McMaster University | HEALTH FORUM

Living Evidence Profile #6.6

(5 August 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
- Clinical presentation
- Diagnosis
- Prognosis
- Treatment

We identified 16 new evidence documents since the last update of this LEP, of which 13 were deemed highly relevant. The newly added highly relevant evidence documents include:

- one systematic review;
- one protocol for a systematic review; and
- 11 single studies.

This LEP also includes evidence documents from the previous version that we deemed to still be highly relevant, for a total of 90 highly relevant documents.

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 1 August 2022. 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.

We outline in narrative form below our key findings related to the question from highly relevant evidence documents, and based on experiences from other 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

The ongoing outbreak of monkeypox continues to escalate across the globe. A day after the last update, the WHO Director-General declared that the outbreak is a Public Health Emergency of International Concern (PHEIC) on 23 July 2022, in response to the rising case count and public-health concern.(1) The twice weekly updated WHO global trends epidemiological report and health emergency dashboard indicated that there are 25,054 confirmed cases and at least 11 deaths,(2) whereas the U.S. CDC global map reported a total of 26,208 confirmed cases as of 3 August 2022.(3) Most of the reported cases are primarily concentrated in the European region and the Region of the Americas.(2,3)

New available evidence on monkeypox continue to emerge. In terms of biology, 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 MPXV-2022 strains, which led the authors of one study to conclude that the current monkeypox virus is prone to novel mutations (published 29 July 2022).(4)

A pre-print medium-quality systematic review and three pre-print single studies confirmed previous research evidence in addition to providing new updates to the epidemiology of monkeypox.(5-8) The pre-print medium-quality systematic review (last updated 24 July 2022) reported that 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. Additionally, of the six countries with increasing confirmed cases, the U.S. 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 authors of the review concluded 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) A network modelling study (pre-print) simulated a monkeypox epidemic among men who have sex with men (MSM), 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).(6) A single study (pre-print) described the global spatial landscape of orthopoxviruses (including monkeypox), and found significant spatial heterogeneity with population susceptibility between 57% to 96% based on demographic changes and waning of cross-protective immunity within a nation (published 30 July 2022).(7) Finally, a single study (pre-print) found that monkeypox virus DNA was consistently detected in wastewater samples across the majority of test sites in the Greater Bay Area in

California, with increasing concentrations of DNA over time between 19 June to 20 July 2022 (last updated 26 July 2022).(8)

Three single studies described the clinical presentation of monkeypox, which all reported similar findings as the last evidence update. A single study reported on clinical features and treatment responses among seven individuals with monkeypox between 2018 and 2020 in the U.K (published August 2022).(9) In addition, a single study characterized the clinical presentation of monkeypox among 197 patients at infectious-disease centres and sexual-health centres in London, U.K. between May and July 2022, and found that all patients were men with a mean age of 38 years, identified as gay or bisexual, and/or part of the MSM community.(10) All individuals presented with mucocutaneous lesions, mostly on genitals or in the perianal area (published 28 July 2022). Similarly, a single study reported on an international case series that describe the presentation, clinical course, and outcomes of 528 PCR-confirmed monkeypox cases between 27 April to 24 June 2022. The authors reported that 98% of patients were men and identified as gay or bisexual. Viral DNA was detected in 29 of 32 of persons in whom seminal fluid was analyzed (published 21 July 2022).(11)

We identified three pre-print single studies and one protocol that reported on the prevention and control of monkeypox, including vaccination and infection prevention. The findings include:

- a single study (pre-print) that reported on the determinants of vaccination intention and self-isolation intention after exposure among 394 people in the MSM community in the Netherlands, where authors suggested that efforts to increase vaccination, intentions to isolate and ability to self-diagnose should be aimed at MSM with the highest risk (last updated 31 July 2022);(12)
- a single study (pre-print) that found robust and durable humoral and cellular immune responses for up to six months after vaccination with the two-dose COH04S1 vaccine in a subgroup of 20 volunteers in a phase one clinical trial (last updated 29 July 2022);(13) and
- a single study (pre-print) that identified widespread surface contamination in occupied patient rooms, on healthcare worker personal protective equipment after use, and in doffing areas, which led the authors to conclude that that there was significant contamination in isolation facilities and potential for aerosolization of monkeypox virus during specific activities (Last updated 21 July 2022).(14)

In addition, the upcoming systematic review and meta-analysis is focused on assessing the effectiveness of monkeypox vaccines (anticipated completion data 25 August 2022).(15)

Finally, we identified one single study focusing on diagnosis, where the authors found 100% clinical performance to detect monkeypox with adapted PCR test kits from SARS-CoV-2 (Published 29 July 2022).(16)

Key findings from the jurisdictional scan

Key findings from the jurisdictional scan are summarized below according to each of the categories in the organizing framework.

