wounds, and can also be spread through droplets from blisters or from mouth and pharynx ○ It cannot be spread through droplets floating in the air • It is suspected that many people have been infected with monkeypox through contact among men who have sex with men <ul style="list-style-type: none"> ○ The variant currently in Europe is not particularly infectious, but there is a lack of understanding in how it has spread to those who are currently sick • The National Institute for Public Health and the Environment report published on 2 August 2022 indicates that anyone can get monkeypox and infections with the virus occurs in all age categories; however, most of the recent infections have involved MSM contact, with the highest risk of infection being among men who have sex with multiple partners <ul style="list-style-type: none"> ○ Monkeypox is transmitted through intimate contact (kissing, making love, and sexual intercourse) with an infected person, and can also be transmitted occasionally through unprotected contact with contaminated materials ○ The virus can spread via droplets of fluid from the blisters or from the mouth and nose, though the risk of this is low ○ The scabs from the blisters can also transmit the virus ○ Blisters may form in less visible locations, including the mouth or inside the rectum, where they may look like ulcers <p>Prevention and control</p>

- According to the [Government of the Netherlands](#), infected individuals must undergo isolation at home
 - [High-risk contacts](#) such as sexual partners, family members, and others in contact with the skin blisters should also quarantine
 - If they take a test and it is negative, they can end their isolation
 - If they are positive, they should continue isolating until no longer being infectious and their skin is healed completely and the scabs have fallen off their skin
- [The Municipal Public Health Service](#) will begin source and contact tracing if someone tests positive
- [The National Institute of Public Health and the Environment](#) describes the Imvanex vaccine, which has been used in Europe to protect against smallpox since 2013 and is now being used for monkeypox
 - Imvanex contains a live attenuated virus that cannot replicate within the body, and has milder side effects than the old smallpox vaccine; it also does not leave a scar
 - The vaccine can be safely administered to immunocompromised people, but they may have a weaker immune response
 - Two vaccinations are required with an interval of at least four weeks
 - It is possible that some people may still develop a mild form of monkeypox and transmit the virus despite vaccination; thus, it is recommended to have all blisters examined by a GP or Public Health Services and to not have any intimate contact or sexual intercourse if symptoms arise
 - The effectiveness of the vaccine in preventing monkeypox has only been studied in animals; during testing, it was found that the vaccine protects against serious infection if animals are exposed to the virus after vaccination, though this is not confirmed in a human trial yet
 - 70,000 vaccines have been made available for preventive vaccination against monkeypox in the Netherlands
 - As of 10 August 2022, 5,441 vaccinations have been administered against monkeypox
 - Side effects of the vaccine include pain, redness, and swelling at the injection site, muscle pain, headache, nausea, fever, or elevated temperature
- Vaccination is available to [those at high risk](#) for contracting monkeypox, which is limited to the following groups:
 - MSM contacts, transgender people and MSM sex workers who either take part in the HIV-PrEP program or are on the waiting list for HIV-PrEP, have HIV and are at higher risk for STIs, or regularly visit the Centres for Sexual Health and have a higher risk for STIs
 - Vaccination is only available if a person has received a personal invitation from the regional Municipal Public Health Service or the HIV treatment centre
- According to [the National Institute for Public Health and the Environment](#), 20,278 vaccine doses have been administered as of 29 September 2022
 - This is up from 10,440 administered doses on 25 August 2022
 - It takes up to six weeks for the full immune response to vaccination to take effect
- If someone was born in the Netherlands before 1975 and received a smallpox vaccine in the past, then only [one vaccine dose is needed](#); those born after this date will require two injections
- Monkeypox DNA was found in [sewage](#) in all eight locations that were sampled, and can be used to track the spread of the virus as an early-warning system

Clinical presentation

	<ul style="list-style-type: none"> • The National Institute for Public Health and the Environment report published on 30 June 2022 stated that 84% of patients have symptoms such as fever, tiredness, muscle pain, or swollen lymph nodes <ul style="list-style-type: none"> ○ Almost all infections occurred after intimate or sexual contact ○ Illness course is usually mild ○ Blisters usually occur around the genitals and on the arms and legs • The National Institute for Public Health and the Environment updated their report on 16 August 2022 <ul style="list-style-type: none"> ○ A number of people have had proctitis, an inflammation of the lining of the rectum, which is sometimes the only symptom ○ The report provides images of monkeypox on the finger ○ A person may already be contagious before developing any visible symptoms ○ Some people develop flu-like symptoms or a skin rash before blisters ○ Blisters may be in the mouth or rectum, where they may resemble ulcers ○ Some people will monkeypox only have one blister ○ Scabs from blisters can also transmit the virus • Symptoms are described as mild, including fever, headache, muscle ache, swollen lymph nodes, chills, and fatigue <ul style="list-style-type: none"> ○ 1-3 days later, an infected person will get a rash that starts on the face and appears on the rest of the body ○ The rash will start as spots that develop, which form scabs that fall off the skin in 2-3 weeks ○ In most cases, the rash started in the anus and pubic region before spreading to the rest of the body • As of 31 May 2022, all 31 cases were men and identified as MSM with an age range of 23-64 years <ul style="list-style-type: none"> ○ 18 cases had reported symptom onset and the most likely date of exposure related to attending an event ○ The 97.5 percentile for the incubation period is estimated to be 19.9 days, and an estimated 2% of all cases would develop symptoms more than 21 days after being exposed ○ The literature indicates that incubation periods differ by route of transmission (non-invasive exposure through skin or droplets is 13 days, and complex and invasive exposure through contact with broken skin or mucous membranes is 9 days), which is consistent with smallpox ○ The authors' estimate of mean incubation period for monkeypox is 8.5 days and all current cases are MSM with lesions in the anal and genital regions, which is consistent with the invasive contact incubation period of 9 days reported in the literature <p>Diagnosis</p> <ul style="list-style-type: none"> • The Netherlands confirmed the first cases of monkeypox on 20 May 2022 • The Health Minister designated monkeypox as a category A disease on 24 May 2022, meaning that doctors must report new or suspected cases immediately to prevent its spread <p>Treatment</p> <ul style="list-style-type: none"> • According to the National Institute of Public Health and the Environment, the current smallpox vaccine can be used during the first few days of possible infection, and can be used preventatively in people at greater risk of infection
Portugal	<p>Biology</p> <ul style="list-style-type: none"> • The government of Portugal characterizes monkeypox as a disease that is transmitted through contact with infected animals, people, or contaminated materials, which is often rare and does not easily spread among humans <p>Epidemiology (including transmission)</p>

- As of [12 October 2022](#), Portugal has reported 930 confirmed cases
- A [Eurosurveillance case report](#) from 29 April to 23 May 2022 described the preliminary results of the outbreak investigation and the epidemiological characteristics of 27 confirmed cases
 - The report found that all cases were among young men age ranging from 20 to 59 years
 - Most commonly reported symptoms include exanthema, inguinal lymphadenopathy, fever, asthenia, headache, genital ulcers and vesicles
 - 14 men reported to also have HIV infection
 - The authors concluded that the MPX outbreak in Portugal shows signs of sustained transmission among a susceptible demographic group (given the lack of exposure to the smallpox vaccination), in addition to hypothesizing that MPX has been circulating below the detection of the surveillance systems
- The [Directorate-General for Health](#) suggested that transmission is occurring through close contact, including sexual intercourse
 - The use of condoms is indicated to not provide effective protection from monkeypox
- According to the [Directorate-General for Health](#), 99.3% of reported cases are male, with only **five** cases being reported in females
 - 43% of cases were reported in those aged 30 to 39

Prevention and control

- A [Eurosurveillance case report](#) from 29 April to 23 May 2022 described the preliminary results of the outbreak investigation and the epidemiological characteristics of 27 confirmed cases
 - The Public Health Emergencies Centre and the Health Authorities in Portugal reported that home isolation was recommended until lesions fade away, and self-monitoring for 21 days from the date of last exposure
 - Healthcare workers are recommended to use standard contact precautions, hand hygiene, and barrier nursing through PPE (i.e., gloves, face mask, gown, goggles)
 - Other measures include identifying the first case, use of standard case definition with prompt sample collection for diagnosis
 - Public health authorities are also engaging with LGBTQI+ communities, including community leaders, on targeted risk communication and social mobilization with non-stigmatizing approaches
- The [Directorate-General for Health](#) disseminated communication materials related to transmission, prevention, and hygiene measures to reduce the risk of monkeypox
 - Dissemination activities include raising awareness at public and private events
- The Directorate-General for Health indicated that as of July 12th, Portugal has received 2700 doses of the Jynneos vaccine, produced by the Bavarian Nordic company
 - An Exceptional Use Authorization was granted for the use of this vaccine as an additional measure in the control of the monkeypox outbreak.
 - The eligibility criteria for vaccination includes people who have had close contact with a case within 4 days and people who have had close contact with a case and remain asymptomatic within 14 days. People with confirmed prior monkeypox infection or who have a full course of smallpox vaccination within 2 years are not eligible for vaccination.
 - 2 vaccine doses are recommended for those who have had potential continuous or intermittent exposure, while 1 dose is recommended for people who are unexposed, or who have had a smallpox vaccine over two years ago.
 - Limited data is available for the use of this vaccine in those who are pregnant or breastfeeding, or under the age of 18

	<ul style="list-style-type: none"> • A news report indicates that the Imvanex vaccine has been administered in Portugal since July 16 <ul style="list-style-type: none"> ◦ Three individuals who have had close contact with infected people were the first to be vaccinated ◦ The Imvanex vaccine has been approved in Europe to prevent smallpox, but is also effective against Monkeypox • According to the Directorate-General for Health, as of 12 September 2022, a total of 437 people have been vaccinated <p>Clinical presentation</p> <ul style="list-style-type: none"> • The government of Portugal indicated that individuals should seek medical attention if they have ulcerative lesions, rash, enlarged lymph nodes
Spain	<p>Biology</p> <ul style="list-style-type: none"> • The Ministry of Health of Spain has developed a guideline for the management of the Monkeypox, which defines Monkeypox (MPX) as a rare viral zoonotic disease <p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> • As of 4 October 2022, Spain has 7,188 cases, which is the highest in the European region, and second highest around the globe • The Ministry of Health highlighted a reduction in the number of new cases which, according to the health authorities, cannot be attributed to vaccination efforts, given that a large vaccination campaign has not taken place in Spain, and most of the people immunized have only received a fraction of a dose • The first human cases were identified in the Democratic Republic of the Congo in 1970 <ul style="list-style-type: none"> ◦ While the majority of documented cases of MPX have occurred in the Democratic Republic of the Congo, the number of cases in other West and Central African countries has increased during the last decade • Since 2016, confirmed cases of MPX have been reported in the Central African Republic, the Democratic Republic of the Congo, Liberia, Nigeria, the Republic of the Congo, and Sierra Leone, and several African countries in these regions are currently experiencing active outbreaks of MPX • Outside of Africa, cases of human MPX infections have been documented in different countries: 47 cases in the United States in 2003 and one in 2021, four cases in the United Kingdom (UK) in 2018/2019 and three in 2021, one case in Israel in 2018 and a case in Singapore in 2019 • Those diagnosis were confirmed after PCR tests carried out by the laboratory of the National Center for Microbiology (CNM) of the Carlos III Health Institute (ISCIII) • An Emergency Committee of the World Health Organization will determine on June 23 if orthopoxvirus is an international threat <p>Prevention and control</p> <ul style="list-style-type: none"> • The Government of Spain has distributed 5,000 vaccines to health clinics, with an anticipated 7,000 more arriving in the country this week <ul style="list-style-type: none"> ◦ Community groups and sexual health associations are focusing their efforts around gay men, bisexuals, and transgender women • The Government of Spain will buy vaccines and antivirals to treat monkeypox, and the Minister of Health announced that the government has already negotiated these acquisitions with the European Medicines Agency (EMA), which is the the health emergency preparedness authority and responsible for making the Imvanex vaccine available • Historically, smallpox vaccination has been shown to protect partially against MPX