Epidemiology (including transmission)

Confirmed case numbers continue to rise, especially in the U.S. where testing capacity has drastically increased in recent weeks. The Public Health Agency of Canada (PHAC) reported a total of 890 cases of monkeypox in Canadian provinces and territories as of 3 August 2022, with 423 cases confirmed in Québec, 373 cases in Ontario, 13 cases in Alberta, 78 cases in British Columbia, two cases in Saskatchewan, and one newly reported case in Yukon. Across other jurisdictions, as of 2 August 2022,

482 cases were reported in Belgium, 2,239 in France, 505 cases in Italy, 925 cases in the Netherlands, 4,577 cases in Spain, 88 in Sweden, 2,759 in the UK, and 6,326 in the U.S. As of 28 July 2022, 45 cases were reported in Australia. As of 27 July 2022 Portugal has reported 536 confirmed cases. In Germany, as of 3 August 2022, 2,781 cases have been reported. Therefore, the highest increased reported cases were in the U.S.(17-25)

Contact with the monkeypox virus has been reported for the first time in Nova Scotia, Newfoundland and Labrador, and the Yukon. On 28 July 2022, Newfoundland and Labrador identified its first probable case of monkeypox.(26) 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.(27) On 21 July 2022, 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.(28)

Jurisdictions continue to monitor patterns of transmission and case characteristics. In Canada, Dr. Tam stated at a press conference on 27 July 2022 that over 99% of the monkeypox cases in Canada for whom information is available are male with a median age of 36 years.(29) The UK Health Security Agency released a technical briefing about the monkeypox outbreak in England on 19 July 2022 which places the monkeypox outbreak at level 2 of potential transmission (transmission within a defined sub-population).(30)

Prevention and control

Several jurisdictions in Canada are providing updates about vaccine procurement, dissemination, and the status of their availability. In Canada, 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.(29) New Brunswick announced on 28 July 2022 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.(31) In Alberta, Alberta residents who self-identify as meeting specific criteria are eligible for vaccination.(32) Additionally, 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.(33)

Reports about vaccine procurement, dissemination, and availability also continue across other jurisdictions. The U.K has now procured a total of 130,000 doses of the smallpox vaccine from Bavarian Nordic to offer to those eligible for vaccination.(30) Two vaccines are available in Australia for the prevention of monkeypox, which are the 3rd generation JYNNEOS and the 2nd generation ACAM2000.(34) In France, more than 32,000 doses have been delivered to the territories as of 27 July 2022. Additionally, the third generation MVA-BN (Imvanex and Jynneos) vaccines, which the High Authority of Health has listed as being interchangeable, is being used for pre-exposure vaccination in France.(35) Further, 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 and a news report indicates that the Imvanex vaccine has been administered in Portugal since July 16.(36,37) In the UK, 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.(38)

As jurisdictions continue to adjust to new procurement and dissemination of vaccines, additional approaches to improve vaccine communication and guidance have occurred. On 25 July 2022, France

began a digital campaign on preventive vaccinations.(39) In the U.S., the CDC indicates that the only FDA-approved dosing regimen for the JYNNEOS vaccine is a two-dose series, with few exceptions and advises that 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 four weeks after orthopoxvirus vaccination before receiving a Moderna, Novavax, or Pfizer-BioNTech COVID-19 vaccine.(40) In Quebec, a list of vaccine side effects has been provided, including relatively common (>10% of people) all the way to extremely rare (0.0001% of people) side effects.(41)

Aside from vaccines, jurisdictions are continuing to release or update guidance to help reduce the risk of transmission. 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. On 21 July 2022, the federal government of Canada announced that it is providing funding for community-based organizations in regions most impacted by the monkeypox outbreak to reach out to 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. 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. Finally, on 26 July 2022, Australia's Chief Medical Officer, Professor Paul Kelly, declared the monkeypox (MPX) situation a Communicable Disease Incident of National Significance.(42-44)

Diagnosis

As case counts rise and strain testing capacity, some jurisdictions are adjusting testing protocols. 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. 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 probably cases. According to a Health Agencies Update in the US, over 8000 tests have been available weekly through more than 67 public health laboratories, however, clinicians continue to face difficulties in ordering tests. Outsourcing tests to commercial laboratories is expected to clear up the backlog in the U.S.(17,45)

Prognosis

Spain has recorded its first two deaths in patients infected with monkeypox, with both deaths occurring in young men who suffered from encephalitis and meningoencephalitis caused by the infection, respectively.(46) Two other deaths have also occurred in Brazil and India. In Canada, 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 with no deaths reported.(47)

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	Clinical presentation	Diagnosis	Prognosis	Treatment
Guidelines (non-robust)	1	-	-	-	1	-	1	1
Full systematic reviews	6	-	4(1)	-	3	1	1	1
Rapid reviews	0	-	-	-	-	-	-	-
Non-systematic reviews	17	4	14	8	5	6	2	3
Protocols for reviews or rapid reviews that are underway	12	-		2(1)	8	-	-	1
Titles/questions for reviews that are being planned	0	-	-	-	-	-	-	-
Single studies	109	16	54(4)	23(7)	20(4)	14(2)	8	14

*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	• 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 MPXV-2022 strains, concluding that the current monkeypox virus is prone to novel mutations (Published 29 July 2022)	• None identified

Epidemiology (including transmission)	• A medium-quality systematic review synthesized the evidence on the reproduction number and incubation period for the monkeypox virus in six countries between May and July 2022
	  ○ 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 men who have sex with men (MSM) 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)
	• A single study (pre-print) described the global spatial landscape of orthopoxviruses (including monkeypox), and found significant spatial heterogeneity with population susceptibility between 57% to 96% based on demographic changes and waning of cross-protective immunity within a nation
		• The Public Health Agency of Canada (PHAC) reported a total of 890 cases of monkeypox in Canadian provinces and territories as of 03 August 2022, with 423 cases confirmed in Québec, 373 cases in Ontario, 13 cases in Alberta, 78 cases in British Columbia, two cases in Saskatchewan, and one newly reported case in Yukon
		• 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 28 July 2022, Newfoundland and Labrador identified its first probable case of monkeypox
		  ○ 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
		• Cases continue to rise across other jurisdictions as well, with as of 02 August 2022, 482 in Belgium, 2,239 in France, 505 cases in Italy, 925 cases in the Netherlands, 4,577 cases in Spain, 88 in Sweden, 2,759 in the UK, and 6,326 in the U.S.
		  ○ As of 28 July 2022, 45 cases were reported in Australia
		  ○ 2,781 cases have been reported in Germany as of 03 August 2022
		  ○ As of, 27 July 2022 Portugal has reported 536 confirmed cases
		• 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 Helath and the Environment report published on 2 August 2022 in the Netherlands indicates that anyone

	○ 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 • 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) • A single study (pre-print) deployed digital PCR assays that target genomic monkeypox virus (MPXV) DNA in the routine wastewater surveillance program in the Greater Bay between 19 June to 20 July 2022, and found that MPXV DNA was consistently detected in samples across the majority of test sites (8/9), with increasing concentrations of DNA over time ○ Robust surveillance of MPXV 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)	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 ○ 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 which places the monkeypox outbreak at level 2 of potential transmission (transmission within a defined sub-population) • 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
Clinical presentation	• A single study reported on the clinical features and treatment responses of seven individuals with monkeypox between 2018 and 2020 ○ 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; 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 an infectious disease centres and sexual health centres in London, U.K. between May and July 2022	• None identified