- Public health authorities are [engaging with LGBTQI+ communities](#), on targeted risk communication and social mobilisation with non-stigmatizing approaches
- [On 30 August 2022 and 31 August 2022, 5,000 more doses of the monkeypox vaccine will arrive](#), in addition to the 5,300 received in June and more than 7,000 arrivals in August
 - With this latest addition, the National Health System (SNS) will add more than 17,000 doses against this virus
- [The doses of Imvanex come from centralized purchasing from European countries](#), to try to control the spread of monkeypox
- The shortage of the vaccine has led [the U.S. and European health authorities to authorize the division of each available dose into five](#), with the aim of immunizing more people with fewer vials
 - Spain approved a new vaccination strategy a week ago in which it indicates applying 0.1 ml in most cases instead of 0.5 ml as before, which would mean that the most recent shipment could translate into up to 25,000 people vaccinated
- The Ministry of Health closed a bilateral purchase of 200 doses of the vaccine with the Netherlands before the European Commission sent the first shipment of 5,300 doses at the end of June. The [remaining 7,120, up to complete 12,420](#), are expected to arrive between July and August.
- The European Medicines Agency (EMA) is reviewing the [Bavarian Nordic vaccine to see if approves the indication in monkeypox infection](#)
 - Until now, in the EU it is only approved against conventional smallpox
 - In the United States, the same vaccine is approved for both viruses

Clinical presentation

- Monkeypox virus infection is usually a self-limited illness, and most people recover within several weeks, however, in some cases serious illness can occur
- The incubation period is 6 to 16 days, but can range from five to 21 days
- The classic initial clinical picture described until this outbreak usually includes fever, headache, muscle aches, lymphadenopathy, and fatigue
- Between one and five days after the onset of fever, a rash develops, often starting on the face and then spreading to other parts of the body with the rash tending to be more concentrated on the face and extremities than on the trunk
- The disease affects the face (in 95% of cases); the palms of the hands and soles of the feet (in 75% of cases); the oral mucosa (in 70% of cases); the genitalia (30%); and the conjunctiva and cornea (20%)
- Areas of erythema or hyperpigmentation of the skin around the lesions are usually seen
- The lesions can vary in size, the rash evolves sequentially from macules to papules, vesicles, pustules, and crusts that dry up and fall off
- In the first reported cases associated with this outbreak, genital and peri-oral lesions have been identified in a high number of cases
- Symptoms usually last between two to four weeks
- The agency of health surveillance in Spain (SiViES) [has complete data of 2,368 patients](#), 2,348 are men and 20 are women
- Age ranges from 3 to 76 years, with a median age of 37 years; the SiViES report indicates that the date of onset of symptoms is available in 2,143 cases, of these, the first reported case started symptoms on April 26 and the last on July 11
- There is also information regarding clinical manifestations, hospitalization and complications in 1,199 cases of the 2,368 notified to the SiViES platform

- Among the [patients with characterization of their symptoms](#), they mainly presented fever (56.6%); exanthema [skin eruption] anogenital (49.8%), oral-buccal (39.9%) and in other locations (40.4%); localized lymphadenopathy (45.5%); and asthenia (38.0%)
- Of the 1,199, a total of 54 patients (4.5%) presented complications throughout their clinical process; the most frequent were secondary bacterial infections and mouth ulcers
- The report adds that 970 of 980 patients with available information were men who have sex with men
- Information is available on the most likely transmission mechanism in 867 cases, with 91.8% of cases due to close contact in the context of sexual intercourse and 8.2% due to close non-sexual contact
- In relation to [attendance at mass events](#), of the 774 cases with available information on this variable, 261 attended an event on the dates prior to the onset of symptoms

Diagnosis

- The clinical differential diagnosis that should be considered includes other exanthematous diseases that can present with a generalized pustular or vesicular eruption, such as smallpox (because of the risk that it could be an intentional event), chickenpox, herpes virus, eczema herpeticum, some enteroviruses (such as coxsackie or echovirus) measles, bacterial skin infections, scabies, syphilis, drug-associated allergies and some dermatological diseases
- Lymphadenopathy during the prodromal stage of the disease may be a clinical feature to distinguish MPX from varicella or smallpox
- The [guideline developed by the Ministry of Health of Spain](#) has recommended that samples to be obtained in a suspected case should be taken from the skin lesion (vesicular fluid, smear of vesicular lesions, exudates or scabs)
- The skin lesion sample must be sent in virus transport medium and kept cold
- If this sample is not available or additional studies are required, other samples may be used by contacting the National Institution of Microbiology in Spain in advance
- Clinical samples are considered category B and, therefore, standard precautions are sufficient for transporting the samples

Prognosis

- The [guideline for the management of monkeypox](#) developed by the Ministry of Health of Spain has indicated that the number of injuries varies from a few to several thousand and, in severe cases, the lesions may coalesce until large sections of skin are shed
- Severe cases occur most often among children, young adults, and immunocompromised persons, and are related to the degree of exposure to the virus and the vulnerability of the person
- Complications may include secondary bacterial infections, bronchopneumonia, sepsis, encephalitis, and corneal infection with subsequent loss of vision
- Its clinical presentation is milder than smallpox, and the case fatality rate for the West African clade has been documented to be [around 1%, while for the Congo Basin clade it can be as high as 10%](#)
- According to [the SiViES health report](#), 48 cases have been hospitalized (4.0%); none of the cases has died
- Spain has recorded its first two deaths in patients infected with monkeypox
 - The Ministry of Health of Andalusia has reported that one of the deaths is a 31-year-old man who was admitted to the Intensive Care Unit of the Reina Sofía University Hospital in Córdoba with [meningoencephalitis caused by the infection](#)
 - The first victim, in the Valencian Community, was also a young man (his age has not been reported) who also suffered from encephalitis

	<p>Treatment</p> <ul style="list-style-type: none"> • Among three antivirals available, the Government of Spain has preferred Tecovimirat, which seems to present the best outcomes • The Government of Spain will join a centralized purchase under the terms agreed with the corresponding pharmaceutical company
Sweden	<p>Biology</p> <ul style="list-style-type: none"> • The Public Health Agency of Sweden defines monkeypox as a rare, sporadic species of the Orthopoxvirus that can be transmitted between animals and humans <ul style="list-style-type: none"> ◦ It has previously infected people in African rainforests where the reservoirs of the virus are primarily wild monkeys <p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> • According to the U.S. Centers for Disease Control and Prevention’s 2022 Monkeypox Outbreak Global Map, Sweden has confirmed 202 cases of monkeypox and no deaths as of 12 October 2022 • The Public Health Agency of Sweden reported that the incubation period of monkeypox is usually six to 13 days but can vary between five and 21 days <p>Prevention and Control</p> <ul style="list-style-type: none"> • According to a local report, the regions of Stockholm and Skane began offering Jynneos monkeypox vaccines to people who have been in contact with infected individuals in the last week • The Public Health Agency of Sweden provides general preventive measures for monkeypox, including avoiding close contact with infected people, particularly sexual contact, and avoiding animals in areas where monkeypox is present <p>Clinical presentation</p> <ul style="list-style-type: none"> • Symptoms of monkeypox often include mild skin rashes and blisters that can spread to different parts of the body, as well as fever and swollen lymph nodes • If the virus is transmitted sexually, blisters on the genitals and around the anus can occur <p>Diagnosis</p> <ul style="list-style-type: none"> • Sweden confirmed its first case of monkeypox on 19 May 2022, and it is unknown how the person became infected
United Kingdom (U.K.)	<p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> • The case count is 3,523 confirmed and 150 highly probable as of 10 October 2022 • The UK Health Security Agency released an eighth technical briefing about the monkeypox outbreak in England on 23 September 2022 <ul style="list-style-type: none"> ◦ The technical briefing places England at level two of four of outbreak transmission potential (transmission within a defined sub-population) ◦ The risk assessment section provides an assessment of the current disease trajectory and observed severity, both in the U.K. and internationally ◦ An epidemiological update is provided which presents insights from newly diagnosed cases, enhanced surveillance questionnaires completed by cases, and testing data ◦ With respect to the observed reduction in incident cases, it is noted that this occurred too soon after the introduction of the vaccination program for it to be a major driver; rather, it is more likely that cases are declining due to some combination of infection saturation, changes in case ascertainment, and behavioural changes

- It was observed that *Shigella* spp and lymphogranuloma venereum (infections that also disproportionately affect men who have sex with men) diagnoses also began decreasing around the time that monkeypox diagnoses began slowing, suggesting that changes in sexual behaviour may have contributed to reductions in incident monkeypox cases in August 2022
- The UK has confirmed the [importation of one case of monkeypox with a travel link to West Africa](#); this patient has been admitted to hospital given that cases imported directly from West Africa are still considered high consequence infectious diseases
- The UK passed [legislation to make monkeypox a notifiable disease](#) in law as of 8 June 2022
 - This legislation means that doctors are required to notify their local council or Health Protection Team if they suspect a patient has monkeypox and laboratories must notify the UK Health Security Agency if they identify monkeypox virus in a sample
 - To ensure anyone concerned about monkeypox seeks appropriate healthcare, the National Health Service regulations were amended to make monkeypox treatment and diagnosis free from charge for all overseas visitors
- The [UK Health Security Agency](#) has reported that a ‘notable proportion’ of cases reported to date have been among individuals who are gay or bisexual and men who have sex with men, and the agency is asking individuals in these groups to be aware of symptoms, especially if they recently had a new sexual partner
- [Contact tracing investigations](#) have identified links to gay bars, saunas, and the use of dating applications in the UK and abroad—but no single factor or exposure that links all cases has been identified
- A [Eurosurveillance report](#) describes the monkeypox outbreak in the UK as of 25 May 2022 that is affecting people with no travel links to endemic countries
 - The mean reporting delay (time between symptom onset and when the case was recorded in the case management system) was 11 days for the 86 cases as of 25 May 2022
 - The outbreak has been grouped into three distinct incidents based on transmission dynamics and travel histories
 - There was a median of four and a maximum of 25 contacts per case; contacts of cases in these incidents included passengers on the same flight as a case, healthcare workers exposed before patients were identified as cases, and community contacts
 - The gay, bisexual, or other men who have sex with men community is overrepresented among the cases, suggesting transmission in these sexual networks
 - While vaccination has been offered to medium- and high-risk contacts uptake has been low, with 69% of healthcare contact and 14% of community contacts having taken up the vaccination offer by 24 May 2022
- Monkeypox clade IIb (B.1 lineage), which is largely circulating during the current outbreak, has [not been classified as a high consequence infectious disease](#) by the UK Health Security Agency; however, the other clades of monkeypox are classified as high consequence infectious diseases and may be subject to different clinical and public-health responses