	○ All 197 patients were men with a mean age of 38 years and identified as gay, bisexual, or MSM, which all presented with mucocutaneous lesions, mostly on genitals or in the perianal area ○ 170 participants reported systemic illness, with the most commons 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 ○ 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)	
Prevention and control	• A single study (pre-print) reported on determinants of vaccination intention and self-isolation intention after exposure among 394 people in the MSM community in the Netherlands ○ 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	*Vaccine procurement, dissemination, and availability* • 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 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

	aimed at MSM 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
	  ○ 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 vs. 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 MPXV from infected patients admitted to isolation rooms in the UK to inform infection prevention and control measures
	  ○ 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 MPXV during specific activities (Last updated 21 July 2022)
		• 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, which are the 3rd generation JYNNEOS and the 2nd generation ACAM2000
		  ○ The Australian Technical Advisory Group on Immunization has identified key risk groups recommended to receive vaccination
		• As of 27 July 2022 in France, 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
		Vaccine communication and guidance
		• 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. 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
		• 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
		  ○ 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 *Other measures* • 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 • 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 • 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: ○ Sexual contact with a new, anonymous, or multiple partners ○ Sexual contact with some 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 (MPX) situation a Communicable Disease Incident of National Significance
Diagnosis	• A single study adapted existing PCR test kits from SARS-CoV-2 for the use in monkeypox diagnoses, which the	• As case counts rise and strain testing capacity, some jurisdictions are adjusting testing protocols

	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)	○ 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 probably cases ○ According to a Health Agencies Update in the US, over 8000 tests have been available weekly through more than 67 public health laboratories, however, clinicians continue to face difficulties in ordering tests • Outsourcing tests to commercial laboratories is expected to clear up the backlog in the US
Prognosis	• None identified	• 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 ○ 99.5% of cases are male, 0.5% are female • 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
Treatment	• None identified	• None identified

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	• One single study that explored the population transmission of Monkeypox virus (MPXV) 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 ○ 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 a newly emerging clade that has genomes from the ongoing 2022 multi-country outbreak (published 12 July 2022) • 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 MPXV 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	• Countries and provinces examined characterize monkeypox as a viral zoonotic disease caused by an orthopoxvirus

	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)	• 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
	  ○ 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)
	• Crowdsourced predictions of global projections for confirmed monkeypox cases and deaths between 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 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 critical considering the current outbreak outside of Africa (published 6 July 2022)
	• A single study that explored the population transmission of Monkeypox virus (MPXV) 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
		• 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
		  ○ 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.
		  ○ 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
		• 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"

	monkeypox strains, with clade CB splitting off 560-860 years ago ○ 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 ○ 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-umbilicated and pseudo-pustular skin lesions (93.8%), asthenia (66.6%), and fever (52.1%) ○ 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	• 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 ○ 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: ○ 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: ○ 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 • 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

	May 2022 identified that all patients were men who have sex with other men (MSM) who presented with skin lesions ○ 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 ○ 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 ○ 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	○ 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 • An infected pregnant women may also pass monkeypox on to their developing fetus

	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 o 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 o Almost half the respondents (47%) feel that their knowledge level about monkeypox is poor or very poor o 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 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 o 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 (MPX) 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 (MSM) sexual contact network, and recommended that ongoing support and public health messaging should be implemented for prevention and early detection within the MSM 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) o 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 o 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: o 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 o 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 ○ 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 MPX cases across nine countries (Austria, Belgium, France, Germany, Italy, Portugal, Spain, Sweden, and the Netherlands) ○ 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)	

	• A single study reported two cases of monkeypox within two white British men
	  ○ 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
	  ○ 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)
	• 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
	  ○ 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)
	  ○ 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
	  ○ 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)
	• 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
	  ○ 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
	  o 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
	  o 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
	  o The highest incidence was among 10-19-year-old males, the cohort reporting the highest proportion of animal exposures (37.5%)
	  o 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
	  o 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
	  o 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 o 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 o Forty-three participants (34.4%) were IgG positive for anti-orthropoxvirus antibodies; however, amongst those born after the era of routine smallpox vaccination only four (6.3%) were positive for anti-orthropoxvirus antibodies o The authors concluded that presence of anti-orthropoxvirus antibodies in individuals born after the era of smallpox vaccination suggests the possibility of asymptomatic circulation of an orhtorpoxvirus (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 documented human outbreak of the west African strain of the monkeypox virus o Data was collected with a standardized form based on a case definition of human monkeypox from previously established guidelines o Diagnosis of the human monkeypox virus infection was confirmed by viral identification with real-time PCR and detection of antibodies o 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 o 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 ○ 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 and other animals in the Central African region (Published 21 August 2017)	
Prevention and control	• 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	• 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 placement, hand hygiene, personal protective equipment, patient transport, cleaning and disinfection, laundry, and waste management • 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