Prevention and control

- The UK Health Security Agency alongside the public health agencies of England, Scotland, Wales, and Northern Ireland have released a [consensus statement regarding principles for monkeypox control in the UK](#)
 - These principles are intended to guide the public health response to ensure there is a proportionate response that encourages engagement with health services, prevents stigma, and controls spread
 - The statement outlines several assumptions about monkeypox transmission and biology that are meant to be regularly updated with new evidence
 - Implications/guidance for the following sectors are presented: community/domestic, ambulatory care, inpatient healthcare, and other residential settings

- Implications/guidance for the following sectors are presented: community/domestic, ambulatory care, inpatient healthcare, and other residential settings
- The [UK Health Security Agency](#) has purchased supplies of Imvanex (a smallpox vaccine supplied by Bavarian Nordic) and is offering this vaccine to close contacts of those diagnosed with monkeypox to reduce their risk of symptomatic infection and severe illness
 - High-risk contacts of confirmed cases are also being asked to isolate at home for up to 21 days
 - At the current time, given global vaccine shortages, the offer of [post-exposure vaccination is being limited](#) to those at highest risk of severe complications, but the program for pre-exposure vaccination is unchanged
- The smallpox vaccine is also being [offered to health workers](#) who will care for monkeypox patients as well as those who work in sexual health centre and may have assessed suspected cases
 - The UK Health Security Agency is also advising that pregnant and severely immunocompromised workers should not assess or provide care for suspected or confirmed monkeypox cases
- The U.K. has procured [150,000 doses of the smallpox vaccine](#) from Bavarian Nordic to offer to those eligible for vaccination
 - As of 10 August 2022, roughly 27,000 doses have been administered, the vast majority of which have gone to gay, bisexual and other men who have sex with men
 - The remainder of the administered doses have gone to contacts of cases and eligible healthcare workers
 - Of the procured doses, roughly 50,000 have arrived in the U.K.; the remaining doses are expected to arrive in September 2022
- There are reports that given vaccine shortages, the U.K. [monkeypox vaccination campaign will be paused](#) to a large extent until new vaccine doses arrive in late September; however, doses are being reserved for post-exposure vaccination
- The UK Health Security Agency is piloting offering [fractional doses](#) (of 0.1 ml as opposed to 0.5 ml) at three vaccination sites given current global vaccine shortages
- [Second doses](#) of the Jynneos vaccine are now being offered to those at highest risk and for whom two to three months have elapsed since their first dose
 - This is enabled by securing more vaccine doses as well as an expansion in using intradermal administration
- The UK Health Security Agency has produced three leaflets about updates to the vaccination program that are targeted at patients
 - The leaflet about the [smallpox \(monkeypox\) vaccine](#) addresses many common questions about the vaccine and includes information about side-effects and how to report adverse events
 - The leaflet about [waiting for vaccination](#) lays out the UK's approach to managing limited vaccine supplies, how they are prioritizing different groups for vaccination, and addresses some concerns of people who are not currently eligible
 - The leaflet about [intradermal injection](#) (which is provided to patients attending clinics that are offering intradermal injection) provides information about this injection technique, its effectiveness, and the rationale for taking this approach
- The [UK Health Security Agency](#) is working with partners to communicate with sexual health service partners as well as the gay, bisexual, or other men who have sex with men community about monkeypox and how to stay safe
 - The agency has noted it is engaging with the dating application Grindr, the LGBT Consortium, Pride organizers, and venue owners to share public health messaging
- The [UK Health Security Agency](#) notes that appropriate respiratory and contact precautions need to be taken and that scabs may be infectious, so bedding, clothing, and other articles need to be handled appropriately

- The monkeypox virus is classified as an Advisory Committee on Dangerous Pathogens (ACDP) Hazard Group 3 pathogen and the live virus must be handled at full containment level 3
- The UK Health Security Agency is [advising men who have confirmed monkeypox infection to use condoms during sex](#) for 12 weeks following recovery from infection, and the agency is offering a monkeypox PCR test on semen samples after these 12 weeks have passed if the patient:
 - Is undergoing fertility treatment or planning pregnancy
 - Is undergoing planned semen storage
 - Has an immunocompromised sexual partner
 - Is concerned about sexual transmission and requests a test
- Public Health England has produced a [guidance document about environmental cleaning and decontamination](#) with sections dedicated to healthcare and domestic settings
- The UK Health Security Agency has produced and updated [recommendations for the use of pre- and post-exposure vaccination during a monkeypox incident](#)
 - This document contains background information regarding the Imvanex vaccine, recommendations regarding pre- and post-exposure vaccination, how to prioritize the vaccine stock, booster doses, and vaccine prescribing and administration
- The UK Health Security Agency has produced a [monkeypox contact tracing classification and vaccination matrix](#) to help guide follow-up and vaccination advice for individuals who have had varying levels of exposure risk with confirmed cases of monkeypox
- The UK Health Security Agency has produced guidance regarding the [cleaning of sex-on-premises venues](#) in light of the monkeypox virus outbreak
- The UK Health Security Agency has produced [guidance regarding monkeypox in prisons and places of detention](#)
- The [Coalition for Epidemic Preparedness Innovations has awarded](#) the UK Medicines and Healthcare products Regulatory Agency and the UK Health Security Agency funding to advance research into tools for assessing current and future vaccines against monkeypox
- The UK Health Security Agency has used surveillance data, survey findings, and expert opinion to estimate that approximately [110,000 individuals are eligible for monkeypox vaccination in](#) the U.K.

Clinical presentation

- The UK Health Security Agency has [updated the monkeypox case definition](#) to now also include “a single lesion or lesions on the genitals, anus and surrounding area, lesions in the mouth, and symptoms of proctitis (anal or rectal pain or bleeding), especially if the individual has had a new sexual partner recently” as a symptom
- The UK Health Security Agency has produced [guidance regarding case definitions](#) of possible, probable, highly probable, and confirmed cases of monkeypox
 - The guidance document also includes actions to take for clinicians when presented with a possible, probable, confirmed or highly probable case

Diagnosis

- The UK Health Security Agency has produced guidance for [collecting, submitting, and processing of samples](#) for the diagnosis of monkeypox
- To increase testing capacity, [some suspected monkeypox samples are now being tested with an orthopox polymerase chain reaction test](#)
 - Those who test orthopox-positive are deemed as highly probable cases

	<ul style="list-style-type: none"> • The rare and imported pathogens laboratory (RIPL) at the UK Health Security Agency Porton Down has been designated as the diagnostic laboratory for monkeypox <ul style="list-style-type: none"> ◦ Professionals are being asked to consult with the imported fever service before sending blood samples for testing • Public Health England has produced a monkeypox guidance document for primary care which provides information on transmission, clinical features, patient assessment, and infection prevention and control <p>Treatment</p> <ul style="list-style-type: none"> • The National Institute for Health and Care Research has commissioned the Placebo-Controlled Randomized Trial of Tecovirimat in Non-Hospitalized Monkeypox Patients (Platinum) trial to test the safety and efficacy of tecovirimat in monkeypox patients <ul style="list-style-type: none"> ◦ The trial has already begun recruiting patients ◦ The trial will examine the following outcomes: time needed for skin and mucosal lesion healing, time for throat and lesion swabs to test negative, rate of hospitalization • The UK Health Security Agency notes that the smallpox vaccine, cidofovir, and tecovirimat can be used to control outbreaks, but monkeypox treatment is mostly supportive • The UK Health Security Agency has released interim guidance about the de-isolation and discharge of monkeypox-infected patients, which pertains both to patients admitted to hospitals as well as those who manage symptoms at home • The UK Health Security Agency has produced guidance regarding home isolation for people who have been diagnosed with monkeypox infection <ul style="list-style-type: none"> ◦ Cases are being asked to isolate at home, if they are well enough, and to avoid contact with others until lesions have healed and scabs have dried • The British HIV Association has released a statement on monkeypox which includes information regarding the impact of HIV on monkeypox, vaccine considerations, as well as pharmacokinetic and renal considerations for treatment
United States (U.S.)	<p>Biology</p> <ul style="list-style-type: none"> • According to the CDC, Monkeypox is a rare disease that is caused by infection with monkeypox virus, which belongs to the orthopoxvirus genus in the family Poxviridae <p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> • As of 12 October 2022, the U.S. has reported a total of 27,022 confirmed monkeypox cases • According to the Morbidity and Mortality Weekly report published by CDC, the incidence of monkeypox was 14 times as high among unvaccinated males compared with those who had received a first vaccine dose ≥ 14 days earlier • The first human case of monkeypox was recorded in 1970 in the Democratic Republic of the Congo (DRC) during a period of intensified effort to eliminate smallpox • Since then, monkeypox has been reported in people in several other central and western African countries: Cameroon, Central African Republic, Cote d'Ivoire, Democratic Republic of the Congo, Gabon, Liberia, Nigeria, Republic of the Congo, and Sierra Leone • Transmission of monkeypox virus occurs when a person comes into contact with the virus from an animal, human, or materials contaminated with the virus • On May 18, 2022, a U.S. resident tested positive for monkeypox after returning to the U.S. from Canada. As of May 18, 2022, no additional monkeypox cases have been identified in the U.S.

- The virus enters the body through broken skin (even if not visible), respiratory tract, or the mucous membranes (eyes, nose, or mouth)
- Animal-to-human transmission may occur by bite or scratch, bush meat preparation, direct contact with body fluids or lesion material, or indirect contact with lesion material, such as through contaminated bedding
- Human-to-human transmission is thought to occur primarily through large respiratory droplets
- Respiratory droplets generally cannot travel more than a few feet, so prolonged face-to-face contact is required
- Other human-to-human methods of transmission include direct contact with body fluids or lesion material, and indirect contact with lesion material, such as through contaminated clothing or linens
- According to the [CDC](#), people who do not have monkeypox symptoms cannot spread the virus to others and at this time, it is not known if monkeypox can spread through semen or vaginal fluids
- According to a [report by the CDC](#), 99% of cases were among men, with 94% reporting male-to-male sexual or close intimate contact during the three weeks before symptom onset
 - The data from this report suggests that widespread community transmission of monkeypox has disproportionately affected gay, bisexual, and other men who have sex with men, and racial and ethnic minority groups
- A [report by the CDC](#) suggests that among the cases with reported classification by health departments, 74% of cases were locally acquired
 - The percentage of locally acquired cases increased from 51% to 82% from 17 May to 2 July and from 3 July to 22 July 2022, respectively

Prevention and control

- The [U.S. national monkeypox vaccine strategy](#) was announced on June 28, 2022. Multiple federal agencies, including the Administration for Strategic Preparedness and Response (ASPR), U.S. Food and Drug Administration (FDA), National Institutes of Health (NIH), and Centers for Disease Control and Prevention (CDC) are coordinating to implement this enhanced vaccination strategy
- [On 15 September, 2022](#), the CDC announced a new opportunity for jurisdictions to submit proposals for collaborative vaccination projects intended to expand access to disproportionately affected populations experiencing vaccination disparities
- [As of 11 October, 2022](#), 906,325 vaccine doses were administered in 54 U.S. jurisdictions
- [On 23 September, 2022](#) CDC updated the Monkeypox Vaccine Equity Toolkit which provides strategies, actions, and resources to increase vaccination among populations most affected by monkeypox, but less likely to be vaccinated
- [A U.S. clinical trial](#) is evaluating intradermal delivery of Jynneos monkeypox vaccine to expand vaccine supply
- The CDC recommends having [safer sex practices and temporarily changing some behaviors](#) in social gatherings to lower the risk of contracting monkeypox
- The CDC calls for the [prioritization of people with HIV infections and STIs](#) for monkeypox vaccinations
 - Screening for HIV and other STIs and other preventive care should be considered for persons evaluated for monkeypox, with HIV care and HIV preexposure prophylaxis offered to eligible persons
- On [29 August 2022](#), HHS announced that it will provide approximately \$11 million to support the first U.S.-based fill and finish manufacturing of JYNNEOS – a vaccine approved to prevent smallpox and monkeypox
- [As of 6 September, 2022](#) HHS awarded \$20 million dollar contract to AmerisourceBergen to expand,
- quicken distribution of vaccines and treatments for monkeypox.

- The Department of Health and Human Services is [increasing the vaccine supply](#), increasing available testing through commercial labs, adjusting vaccine allocation strategy, and educating the public about monkeypox
- The [CDC](#) indicates that the only FDA-approved dosing regimen for the Jynneos vaccine is a two-dose series
 - Exceptions to the two-dose series include a person who is diagnosed with monkeypox virus infection after their first dose or a person who has already been diagnosed with monkeypox virus infection as monkeypox virus infection likely confers immune protection
 - An immunocompromised person who is diagnosed with monkeypox after their first dose of Jynneos may be eligible to receive a second dose of Jynneos
 - People who receive Jynneos are considered to reach maximal immunity 14 days after their second dose
 - The FDA-approved Jynneos vaccine dosing interval is 28 days
 - The second dose may be given up to 4 days before the minimum interval of 28 days (i.e., 24 days after the first dose) or up to 7 days after the minimum interval of 28 days (i.e., 35 days after the first dose) based on ACIP's general best practices and clinical study data
- The [CDC](#) advises that Jynneos may be administered regardless of the timing of other vaccines. However, because of the observed risk for myocarditis after the ACAM2000 and mRNA COVID-19 vaccines, people might consider waiting 4 weeks after orthopoxvirus vaccination before receiving a Moderna, Novavax, or Pfizer-BioNTech COVID-19 vaccine
- The [U.S. CDC](#) recommends that individuals should be vaccinated within four days from the date of exposure to prevent onset of the disease to prevent the onset of the disease, but if it is given between four to 14 days after exposure, the vaccination may reduce symptoms but not prevent the disease
- According to the [U.S. CDC](#), there is currently a limited supply of Jynneos but more is expected in the coming weeks and months, and there is an ample supply of ACAM2000
- Individuals are fully vaccinated after two weeks of the second dose of Jynneos, and four weeks after receiving ACAM2000
- Vaccination strategies can include post-exposure prophylaxis (PEP), expanded PEP (e.g., targeting people who have certain risk factors), and PrEP (e.g., individuals who are at high risk such as clinicians and laboratory workers who handle specimens that might contain monkeypox virus)
- A recent [Morbidity and Mortality Weekly Report published by CDC](#) recommended the following vaccination for persons at risk for occupational exposure to orthopoxviruses:
 - For Primary Vaccinations, the Advisory Committee on Immunization Practices unanimously voted in favor of the Jynneos vaccine as an alternative to ACAM2000
 - For booster doses, ACIP unanimously voted in favor of the Jynneos booster vaccine after the 2-dose Jynneos primary series
 - ACIP recommended that the Jynneos booster dose be administered every 2 years to persons working with more virulent orthopoxviruses and every 10 years to persons working with less virulent orthopoxviruses.
 - For the option of transitioning from Jynneos for a booster dose in persons who had received primary vaccination with ACAM2000, ACIP unanimously voted in favor of recommending Jynneos boosters as an alternative to ACAM2000 boosters in persons who received ACAM2000 as the primary vaccine
 - The report also states that the benefit/risk ratio should be considered when administering vaccination to special populations
 - In the United States, [the two-dose Jynneos vaccine](#) is licensed to prevent smallpox and specifically to prevent monkeypox
 - According to the [CDC](#), the following measures can be taken to prevent infection with monkeypox virus:

- Avoid contact with animals that could harbor the virus (including animals that are sick or that have been found dead in areas where monkeypox occurs)
- Avoid contact with any materials, such as bedding, that has been in contact with a sick animal
- Isolate infected patients from others who could be at risk for infection
- Practice good hand hygiene after contact with infected animals or humans (e.g., washing your hands with soap and water or using an alcohol-based hand sanitizer)
- Use personal protective equipment (PPE) when caring for patients
- On 4 August 2022, the [U.S. Department of Health and Human Services](#) declared the U.S. monkeypox outbreak to be a public-health emergency
- A [report by the CDC](#) of 2,891 monkeypox cases reported in the U.S. between May 17 and July 22 by 43 states, Puerto Rico and the District of Columbia indicated that among 339 persons with vaccination status available, 48 (14%) reported previous receipt of smallpox vaccine, including 11 (23%) who received one of two JYNNEOS doses during the current outbreak, 11 (23%) who received pre-exposure prophylaxis at an unknown time before the current outbreak, and 26 (54%) who did not provide information about when vaccine was administered
- As of 23 August 2022, [207,728 vaccination doses were administered](#) in the 19 U.S. jurisdictions reporting data

Clinical Presentation

- In humans, the [symptoms of monkeypox](#) are similar to, but milder than the symptoms of smallpox
- Monkeypox begins with fever, headache, muscle aches, and exhaustion
- The main difference between symptoms of smallpox and monkeypox is that monkeypox causes lymph nodes to swell (lymphadenopathy) while smallpox does not
- The incubation period (time from infection to symptoms) for monkeypox is usually seven to 14 days but can range from five to 21 days, and the illness typically lasts for two to four weeks
- The development of initial symptoms (e.g., fever, malaise, headache, weakness, etc.) marks the beginning of the prodromal period
- According to a [report by the CDC](#), 42% of persons with monkeypox did not report the typical prodrome as their first symptom, 46% reported one or more genital lesions during their illness, and 41% had HIV infection
 - The most frequently reported signs and symptoms indicated by the CDC include rash (100%), fever (63%), chills (59%) and lymphadenopathy (59%)
 - Rectal symptoms reported include purulent or bloody stools (21%), rectal pain (22%), and rectal bleeding (10%)
 - Rash was most frequently reported on the genitals (46%), arms (40%), face (38%), and legs (37%)
 - This report recommends that clinicians should test patients with rash consistent with monkeypox, regardless of whether the rash is disseminated or was preceded by prodrome

Diagnosis

- On 7 September 2022, the HHS secretary signed [a declaration under section 564](#) of the Federal Food, Drug, and Cosmetic Act to allow the U.S. Food and Drug Administration (FDA) Commissioner to issue emergency use authorizations for in vitro diagnostics to expand the availability of tests for monkeypox

- According to a [Health Agencies Update](#), over 8000 tests have been available weekly through more than 67 public health laboratories, however, clinicians continue to face difficulties in ordering tests
 - To increase the accessibility of monkeypox testing, the US Department of Health and Human Services began shipping monkeypox tests in late June to 5 commercial laboratory companies
 - Outsourcing tests to commercial laboratories is expected to clear up the backlog
- [Clinicians can recognize potential monkeypox](#) infection based on the similarity of its clinical course to that of ordinary discrete smallpox
- The [CDC](#) indicates that cases should be confirmed by PCR demonstrating the presence of monkeypox virus DNA or isolation of monkeypox virus in culture from a clinical specimen
 - Cases in which an alternative diagnosis can fully explain the illness, an individual with symptoms does not develop a rash within 5 days of illness onset, or a case where high-quality specimens do not demonstrate the presence of the virus or antibodies may be excluded
- A feature that distinguishes infection with monkeypox from that of smallpox is the development of swollen lymph nodes (lymphadenopathy)
- Swelling of the lymph nodes may be generalized (involving many different locations on the body) or localized to several areas (e.g., neck and armpit).
- Shortly after the prodrome, a rash appears
- Lesions typically begin to develop simultaneously and evolve together on any given part of the body
- The evolution of lesions progresses through four stages—macular, papular, vesicular, to pustular—before scabbing over and resolving
- This process happens over a period of two to three weeks

Prognosis

- The severity of illness can depend upon the initial health of the individual, the route of exposure, and the strain of the infecting virus (West African vs. Central African virus genetic groups, or clades)
- Most people with monkeypox [recover fully within two to four weeks](#) without the need for medical treatment

Treatment

- According to the [U.S. CDC](#), there is currently no treatment available specifically for MPX infections, however there are medical countermeasures available through the Strategic National Stockpile (SNS) with limited available evidence on its effectiveness for the treatment of monkeypox such as: 1) Tecovirimat; 2) Vaccinia Immune Globulin Intravenous (VIGIV); 3) Cidofovir; and 4) Brincidofovir
- The [Morbidity and Mortality Weekly Report \(MMWR\)](#) for treatment of monkeypox dated 9 September 2022 concluded that Tecovirimat is tolerated and current data supports continued treatment for monkeypox
- The [NIAID states that Intravenous vaccinia immune globulin \(VIGIV\)](#) may be authorized for use to treat monkeypox during an outbreak
- [On 7 October, 2022 CDC updated the Interim Clinical Considerations for management of ocular monkeypox virus infection](#)
 - It provides guidance for healthcare facilities and healthcare professionals providing care for people infected with monkeypox virus
- [On 4 October, 2022 the CDC updated the Clinical Considerations for monkeypox in children and adolescents less than 18 years old](#)
- [A U.S. clinical trial is evaluating the antiviral \(tecovirimat TPOXX\) for monkeypox](#)

Appendix 5: Experiences in Canadian provinces and territories related to available evidence about monkeypox [yellow highlights = newly added or revised content in this version of the living evidence profile]