	• 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
	  ○ 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
	  ○ 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
	  ○ These tools were deployed within 24 hours of identification of a patient with suspected MPX, with the full suite in production within 4 days of confirmation of the diagnosis of MPX (Published 16 June 2022; Pre-print)
		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
		  ○ 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
		• 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
		  ○ 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

	• The WHO developed the following interim guidance on risk communication and community engagement (Published 2 June 2022):
	  ○ "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
	  ○ 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)
	  ○ 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
		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
		  ○ 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 U.K. for monkeypox; people with atopic dermatitis may have more intense and frequent reactions after vaccination
		• The Provincial Infection Control Network of British Columbia has released interim infection prevention and control guidance for monkeypox in health care settings
		  ○ 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

	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 monkeypox and many patients were born after the cessation of smallpox eradication program (Published 12 November 2020) • 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) ○ 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-	• 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: ○ 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 • In Germany, The Standing Committee on Vaccination (STIKO) has put forth a recommendation to vaccinate individuals against the Monkeypox virus with Imvanex ○ 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)

	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): o 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 o 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 o 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) o 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	• 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 o 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 o Talking to sexual partners about sexual health and using barriers such as gloves and condoms o Avoid sharing toothbrushes, sex toys, and drug use supplies o Avoid prolonged face-to-fact contact, especially indoors o 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 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) o An AIIR is not required for specimen collection o 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 o 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 o 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 o 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 ○ 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 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
		  ○ 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
		  ○ 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
		  ○ 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 • 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: ○ 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 ○ 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 ○ 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.

		○ 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
Clinical presentation	• A medium quality systematic review (pre-print) that investigated the neurological and psychiatric presentations of monkeypox (MPX) virus infection found that the most frequent clinical feature of neuropsychiatric presentations of MPX 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 critical considering the current outbreak outside of Africa (published 6 July 2022) • 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) ○ 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	• 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 ○ 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 • 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 ○ 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 MSM with an age range of 23-64 years ○ 18 cases had reported symptom onset and the most likely date of exposure related to attending an event

	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
	  ○ 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, 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%) (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)
	  ○ Viraemia, prolonged virus DNA detection in upper respiratory tract swabs, low mood, and PCR-positive deep tissue abscess were some of the disease features
		○ 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 parts of the body with the rash tending to be more concentrated on the face and extremities than on the trunk
		  ○ 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
		• 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

	• A pre-print of a prospective observational study conducted in the Democratic Republic of Congo reported the findings from 216 patients with monkeypox
	  ○ 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 within one to 10 days spread over the body) (Published 12 November 2020)
	• A non-systematic review described that monkeypox is similar to smallpox but generally less severe (Published December 2019)
	  ○ 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 cclinical 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) • 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 ○ 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)	
Diagnosis	• 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 was able to assess 2,009 samples, 36.6% (n=395 individuals) of which were non-variola Orthopoxvirus positive ○ 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) ○ 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	• 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 ○ 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

	• 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	

Prognosis	• 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)
	  ○ Five (12.5%) of the cases died
	  ○ 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)
		• 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
		• 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)

	○ 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) ○ The study concluded that maternal monkeypox infection may have adverse consequences for the fetus without apparent correlation with severity of maternal disease	
Treatment	• 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 ○ 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) (Published 24 May 2022) • A non-systematic review noted that monkeypox is primary 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) ○ 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	• 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 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 • 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 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)

	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) ○ 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)	• 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 vaccina 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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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 to COVID-19. 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	• Epidemiology (including transmission)	• 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 between May and 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 Source 5/10 (McMaster forum AMSTAR rating)	Last updated 26 July 2022
Rapid reviews	None identified		
Non-systematic reviews	None identified		
Protocols for reviews that are already underway	• Prevention and control	Monkeypox vaccine effectiveness: A systematic review and meta-analysis Source	Anticipated completion date 25 August 2022
Titles and questions for reviews being planned	None identified		

Single studies	• Clinical presentation	• This study reports the clinical features, longitudinal virological findings, and response to off-label antivirals in 7 patients with monkeypox who were diagnosed from 2018-2020 (4 men and 3 women) • 3 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 • Symptoms include viraemia and reactive low mood; 5 patients spent more than 3 weeks in isolation due to prolonged PCR positivity • 3 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 2 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 6 weeks after hospital discharge Source	Published August 2022