Province/territory	Summary of experiences
Pan-Canadian	<p>Biology</p> <ul style="list-style-type: none"> • According to the Government of Canada’s website, monkeypox is a viral disease that can enter the body through broken skin, the respiratory tract, or the mucous membranes of the eyes, nose or mouth • The virus naturally occurs in Western and Central Africa, and the cessation of smallpox vaccination appears to have increased humans’ susceptibility to severe monkeypox <p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> • The Public Health Agency of Canada (PHAC) reported a total of 1,411 cases of monkeypox in nine Canadian provinces and territories as of 12 October 2022 • The Director-General of the WHO, Tedros Adhanom Ghebreyesus, said at a press conference on 31 August 2022 that the “sustained downward trend” of monkeypox cases in Canada is an encouraging sign, and highlighted that despite several countries in the Americas seeing increased case counts, Canada appears to be an outlier • According to Dr. Tam’s remarks at a press conference on 27 July 2022, over 99% of the monkeypox cases in Canada for whom additional information is available are male with a median age of 36 years • Confirmed cases of monkeypox in Canada are reported to the Public Agency of Canada (PHAC) and updated weekly by province or territory on their website • In recent weeks, the province of Ontario has become the epicentre of the monkeypox disease in Canada, with 631 monkeypox cases being reported as of 9 September 2022 • Monkeypox can spread in three ways: 1) animals (e.g., rodents, primates) to humans; 2) person-to-person; and 3) through contaminated objects • Humans may also become infected by eating uncooked contaminated meat or through contact with body fluids from infected animals or humans • An infected pregnant women may also pass monkeypox on to their developing fetus • The virus is contagious between one to five days before the stage-two rash develops up until the scabs fall off and the skin heals • At a news conference on 3 June 2022, Canada’s Chief Public Health Officer, Dr. Theresa Tam, reported that a disproportionate number of the confirmed cases in Canada are among gay and bisexual men but warned that anyone can be potentially susceptible to the disease <ul style="list-style-type: none"> ○ She encouraged public health officials to learn from the experience of the HIV/AIDS epidemic and to involve communities that are most impacted right from the start ○ Officials have stayed clear of confirming the origin of monkeypox in Canada citing privacy and stigmatization concerns • In an announcement on 4 July 2022, the Public Health Agency of Canada (PHAC) noted that the possibility and extent of respiratory transmission is of monkeypox is “unclear at this time.” <p>Prevention and control</p>

- Since monkeypox primarily spreads through close contact, people can lower their risk of contracting monkeypox by [maintaining physical distance and using frequent hand hygiene](#) and respiratory hygiene, such as masking
 - In the coming days, the [federal government will release updated guidance for infection prevention and control](#) considering the recent confirmed cases of monkeypox
- The Public Health Agency of Canada has issued a [travel health notice, last updated 20 June 2022](#), to practise enhanced health precautions when traveling to certain countries
 - Enhanced health precautions may include using personal protective equipment, delaying travel until risk is lower, avoiding higher risk activities, and additional vaccinations for certain groups
- According to PHAC's press release on [23 July 2022](#), the Government of Canada has provided over 70,000 doses of Imvamune vaccines to provinces and territories and is also providing treatments for case management as requested
- On 8 June 2022, the National Advisory Committee on Immunization (NACI) released [interim guidance on the use of Imvamune](#), a third-generation smallpox vaccine, for post-exposure prophylaxis (PEP) against monkeypox:
 - A single dose of Imvamune may be offered to individuals with high-risk exposures of a probable or confirmed case of monkeypox, or in setting where transmission is occurring, ideally within four days of exposure
 - PEP should not be offered to individuals who already have a monkeypox infection
 - A second dose of Imvamune may be offered after 28 days of the first dose if continued risk of exposure is indicated
 - NACI also recommended Imvamune pre-exposure prophylaxis (PrEP) for adults at high risk of occupational exposure in a laboratory research setting and for special populations, such as individuals who are immunocompromised, pregnant, lactating, children and youth who are less than 18 years old, and individuals with atopic dermatitis based on exposure risk
- **The National Advisory Committee on Immunization (NACI) updated its [interim guidance on the use of Imvamune](#) on 16 September 2022 after considering the impact of dose-sparing strategies during periods of limited vaccine supply**
 - The new guidance recommended that specific groups should be considered for vaccination, including men who have sex with men, individuals who self-identify as sex workers regardless of their self-identified sex/gender, and staff or volunteers who are in sex-on-premises venues where workers may have contact with fomites that are potentially contaminated with monkeypox
 - It also recommends that in the context of limited vaccine supply, those with prior history of monkeypox infection **do not need to be vaccinated, first doses should be prioritized to meet demand for vaccinations before second doses are offered, and off-label intradermal administration can be used for immunocompetent adults as a second dose**
- According to a [4 July 2022 news report](#), a total of 8,101 doses of IMVAMUNE vaccine have been administered in Québec since 27 May, and as of 30 June, nearly 6,000 people in Toronto have been vaccinated against monkeypox
 - [Vaccination also began in Alberta](#) on 4 July 2022
- Canada's Chief Public Health Officer, Dr. Theresa Tam, indicated that [negotiations are underway to procure more monkeypox vaccine](#) from the Danish manufacturer Bavarian Nordic
 - The manufacturer said in early June that PHAC had agreed to a US\$56 million, five-year contract to purchase IMVAMUNE vaccine, with expected delivery beginning in 2023
- As of [11 August 2022](#), the Government of Canada has distributed over 99,000 doses of Imvamune vaccine to provinces and territories

- More than 50,000 people have been vaccinated in Canada since 11 August
- The Public Health Agency of Canada has provided [resources](#) on their website for health professionals administering IMVAMUNE vaccinations
- To reduce the risk of becoming infected or spreading monkeypox, [PHAC recommends](#) that Canadian residents:
 - stay home and limit contact with others if they have symptoms or are recommended to do so by a healthcare provider
 - avoid close physical contact with anyone who is infected with or may have been exposed to the monkeypox virus
 - maintain good hand hygiene and respiratory etiquette
 - clean and disinfect high-touch surfaces and objects in the home, especially after having visitors
 - use condoms and practice safe sex with fewer sexual partners
- On [21 July 2022](#), the federal government announced that it is providing funding for community-based organizations in regions most impacted currently by the monkeypox outbreak to reach at-risk populations on how to protect themselves
- At a recent [press conference](#), Dr. Theresa Tam responded to questions about whether governments are looking at how to financially support those who need to isolate by saying that she is encouraging provinces and territories to implement these types of supports
- On [12 August 2022](#), the Government of Canada announced funding from the HIV and Hepatitis C Community Action Fund to support community-based organizations in Vancouver and Edmonton in addressing the monkeypox outbreak
 - This is part of a [\\$1 million commitment](#) to support community-based organizations across the country

Clinical presentation

- The [Government of Canada describes the symptoms of monkeypox in two stages](#) that typically develop five to 21 days after exposure and last between two and four weeks:
- Stage one symptoms may include fever, headache, chills, swollen lymph nodes, muscle pain, back pain, joint pain, and exhaustion
- Stage two symptoms include a rash that develops on the face, extremities, or other parts of the body one to three days after the fever, and usually lasts between 14 and 21 days as it changes through different stages before it falls off as a scab

Diagnosis

- Diagnosis of monkeypox can be done by a healthcare provider, according to the [Government of Canada's website](#)
- Symptoms usually resolve within a few weeks and are often mild, but in rare cases, death can occur
- One recent [news report](#) indicated that the limited surveillance of monkeypox in Canada and the time it takes to diagnose and send samples for confirmation to the National Microbiology Laboratory in Winnipeg makes it likely that Canada is weeks behind in identifying the true scope of the spread of monkeypox in the country
- As of 25 May 2022, there were [16 confirmed cases of monkeypox in Canada](#), a large increase from the first case count only a week prior
- To [support the monkeypox response in Canada](#) and conduct testing for jurisdictions that are not performing their own, PHAC's Health Portfolio Operations Centre, Incident Management Structure and the National Microbiology Laboratory (NML) have been activated to Level 2
- PHAC [defines a probable case](#) of monkeypox as a person of any age who presents with an unexplained acute rash or lesion(s) as well as one or more of the following:

	<ul style="list-style-type: none"> ○ Has an epidemiological link to a probable or confirmed case of in the 21 days prior to the onset of symptoms ○ Has reported travel history to or residence in a location where monkeypox was reported in the 21 days prior to the onset of symptoms ● A confirmed case of monkeypox is defined by PHAC as a person who is laboratory confirmed for monkeypox by detection of unique sequences of viral DNA either by real-time PCR and/or sequencing <p>Prognosis</p> <ul style="list-style-type: none"> ● Vaccination with the smallpox vaccine within four days and up to 14 days after initial contact with an infected monkeypox case can protect against monkeypox with greater than 85% efficacy ● Canada’s Minister of Health, Jean-Yves Duclos announced on 24 May 2022 that Canada has a supply of Imvamune vaccines and therapeutics from the National Emergency Strategic Stockpile (NESS) that they will maintain as they work on rolling out a response plan <p>Treatment</p> <ul style="list-style-type: none"> ● Treatment for monkeypox is mainly supportive and there are no licensed antiviral drugs available to treat monkeypox ● According to a Montreal news report, the federal government will be sending vaccines and other “therapeutics” to Québec to help the province address the recent outbreak of monkeypox
British Columbia	<p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> ● As of 30 August 2022, there are 137 cases of monkeypox in British Columbia ● The British Columbia Centre for Disease Control maintains a webpage about monkeypox for healthcare providers with information about clinical presentation, transmission, management of suspected cases (including diagnosis and testing), infection prevention and control, and treatment ● The British Columbia Centre for Disease Control also maintains a webpage about monkeypox for the public that contains information about the current situation, how it spreads, symptoms, what to do if you have been exposed, what to do if you become ill, vaccination, travel, and recommendations for Two-spirit, gay, bisexual, transgender and queer communities, and guidance for event planning during Pride ● The British Columbia Centre for Disease Control publishes a weekly monkeypox epidemiological summary to provide insights into the populations affected by monkeypox in the province <ul style="list-style-type: none"> ○ Current data from British Columbia points to the importance of close, intimate contact during sex in driving the spread of monkeypox <p>Prevention and control</p> <ul style="list-style-type: none"> ● The British Columbia Centre for Disease Control maintains a webpage about monkeypox for healthcare providers with information about clinical presentation, transmission, management of suspected cases (including diagnosis and testing), infection prevention and control, and treatment ● On 20 May 2022, the Provincial Health Officer of British Columbia issued a notice of duty to report all suspected cases of monkeypox as per the Reporting Information Affecting Public Health Regulation of the <i>Public Health Act</i> ● The British Columbia Centre for Disease Control has produced a factsheet with recommendations for Two-Spirit, gay, bisexual, transgender and queer communities

- The [Provincial Infection Control Network of British Columbia](#) has issued interim infection prevention and control guidance for monkeypox in health care setting which covers patient placement, hand hygiene, personal protective equipment, patient transport, cleaning and disinfection, laundry, and waste management
- The [monkeypox vaccination campaign in British Columbia](#) is guided by the principles of maximizing benefit, equity and transparency
- Currently, populations at greatest risk for being exposed to monkeypox [are eligible for vaccination](#)
 - This includes individuals who are transgender people or those who identify as belonging to the gay, bisexual and other men who have sex with men community and have one or more risk factors for monkeypox exposure
- Given [current vaccine shortages](#), the British Columbia Centre for Disease Control notes that the monkeypox vaccine is reserved for Canadian residents and those visiting British Columbia for extended periods of time, and people should not travel to the province for the purpose of obtaining the vaccine
- Eligible patients are now able to receive a [second dose](#) of vaccine 28 days after their first dose
- Currently, second doses are being offered as either a [subcutaneous or intradermal injection](#)

Clinical presentation

- The [British Columbia Centre for Disease Control](#) maintains a webpage about monkeypox for healthcare providers with information about clinical presentation, transmission, management of suspected cases (including diagnosis and testing), infection prevention and control, and treatment
- The British Columbia Centre for Disease Control highlights that clinicians should be aware of the [differential diagnosis](#) of lesions associated with monkeypox as these symptoms may also present with the following infections:
 - Herpesviruses
 - Syphilis
 - Chancroid
 - Other poxviruses
 - Lymphogranuloma venereum
- The British Columbia Centre for Disease Control states that the [disease generally occurs in two stages](#)
 - The first stage often includes symptoms such as fever, chills, headache, swollen lymph nodes, body pain, and fatigue and lasts two to three weeks
 - The second stage typically starts one to five days after the first stage and includes rashes as well as sores that change over time

Diagnosis

- Vancouver Coastal Health has produced [standard operating procedures](#) for health professionals for the clinical assessment, testing, and public health follow up of monkeypox
- The British Columbia Centre for Disease Control has published [monkeypox testing guidelines for primary care](#) which has information regarding the clinical presentation, who to test, how to collect specimens, swab types, and how to advise patients with suspected monkeypox

	<ul style="list-style-type: none"> • The British Columbia Centre for Disease Control maintains a webpage about monkeypox for healthcare providers with information about clinical presentation, transmission, management of suspected cases (including diagnosis and testing), infection prevention and control, and treatment • The British Columbia Centre for Disease Control runs in-house PCR testing for monkeypox <ul style="list-style-type: none"> ○ Sample collection from individuals with skin lesions involves dry swabs or swabs in Universal Transport Medium and does not require approval from the British Columbia Centre for Disease Control Microbiologist ○ For individuals without skin lesions and who are suspected to be in the first stage of illness, oropharyngeal swabs, nasopharyngeal swabs, EDTA blood and urine can be considered for testing, but clinicians must contact the British Columbia Centre for Disease Control Microbiologist or their local hospital microbiologist before sample collection ○ For individuals who are suspected to have passed the first and second clinical stages of illness, urine collection can be considered, but clinicians must contact the British Columbia Centre for Disease Control Microbiologist or their local hospital microbiologist before sample collection <p>Treatment</p> <ul style="list-style-type: none"> • The British Columbia Centre for Disease Control maintains a webpage for health professionals about monkeypox treatment options that briefly outlines the potential for using tecovirimat, cidofovir, brincodofovir, and vaccinia immunoglobulin <ul style="list-style-type: none"> ○ It is noted that treatment with oral tecovirimat can be considered on a case-by-case basis ○ The use of cidofovir, brincodofovir, and vaccinia immunoglobulin is not recommended
Alberta	<p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> • As of 25 August 2022, 31 cases of monkeypox have been confirmed in Alberta • The Chief Medical Officer’s 3 June 2022 notice stresses that the risk is low to the general population, but the virus can affect anyone in close contact with a case (and is not limited to spread via intimate sexual activities) • The Chief Medical Officer’s 20 May 2022 notice for Alberta Health Services medical staff included a note about monkeypox <ul style="list-style-type: none"> ○ The note included background information about monkeypox and reminded physicians about mandatory reporting for rare or emerging communicable diseases and the need to notify the Medical Officer of Health regarding any suspected cases of monkeypox • The Government of Alberta has produced a factsheet about the Monkeypox virus outbreak that covers the following topics: transmission, symptoms, prevention (both on an individual and community level), testing, treatment, vaccination, and travelling outside Canada • The Alberta Medical Association hosted a webinar on 29 June 2022 about Monkeypox in Alberta for community physicians • The Alberta Health Service and Alberta Precision Laboratories have produced a vlog about monkeypox and the testing infrastructure for monkeypox available in Alberta <p>Prevention and control</p> <ul style="list-style-type: none"> • Currently, Alberta residents who self-identify as meeting the following criteria are eligible for vaccination: <ul style="list-style-type: none"> ○ Individuals who belong to the gay, bisexual and other men who have sex with men community and have either a recent diagnosis of a sexually transmitted infection, are planning to (or have in the past 90 days) have sex outside of a mutually monogamous relationship, or have attended or worked in a venue for sexual contact in the past 90 days ○ Sexual contacts of the above-described groups

	<ul style="list-style-type: none"> ○ Staff and volunteers in setting, venues, or events where sexual activities between men take place ● Pre-exposure vaccination for eligible individuals is available in nine cities across Alberta ● The Alberta Health Service has produced vaccine information sheets for the Imvamune Monkeypox/smallpox vaccine (Bavarian Nordic) targeted at both clinicians as well as a separate sheet targeted at the public ● The Alberta Health Service has produced infection prevention and control measures for healthcare providers working with patients suspected to have monkeypox <p>Diagnosis</p> <ul style="list-style-type: none"> ● The Public Health Laboratory and Alberta Precision Laboratories produced a memo for all physicians and clinicians regarding testing for Monkeypox, which contains in-depth background information, information about the virological diagnosis of Monkeypox, what to do if clinicians suspect a patient has Monkeypox, and details about specimen collection ● Monkeypox testing is recommended for individuals with acute rash or ulcers with or without systemic symptoms and in the past 21 days had one or more of the following risk factors: <ul style="list-style-type: none"> ○ Sexual contact with a new, anonymous, or multiple partners ○ Sexual contact with someone who had a new, anonymous, or multiple partners ○ Significant contact with someone who has skin lesions with no known alternate cause ○ Contact with a known or probable case of monkeypox ● Clinicians must consult with the virologist on-call at the provincial laboratory prior to the collection of samples for monkeypox testing
Saskatchewan	<p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> ● Monkeypox does not spread easily from person to person and is primarily spread through prolonged face-to-face close contact, touching bodily fluids of a person who is sick with the disease, or from exposure to contaminated objects ● On 15 July 2022, Saskatchewan’s second case was reported not to be epidemiologically linked to the first case identified 13 July 2022 ● On 13 August 2022, the Saskatchewan Health Authority warned the public about an “elevated risk” of contracting monkeypox through anonymous sexual contact as a result of the recently identified cases associated with this source of transmission <p>Prevention and Control</p> <ul style="list-style-type: none"> ● An information sheet on Imvamune, including general information about the vaccine, its administration (including intradermal injection), and eligibility criteria, was updated on 3 October 2022 ● The Saskatchewan Health Authority released Interim Infection Prevention and Control Guidelines for monkeypox ● Saskatchewan will be offering vaccines offering protection against monkeypox to close, high-risk contacts of an infected person if cases are found in the province ● Information about eligibility for Imvamune smallpox and monkeypox vaccine is available in English and French through the Saskatchewan government website
Manitoba	<p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> ● Spread occurs when a person comes into close contact with an infected animal, human, or materials contaminated with the virus

	<p>Prevention and control</p> <ul style="list-style-type: none"> • As of 6 October 2022, Manitoba health has set the eligibility criteria for monkeypox vaccination as cisgender, transgender or two-spirit people who self-identify as belonging to the gay, bisexual and other men who have sex with men (gbMSM) community and who meet at least one of the following criteria: <ul style="list-style-type: none"> ○ Have received a diagnosis of a sexually transmitted infection in the past year ○ Have had two or more sexual partners in the past 90 days ○ Have attended locations for sexual contact (e.g., bathhouses or sex clubs) or are planning to ○ Have had anonymous sex in the past 90 days (i.e., using apps, online sites, formal/informal gatherings) or are planning to ○ Engaged in sex work or plan to, as a worker or client ○ Any sexual contacts of individuals described above ○ Individuals who self-identify as sex workers, regardless of self-identified sex/gender • Eligible Manitobans can begin booking monkeypox vaccine appointments again as of 11 August 2022 • Following Manitoba's first confirmed monkeypox case, the province announced on 26 August 2022 that it has expanded the criteria for vaccination eligibility • As of 13 September 2022, 902 doses of vaccine have been administered across Manitoba <p>Clinical presentation</p> <ul style="list-style-type: none"> • Symptoms include fever, malaise, headache, backache, chills, weakness, and swollen lymph nodes <p>Diagnosis</p> <ul style="list-style-type: none"> • Manitoba is actively monitoring for monkeypox cases, although none have been identified yet <p>Treatment</p> <ul style="list-style-type: none"> • Treatment of monkeypox is mainly supportive, but in severe cases antivirals may be considered
Ontario	<p>Biology</p> <ul style="list-style-type: none"> • Monkeypox is an orthopoxvirus caused by the Monkeypox virus <p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> • Monkeypox can be transmitted from animals to humans or by contact with infected lesions, skin scabs, body fluids, or respiratory secretions, and by being in contact with materials contaminated with the virus (clothing, bedding) <ul style="list-style-type: none"> ○ Human-to-human transmission of monkeypox is uncommon, but it may occur through respiratory droplets or contact with bodily fluids, skin lesions, and contaminated materials • There is possible transmission during the prodromal period (when early symptoms such as fever, malaise, and headache appear) and the potential for airborne transmission • A Toronto report dated 7 June 2022 also noted that monkeypox can be transmitted from contact with infected animals through bites/scratches and wild game meat preparation <ul style="list-style-type: none"> ○ It is not as transmissible as COVID-19 ○ Monkeypox is most infectious from onset of initial lesions until the scabs have fallen off and new skin is present • A report by Public Health Ontario dated 13 June 2022 indicated that transmission from mother to infant may occur via vertical transmission across the placenta (which can lead to congenital monkeypox) or during close contact after birth • As of 4 October 2022, there are 674 confirmed cases of monkeypox in Ontario

- Of the confirmed cases, 73.6% are reported by Toronto Public Health
 - Of the confirmed cases, 99.3% are in males and 0.7% in females
 - In addition to the confirmed cases, there are 11 probable cases: 10 in males and one in a female
 - [Data collection on Monkeypox](#) cases and epidemiology is conducted through information entered in the Ontario Ministry of Health (MOH) integrated Public Health Information System (iPHIS) database and the Public Health Ontario Laboratory Information Management System
- Prevention and control**
- The [Ontario Monkeypox Investigation Tool](#) was created to record patient information and prevent future illness caused by Monkeypox
 - People can [lower their risk of exposure](#) by maintaining physical distance, frequently washing their hands, and wearing masks
 - [Precautions](#) should be taken until all scabs have fallen off and new skin is present
 - The airborne/droplet/contact precautions should be used: measures include airborne isolation rooms (AIR) with negative pressure ventilation and when AIRs are not available, a patient can be placed in a single room with the door closed with a single toilet
 - If these measures are not feasible, patients should wear a medical mask and cover exposed lesions with clothing, sheets, or a gown, especially during transport across hospital facilities
 - Healthcare workers should wear a fit-tested and sealed N-95 mask, gloves, gown, and eye protection (face shield or goggles)
 - Soiled linens should be cleaned to prevent dispersal of microorganisms
 - Waste (dressings) should be disposed according to facility-specific guidelines for infectious waste
 - Healthcare-grade cleaning agents with a Drug Identification Number (DIN) should be used
 - [Precautionary measures](#) include isolation, wearing PPE, good hand hygiene, avoiding contact with animals that could carry the virus, avoiding contact with bedding or laundry in contact with sick animals or humans
 - Standard household cleaning disinfectants can be used to kill the virus
 - Talking to sexual partners about sexual health and using barriers such as gloves and condoms
 - Avoid sharing toothbrushes, sex toys, and drug use supplies
 - Avoid prolonged face-to-face contact, especially indoors
 - Stay home if you are sick, and encourage others to do the same
 - [Asymptomatic patients](#) can be managed in a primary care setting, vaccination clinics and other outpatient settings such as sexual health clinics
 - A [report by the Ontario Ministry of Health](#) dated 29 August 2022 provides updated Imvamune guidelines for healthcare providers
 - Given the current supply constraints, Ontario is using a single dose of Imvamune to limit transmission; two doses are recommended for moderately to severely immunocompromised individuals and certain laboratory employees
 - Individuals who have had a confirmed case of monkeypox are not recommended to receive the monkeypox vaccine at this time due to the limited utility of the vaccine
 - Imvamune may contain trace amounts of antibiotics (gentamicin and ciprofloxacin) and egg products, so these individuals should be monitored for an extra 15 minutes after getting vaccinated
 - People with atopic dermatitis may have more frequent and intense reactions after vaccination