	• Epidemiology (including transmission)
	• Prevention and control
		• This study uses a network model to simulate a monkeypox epidemic among men who have sex with men (MSM)
		• This model follows a separable temporal exponential family random graph model of a Belgian population of MSM
		  ○ Additionally, a population of men who have sex with men with a high rates of partner change (HR-MSM) was included in this model
		  ○ The model was refined to include main and casual partnerships among low-risk and HR-MSM 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
			Last updated 31 July 2022 (Pre-print)

		○ 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 probability and how this varies according to the type of sexual contact • Additionally, the model did not capture superspreading events Source	
	• Prevention and control • Diagnosis	• This study investigated the ability to self-diagnose a potential monkeypox infection, and determinants of vaccination intention and self-isolation intention after exposure among MSM in the Netherlands • A cohort of 394 men who have sex with men (MSM) 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 ○ 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 ○ Among socio-demographic determinants, MSM 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 ○ Those who were retired, first-generation and second-generation migrants showed higher intentions to self-isolate	Last updated 31 July 2022 (Pre-print)

		○ MSM 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 • The study suggests that efforts to increase vaccination, intentions to isolate and ability to self-diagnose should be aimed at MSM 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 Source	
	• Epidemiology (including transmission)	• The single study (pre-print) described the global spatial landscape of orthopoxviruses (including monkeypox), and found significant spatial heterogeneity with population susceptibility between 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 ○ The authors noted that large countries such as India, China, Brazil, the U.S., and central and western Africa were notable areas for susceptibility Source	Last updated 30 July 2022 (Pre-print)
	• Biology	• 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 MPXV-2022 strains • The authors also reported that ten proteins in the monkeypox virus are prone to novel mutations	Published 29 July 2022

		Source	
	•		
	• Prevention and control	• 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 • 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 Source	Last updated 29 July 2022 (Pre-print)
	• Prevention and control • Diagnosis	• 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 Source	Published 29 July 2022
	• Clinical presentation	• 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 between May and 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	Published 28 July 2022

		• 170 participants reported systemic illness, with the most commons 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 Source	
	• Epidemiology (including transmission) • Prevention and control	• To determine whether monkeypox viral DNA can be detected and monitored in wastewater, this study deployed digital PCR assays that target genomic monkeypox (MPXV) 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 MPXV 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 MPXV was used on a subset of samples ○ There was no significant difference between results of the two assays, proving that MPXV DNA detections using the first assay were true positives • Robust surveillance of MPXV 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 Source	Last updated 26 July 2022 (Pre-print)
	• Epidemiology (including transmission) • Prevention and control	• This study investigated environmental contamination with MPXV 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	Last updated 21 July 2022 (Pre-print)

		○ 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) • This study identified widespread surface contamination in occupied patient rooms, on healthcare worker personal protective equipment after use, and in doffing areas ○ 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 MPXV DNA (7/12) ○ 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 MPXV 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 Source	
	• Clinical presentation	• 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	Published 21 July 2022

		• 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 • 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 Source	
	• Biology	• In this study, a new metagenomic sequencing approach for extraction and enrichment of monkeypox (MPXV) 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 • Specifically, when comparing the original read counts with the final quality controlled read counts, the MPXV 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 Source	Last updated 31 July 2022 (Pre-print)

	• Epidemiology (including transmission)
	• Clinical presentation
		• This study uses the Zeno SWATH MS to study the plasma proteome of a group of MPX patients with a similar infection history and clinical severity
		• The study population includes five patients with PCR-confirmed MPXV infection
		  ○ 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
			Last updated 29 July 2022 (Pre-print)

		• Proteomic measurements were performed on day 1-3 after admission to the hospital
		  ○ The proteomes of MPX 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
		  ○ All MPX 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 MPX and COVID-19 infection
		• This study demonstrates the utility of proteomics in analyzing rare diseases
		• This study indicated that the partial overlap between MPX 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 MPX patients
		Source	

	• Epidemiology (including transmission)	• This study quantified the population of men who have sex with men (MSM) 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 MSM and an estimated 65,100 men in North Carolina identify as MSM • 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 MSM in North Carolina to reduce the risk of monkeypox infection Source	Last updated 21 July 2022 (Pre-print)