- A [report by Public Health Ontario](#) dated 13 June 2022 indicated that self-isolation must be maintained until all scabs have fallen off, new skin is present, and they have been cleared by their public health unit (no longer considered infectious)
 - An AIIR is not required for specimen collection
 - It is recommended that hand hygiene facilities be available in laundry areas, and that clothes from monkeypox cases be machine washed using 70-degree Celsius hot water and regular laundry detergent
 - Routine environmental disinfection must occur in emergency rooms and outpatient settings, inpatient rooms, and shared showering facilities
- A [technical report by Public Health Ontario](#) dated 28 May 2022 describes interim case and contact management guidelines for local public health units based on information from selected public health organization such as the CDC, the United Kingdom Health Security Agency, and the WHO
 - For those self-isolating, it is recommended to cover skin lesions by wearing long clothing, designating one person to care for the person who is self-isolating
 - It is recommended to wear gloves when handling laundry, to not shake or agitate soiled laundry dispersing infectious particles
 - Contaminated dressings and bandages should not be disposed of with household garbage or in landfills, so consider using a biohazard/environmental remediation company to transport waste safely to the hospital for safe processing
 - A detailed guide to assessing risk of exposure is provided in the document
- On 15 September 2022, Ontario's Chief Medical Officer Dr. Kieran Moore reported that Ontario has [administered 32,175 first doses of monkeypox vaccine](#)
- A [City of Toronto report dated 19 July 2022](#) discussed the side effects of the Imvamune vaccine, including redness, pain or swelling at the injection site, tiredness, headaches, and muscle aches
 - It is recommended to contact a healthcare provider or to go to the emergency department if the following symptoms appear: hives, swelling of the face or mouth, trouble breathing or shortness of breath, chest pain or a pounding heart
 - Adverse events following immunization should be reported to Toronto Public Health (TPH)
- A [report dated 21 June 2022](#) indicated that the Imvamune vaccine is approved in Canada as prophylaxis for protection against monkeypox pre-exposure or post-exposure to monkeypox (post-exposure vaccines should be given within 4 days but can be given up to 14 days after last exposure)
 - Based on Ontario Ministry of Health guidelines, Imvamune vaccine clinics are available for people 18 years or older who are transgender, nonbinary, two-spirited, or cisgender who self-identify as a man and belong to the community of gay, bisexual and other men who have sex with men as well as one of the following:
 - Diagnosed with a bacterial STI in the past 2 months
 - Had 2 or more sexual partners within the past 21 days or are planning to
 - Attended venues for sexual contact within the past 21 days or plan to or work/volunteer in these settings
 - Had casual or anonymous sex in the past 21 days
 - Engage in sex work or plan to, and their sexual contacts
 - Cis-gender women are not eligible for the vaccine unless identified as a close contact of a case
- [Prior vaccination against smallpox](#) provides some cross-protection to monkeypox

- A [report by the Ontario Ministry of Health](#) dated 28 May 2022 provides guidance for the Imvamune vaccine as post-exposure prophylaxis (PEP)
 - Imvamune is a live 3rd generation replication deficient smallpox vaccine, developed to provide an alternative for the vaccination of immunocompromised individuals with atopic dermatitis who couldn't receive replicating smallpox vaccines
 - Based on extrapolation from animal studies and smallpox vaccines in humans, a 0.5 mL dose of Imvamune within 4 days of exposure may prevent infection or lessen disease severity
 - It was authorized by Health Canada in 2020 for active immunization against smallpox, monkeypox, and related orthopoxviral infections in adults at high risk of exposure from a confirmed or probable case
 - Individuals who have been in the same premises as a confirmed or probable case but with no known risk exposure are not recommended to received PEP
 - There is limited data on the use of Imvamune in pregnancy and for individuals with severe immunosuppression, and the vaccine is not authorized for use in individuals under 18 years of age (although it has been offered to children in previous U.K. monkeypox incidents)
 - It is not recommended to co-administer Imvamune with other vaccines and to reschedule other vaccines until 14 days after Imvamune; however, Imvamune should not be delayed for individuals who have recently received another vaccine
 - Side effects of Imvamune include pain, erythema, induration, and swelling at injection site, and fatigue, headache, myalgia, and nausea, and reactions resolved within the first 7 days following vaccination
 - Older generations of smallpox vaccines have been associated with myocarditis, while cardiac events of special interest (AESIs) were found in 1.4% of Imvamune recipients
 - Imvamune should be stored frozen or and thawed at room temperature, with more details indicated in [this report](#)
- A [report by the Ontario Ministry of Health](#) dated 14 June 2022 (revised 30 September 2022) provides Imvamune guidelines for healthcare providers
 - The report provides an overview of using Imvamune in special populations: clinical trials have included people living with HIV, moderately to severely immunocompromised individuals eligible for pre-exposure vaccinations are recommended to receive two-doses; pre- versus post-exposure data is also discussed; no clinical trials have been conducted in pregnant individuals, although approximately 300 pregnancies have been reported to the manufacturer with no safety issues, and there is no data on whether the vaccine is excreted in breastmilk although this is unlikely since the vaccine is nonreplicating; the vaccine has not been studied in youth under 18 although it has been given to children as PEP in the U.K. for monkeypox; people with atopic dermatitis may have more intense and frequent reactions after vaccination
- A [report by Ottawa Public Health](#) dated 2 August 2022 states that people who have an allergy to the following ingredients are not eligible for the Imvamune vaccine: tromethamine, sodium chloride, hydrochloric acid, bromobutyl rubber stopper, gentamicin, ciprofloxacin, egg cell DNA and protein, and benzonase
 - For pre-exposure prophylaxis, it is recommended that people wait at least 4 weeks after receiving a live vaccine and at least 2 weeks after receiving an inactivated vaccine before receiving the monkeypox vaccine
- An [environmental scan by Public Health Ontario](#) published in August 2022 on guidance for monkeypox waste disposal indicates that items contaminated in the care of a monkeypox patient should be considered infectious waste and discarded according to jurisdictional protocols

- It is recommended that individuals use strong bags, double bag waste, and ensure good hand hygiene and gloves when managing waste
- On 30 September 2022, the Ontario Ministry of Health released an updated version of guidelines for the storage and handling of monkeypox vaccines
 - The guideline is aimed at Public Health Units and those handling vaccines storage and administration

Clinical presentation

- The [Ministry of Health released a fact sheet](#) comparing monkeypox, chickenpox, and hand-foot-and-mouth disease (HFMD) dated 13 July 2022
 - The incubation period of monkeypox is 5-21 days, while chickenpox is 10-21 days, and HFMD is 3-7 days
 - Fever occurs 1-3 days before rash onset for monkeypox, while those unvaccinated to chickenpox have mild fever 1-2 days before rash with fevers in vaccinated individuals being less common, and in HFMD fever occurs 1-2 days before oral vesicles
 - Lymphadenopathy may occur in monkeypox patients, while less common in chickenpox and HFMD
 - Rashes usually appear at site of inoculation for monkeypox; in chickenpox rashes usually appear on the chest, back, and face, then spreading to the rest of the body (and may appear on the hands and soles of feet in immunocompromised people); for HFMD, vesicles usually appear on the mouth and then appear on other parts of the body
 - In monkeypox, rashes usually progress through macules, papules, vesicles, pustules, and crusting/scab and may have central umbilication; in chickenpox, the pleomorphic rash rapidly progresses through macules, papules, vesicles, and crusting/scab; in HFMD, macules at times with vesicles may break open and progress to crusting/scab
 - Rash duration is usually 14-28 days for monkeypox, 4-7 days for unvaccinated chickenpox; 7-10 days for HFMD
- [Most people recover from monkeypox within two to four weeks](#), although severe illness can occur in some individuals
- [Symptoms](#) include fever, chills, headache, myalgias, swollen lymph nodes in the neck and groin area, fatigue, and rashes (on face, limbs, palm of hands and soles of feet, mucous membranes like mouth and genitals) that follow one to three days after the onset of other symptoms
- The [Ontario Ministry of Health](#) recorded other symptoms including chills/sweats, back pain/ache, sore throat/cough, coryza (inflammation of the mucous membrane of the nose), and distress
- [Public Health Ontario](#) stated that in the 33 confirmed cases as of 21 June 2022, the most commonly reported symptoms included rashes, oral/genital lesions, swollen lymph nodes, headache, fever, chills, myalgia, and fatigue
- An [updated report](#) dated 13 June 2022 indicates that the incubation period averages 6-13 days (range 5-21 days), during which individuals are not considered infectious
- [The rashes or lesions](#) often begin on the face and spread to other parts of the body, and generally appear [1-3 days after fever](#), though in some recent cases, it appears before fever or other symptoms
- In [recent cases](#), the rashes appear around the mouth, genital or anorectal areas

Diagnosis

- A [report by Public Health Ontario](#) updated on 25 July 2022, which outlines testing indications, states that no cases of monkeypox have been reported in children in Ontario; PHO conducts laboratory testing on all pediatric specimens requesting monkeypox, of which 80% of patients are detected for enterovirus

	<ul style="list-style-type: none"> ○ Children with rashes consistent with enterovirus and without contact with a confirmed case do not require monkeypox testing ○ It is recommended to submit a maximum of 3 skin lesion specimens per patient as detection sensitivity from skin specimens is high (90%) in patients with confirmed monkeypox infection ○ Nasopharyngeal throat swabs and blood specimens are not recommended in patients who have skin lesions that can be swabbed or material that can be submitted for testing as skin lesions have higher viral loads ○ Testing for herpesviruses may be ordered on the same specimens being tested for monkeypox ○ Urine is not a routine specimen for monkeypox testing but may be considered for collection ● According to a report by the City of Toronto dated 27 July 2022, people can get tested for mokeypox at a healthcare provider’s office, walk-in clinic, or sexual health clinic ● Monkeypox can be diagnosed with symptoms, a laboratory test, and risk factors such as exposure to a monkeypox case as well as travel to a region with a confirmed case ● Last updated on 17 June 2022, Public Health Ontario released a set of comprehensive testing indications related to specimen collection and handling, preparation of specimen prior to transport, requisitions and testing kit ordering, test frequency and turnaround time, test methods, PCR test interpretation, as well as reporting guidelines <p>Prognosis</p> <ul style="list-style-type: none"> ● As of 22 August 2022, of the 582 confirmed cases of monkeypox in Ontario, 99.5% are male, 3.1% have been hospitalized, 0.3% have been admitted to the ICU, and no deaths have been reported ● As of September 6, 2022, of the 631 confirmed cases of monkeypox in Ontario, 99.4% are male and 0.6% female, 2.9% have been hospitalized, 0.3% have been admitted to the ICU, and no deaths have been reported ● As of 4 October, 2022, of the 674 confirmed cases of monkeypox in Ontario, 99.3% are male and 0.7% female, 2.8% have been hospitalized, 0.3% have been in the ICU, and no deaths have been reported ● The most infected people will recover on their own within 2-4 weeks, and that the infection is rarely fatal <p>Treatment</p> <ul style="list-style-type: none"> ● The report also mentioned Tecovirimat (TPoxx) treatment in Canada (three 200 mg capsules twice daily for 14 days), which is not authorized for monkeypox, but can be given by a licensed healthcare professional for severe monkeypox infections
Québec	<p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> ● The Ministry of Health and Social Services in Quebec states that monkeypox contagiousness is limited compared to other viruses like the flu and COVID-19 because it is contracted by prolonged and close contact with an infected person ● As of 11 October 2022, 520 cases of monkeypox have been reported in Québec <p>Clinical presentation</p> <ul style="list-style-type: none"> ● Infected people have mild symptoms, disappearing after 14-21 days and do not require hospitalization ● Symptoms include fever, headache, muscle aches, back pain, swollen lymph nodes, chills, and fatigue ● Rashes also occur often on the face and may spread to other parts of body such as the genitals <p>Prevention and control</p> <ul style="list-style-type: none"> ● People who think they are infected should self-isolate at home, wear a mask, cover legions, and avoid direct contact with others

- They should also monitor themselves for symptoms for 21 days and avoid sexual relations until 21 days after last contact
- A [report](#) last updated on 20 May 2022 stated that high-risk contacts of a confirmed or probable case of monkeypox may be vaccinated with a single dose within 4 days of exposure, and a second dose only if risk of exposure is present 28 days later
- In Quebec, a [vaccine](#) is available to protect against monkeypox, which can be administered before or after exposure, but the vaccine is reserved for people targeted by public health authorities
 - A post-exposure vaccine may be given within the past 14 days if you have had: direct contact with skin, fluids, or items that have been contaminated with fluids or secretions of someone with monkeypox symptoms, or prolonged close contact with someone with monkeypox symptoms (3 or more hours less than 1 metre away without a mask)
 - If a person has symptoms of monkeypox at time of vaccination, the post-exposure vaccine may not be given
 - A pre-exposure vaccine may be giving if you are a man who is having or will have sex with another man in Montreal in the following situations: sex with more than one regular partner, sex in a place where sexual activities take place, sex in exchange for money, goods, or services
 - Staff and volunteers in a social setting or event where sexual activities take place may also receive the pre-exposure vaccine
 - Men with one regular sex partner do not need to receive the pre-exposure vaccine
- [Vaccine side effects](#) for less than 10% of people include pain, redness, swelling, induration, itching at the injection site, nausea, headache, fatigue, and muscle pains
 - Side effects for less than 1% of people include heat, nodule, hematoma, discolouration at the injection site, limb pain, joint pain, fever and chills
 - Side effects for less than 0.001% of people include swollen gland, skin peeling, nose or throat injection, difficulty sleeping, dizziness, and numbness
 - Side effects for less than 0.0001% of people include pimples, anesthesia, nerve damage, hives, facial swelling, night sweats, profuse sweating, weakness, and migraines
- According to a report by the [Government of Quebec](#) dated 25 August 2022, people suspected of having monkeypox will be contacted by the public-health authority and will be required to cover the lesions, avoid contact with people who are more at risk (pregnant women, children under 12, immunocompromised people), avoid sexual contact, wear a mask when less than one metre from another person indoors and outdoors, avoid sharing any items, avoid any activities in which uncovered lesions may be in contact with the skin, mucous membranes, or objects of another person, adopt general hygiene measures, inform sexual partners with whom they have been in contact with since the onset of symptoms
- As of [12 July 2022](#), Québec's Ministry of Health and Social Services stated that healthcare workers have administered 10, 832 doses of the smallpox vaccine
- As of [4 August 2022](#), Québec's public health director announced that the province is expanding access to the monkeypox vaccine beyond Montreal to other regions across the province
- [Second doses of monkeypox vaccine](#) began to be administered on 6 October 2022 after Quebec received a new supply of vaccines
 - In the city of Montreal, vaccinations are being offered at five clinics with or without appointments

Diagnosis

	<ul style="list-style-type: none"> • The Ministry of Health and Social Services in Quebec confirmed the first two cases of monkeypox on 19 May 2022, and 20 other cases of genital ulcer lesions are under investigation • As of 19 May 2022, all suspected cases have affected men who have sex with other men <p>Treatment</p> <ul style="list-style-type: none"> • Antivirals could be an option, but their clinical usefulness must be evaluated before they are recommended
New Brunswick	<p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> • New Brunswick confirmed its first monkeypox case on 12 August 2022 <p>Prevention and control</p> <ul style="list-style-type: none"> • On 16 September 2022, Public Health New Brunswick expanded access to monkeypox vaccines and encouraged the following groups to get a monkeypox vaccine: cisgender, transgender or two-spirit individuals who are 18 years of age and older and who also self-identify as belonging to the gay, bisexual or men-who-have-sex-with-men community, and who are or plan to become sexually active with more than one partner • On 28 July 2022, New Brunswick announced that it has 140 doses of vaccine and is continuing to develop guidance on how to manage cases and contacts, and surveillance activities as Newfoundland announces its first probable case • New Brunswick is staying informed on the monkeypox outbreak to better prepare if the virus arrives in the Maritimes <p>Diagnosis</p> <ul style="list-style-type: none"> • New Brunswick identified a suspected case of monkeypox, but the patient was not assessed until after symptoms had passed
Nova Scotia	<p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> • Nova Scotia reported two cases of visitors from out-of-province who experienced symptoms while in Nova Scotia and later tested positive in their home province, but has not identified any cases fully within the province • On 23 August 2022, Nova Scotia confirmed its first confirmed monkeypox case in a resident of the province <p>Prevention and control</p> <ul style="list-style-type: none"> • Nova Scotia released guidance for management of cases and contacts of monkeypox on 15 September 2022 • Nova Scotia is actively monitoring the monkeypox outbreak but to date has no reported cases • On 15 September 2022, the first pre-exposure clinic opened in the province and offers the monkeypox vaccine to people at highest risk of exposure, such as members of the LGBTQ community
Prince Edward Island	<p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> • Prince Edward Island is actively monitoring the monkeypox outbreak, but to date has no reported cases <p>Prevention and control</p> <ul style="list-style-type: none"> • On 14 September 2022, Prince Edward Island released an information sheet on Imvamune detailing eligibility and general information about the vaccine • As of 23 June 2022, the provincial health organization is starting to prepare for potential cases <ul style="list-style-type: none"> ○ The province’s Chief Public Health Officer stated that the province has 140 doses of vaccine to be given four weeks apart for anyone who is identified as a close contact to a confirmed or suspected case, and multiple courses of antiviral treatment

	<ul style="list-style-type: none"> ○ As of 11 August 2022, the province is offering monkeypox vaccinations to people travelling to areas where case counts are high and those who might be at a higher risk of exposure ● Prince Edward Island’s chief public health officer announced that the province has a supply of TPOXX (tecovirimat) antiviral treatment for anyone who becomes ill with the monkeypox virus and a limited supply of Imvamune vaccine for post-exposure prophylaxis (PEP) available for anyone identified as a close contact of a positive case
Newfoundland and Labrador	<p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> ● On 28 July 2022, Newfoundland and Labrador identified its first probable case of monkeypox ● Newfoundland and Labrador is actively monitoring the monkeypox outbreak, but to date has no reported cases <p>Diagnosis</p> <ul style="list-style-type: none"> ● Newfoundland and Labrador can test for monkeypox through Canada’s National Microbiology Laboratory <p>Prevention and control</p> <ul style="list-style-type: none"> ● Newfoundland and Labrador is receiving an increased supply of Imvamune and will be expanding eligibility for doses of Imvamune, a vaccine used for smallpox that also provides protection against monkeypox <ul style="list-style-type: none"> ○ A focused vaccination campaign for those at highest risk of infection based on the current evidence and knowledge base of monkeypox will be launched ● As of 22 August 2022, two-spirit (Indigenous people who identify as non-binary in Indigenous culture) transgender and non-transgender males who self-identify as being part of the LGBTQ2S+ community and have had intercourse with two or more partners within the last 90 days can receive vaccination ● Sexual contacts of people who fall into the eligible categories and sex workers are also eligible for vaccination
Yukon	<p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> ● On 21 July, the Government of Yukon confirmed their first case of monkeypox, but did not provide any other details in order to protect the privacy of the individual ● In Canada, the majority of cases at this time are men who reported intimate sexual contact with other men; however, it's important to stress that the risk of exposure to the monkeypox virus is not exclusive to any group or setting <p>Prevention and control</p> <ul style="list-style-type: none"> ● The Government of Yukon is actively working with Public Health Agency of Canada and other public health partners to investigate the spread of monkeypox and assess the situation ● Contacts of a known case of monkeypox may be offered vaccination to reduce their risk of severe disease ● On 3 October 2022 Yukon updated the Yukon immunization program manual, adding the smallpox and monkeypox vaccine
Northwest Territories	<p>Diagnosis</p> <ul style="list-style-type: none"> ● The Government of Northwest Territories released an algorithm for health professionals to identify suspect cases of monkeypox <p>Prevention and control</p> <ul style="list-style-type: none"> ● A news report indicates that a limited supply of the Imvamune vaccine has been distributed to the Northwest Territories ● These doses are reserved for people who have been identified as close contacts of probable or confirmed cases of monkeypox

	<ul style="list-style-type: none"> • The province is following the National Advisory Committee on Immunization's guidance on administering the Imvamune vaccine • On 23 September 2022 the Government of Northwest Territories released a vaccine information sheet about monkeypox vaccine
Nunavut	<p>Epidemiology (including transmission)</p> <ul style="list-style-type: none"> • As of 25 August 2022, there have been no positive or suspected cases in the territory <p>Prevention and control</p> <ul style="list-style-type: none"> • The Nunavik Regional Board of Health and Social Services indicated that vaccines are available in the territory; however, there is limited available information on which and what type of vaccine • The vaccine Imvamune is being supplied by the federal government in limited regions in the country with confirmed outbreaks; the vaccine is used for the treatment and prevention of monkeypox • The Nunavut territorial government has received 140 doses of the vaccine from the federal government stockpile, with plans for more to follow <ul style="list-style-type: none"> ○ For now, the vaccine is being reserved for those who have had close contact with someone who has tested positive and for men who have had or will have sexual contacts with at least one new male partner • The Nunavik Regional Board of Health and Social Services recommends that anyone with symptoms should call their local community service centers or Nursing Stations to ask for an appointment to confirm • Public health measures, such as self-isolating, wearing a mask and covering skin lesions until healed are also suggested <p>Clinical presentation</p> <ul style="list-style-type: none"> • According to the Nunavik Regional Board of Health and Social Services, signs and symptoms include headache, fever, chills, sore throat, general discomfort, fatigue, muscle and back pain, joint pain, swollen lymph nodes, night sweats, rash and skin lesions <p>Prognosis</p> <ul style="list-style-type: none"> • According to the Nunavik Regional Board of Health and Social Services, the illness is mild and resolves on its own within 2 to 4 weeks for most people • Some people could develop complications such as secondary infections, pneumonia, sepsis, encephalitis, meningitis and eye infections