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	• Prevention and control • Prognosis • Treatment	• 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
Full systematic reviews	• Clinical presentation	• The aim of this systematic review was to investigate the neurological and psychiatric presentations of monkeypox (MPX) 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 • The most frequent clinical feature of neuropsychiatric presentations of MPX was myalgia, followed by headache, fatigue, seizure, confusion, and encephalitis • Less evidence regarding the psychiatric sequelae of MPX 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 MPX outbreak Source (8/11 AMSTAR rating)	Published 11 July 2022 (pre-print)
	• Clinical presentation • Diagnosis • Prognosis • Treatment	• 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	Published 14 June 2022 (pre-print)

Type of document	Relevance to question	Key findings	Recency or status

		• The results of the databases and grey literature search showed:
		  ○ 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
		• 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
		Source (7/9 AMSTAR rating)	

	• Epidemiology (including transmission)	• 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	Literature last searched 7 September 2020

Type of document	Relevance to question	Key findings	Recency or status
		• 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 Source (4/11 AMSTAR rating)	
	• Epidemiology (including transmission)	• 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 Republic, but data are insufficient to measure trends in secondary attack rates and case-fatality rates • 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 Source (AMSTAR rating 6/11)	Literature last searched 15 August 2018

Type of document	Relevance to question	Key findings	Recency or status
Rapid reviews	No rapid reviews identified		
Non-systematic reviews	• Prevention and control	• 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 Source	Published 28 June 2022
	• Prevention and control	• The WHO released interim guidance on vaccines and immunization for monkeypox • 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 o 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 o Children, pregnant women, and immunocompromised persons (including persons living with HIV) may be considered	Published 14 June 2022

Type of document	Relevance to question	Key findings	Recency or status
		• 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 Source	
	• Epidemiology (including transmission)	• 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 • 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 Source	Published 9 June 2022
	• Epidemiology (including transmission) • Clinical Presentation	• 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	Published 8 June 2022

Type of document	Relevance to question	Key findings	Recency or status
		sex, human immunodeficiency virus positivity, and a history of previous sexually transmitted infections Source	
	• Epidemiology (including transmission)	• 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 o 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 o 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	Published 4 June 2022

Type of document	Relevance to question	Key findings	Recency or status
		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: o 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 o 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 o 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 Source	
	• Prevention and control	• 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: o Predominantly affected communities, which needs to be properly considered in all RCCE activities and consideration for a risk of stigmatization o Uncertainty, in which there are many unknown aspects of the disease in this early stage of the outbreak	Published 2 June 2022

Type of document	Relevance to question	Key findings	Recency or status
		○ 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: ○ 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 ○ 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 Source	
	• Epidemiology	• Monkeypox cases have been growing across an expanding number of non-endemic countries in recent months	Published 31 May 2022

Type of document	Relevance to question	Key findings	Recency or status
		○ 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 Source	
	• Epidemiology (including transmission) • Prevention and control	• 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 • 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	Published 22 May 2022

Type of document	Relevance to question	Key findings	Recency or status
		• Quarantine or exclusion from work are not necessary during the contact tracing period if there are no symptoms present or begin to develop Source	

	• Epidemiology
	• Prevention and control
		• 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)
		  ○ 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
		  ○ 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
		Source
			Published 23 May 2022

	• Biology
	• Epidemiology (including transmission)
	• Prevention and control
	• Clinical presentation
	• Diagnosis
	• Treatment
		• 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
		  ○ 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
			Published 12 November 2020

Type of document	Relevance to question	Key findings	Recency or status
		• 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 • Antivirals such as Tecovirimat, Cidofovir and Brincidofovir have shown efficacy in in vitro and animal studies, but their effectiveness in humans is unknown o Brincidofovir may have an improved safety profile compared to Cidofovir o Cidofovir and Brincidofovir may be considered in severe cases of monkeypox o Human clinical trials of Tecovirimat suggested that the drug was safe and tolerable with only minor side effects Source	
	• Epidemiology (including transmission) • Prevention and control • Clinical presentation • Diagnosis • Prognosis • Treatment	• The frequency and geographic distribution of human monkeypox cases across West and Central Africa have increased in recent years o Monkeypox is largely found in rodents and has been detected in squirrels, rats, mice, and monkeys o Indirect or direct contact with live or dead animals is assumed to be the main source of human monkeypox infections o 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

Type of document	Relevance to question	Key findings	Recency or status

		• The clinical presentation of monkeypox is similar to smallpox but generally less severe
		  ○ 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
		• 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
		  ○ 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
		  ○ 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
		Source	

Type of document	Relevance to question	Key findings	Recency or status
	• Biology • Epidemiology (including transmission) • Prevention and control • Clinical presentation • Diagnosis • Prognosis • Treatment	• 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 • 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 Source	Published April 2019
	• Biology • Epidemiology (including transmission) • Clinical presentation	• 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	Published January 2019

Type of document	Relevance to question	Key findings	Recency or status
		• The exact mode of transmission of the monkeypox virus to humans remains unknown ○ 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 • The authors noted that there is a need to build public health and surveillance capacities across Africa Source	
	• Epidemiology (including transmission)	• 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
	• Prevention and Control	• 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	Published February 2019

Type of document	Relevance to question	Key findings	Recency or status
		• The smallpox vaccine can offer a secondary prevention strategy to prevent infection of monkeypox in healthcare workers Source	
	• Biology • Clinical presentation • Diagnosis • Treatment	• Human monkeypox - After 40 years, an unintended consequence of smallpox eradication Source	Published 14 July 2020
Protocols for reviews that are already underway	• Epidemiology (including transmission)	Monkeypox as a sexually transmitted disease: a systematic review Source	Anticipated completion date 23 December 2022
	• Clinical presentation	• The prevalence and spectrum of neurological and psychiatric presentations in infections with monkeypox: a systematic review Source	Anticipated completion 8 July 2022
	• Epidemiology (including transmission)	• The epidemiology of monkeypox disease Source	Anticipated completion 8 July 2022
	• Epidemiology (including transmission)	• Epidemiology of monkeypox in Africa: A systematic review Source	Anticipated completion 10 July 2022
	• Clinical presentation	• The human monkeypox virus and the neurologist: A systematic review Source	Anticipated completion 31 July 2022
	• Clinical presentation	• Prevalence of clinical manifestations and complications in monkeypox patients: A systematic review and meta-analysis Source	Anticipated completion 31 July 2022
	• Epidemiology (including transmission) • Clinical presentation	• Epidemiology, clinical manifestations, and outcomes of monkeypox infection in humans: a systematic review and meta-analysis Source	Anticipated completion 30 August 2022
	• Epidemiology (including transmission) • Prevention and control	• 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
	• Clinical presentation	• The prevalence and spectrum of neurological and psychiatric presentations in infections with monkeypox: A systematic review Source	Anticipated completion 1 July 2022

Type of document	Relevance to question	Key findings	Recency or status
	• Clinical presentation • Prevention and control	• Maternal, congenital, and paediatric monkeypox infection – consequences and prevention – A living systematic review Source	Anticipated completion 31 August 2022
	• Epidemiology	• 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
	• Epidemiology	• Prevalence of monkeypox transmission by sexual contact transmission: Systematic review Source	Anticipated completion 30 July 2022
	• Epidemiology	• The epidemiology of monkeypox disease Source	Anticipated completion 8 July 2022
	• Epidemiology • Clinical presentation	• 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	• Prevention and control	• 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 Source	Published 17 July 2022 (pre-print)
	• Diagnosis	• 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	Published 15 July 2022

Type of document	Relevance to question	Key findings	Recency or status

		• This study reports that 2,009 samples were received and of those samples, 36.6% (n=395 individuals) were non-variola Orthopoxvirus positive
		  ○ 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
		• 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
		Source	

	• Epidemiology (including transmission)	• 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 Source	Published 15 July 2022 (pre-print)
	• Biology • Epidemiology (including transmission)	• MPXV is genetically structured in two major clades: clades 1 and 2/3 • This study explored the population transmission of Monkeypox virus (MPXV) in West Africa (WA) (clade 2/3), and the Congo Basin (CB) (clade 1)	Published 14 July 2022

Type of document	Relevance to question	Key findings	Recency or status
		• Complete MPXV 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 • 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 ○ 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 Source	
	• Biology	• 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	Published 12 July 2022

Type of document	Relevance to question	Key findings	Recency or status
		• 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 Source	
	• Prevention and control • Diagnosis	• 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 • 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 Source	Published 11 July 2022
	• Epidemiology (including transmission) •	• 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 ○ 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	Published 10 July 2022

Type of document	Relevance to question	Key findings	Recency or status
		• 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 • 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 Source	
	• Epidemiology (including transmission)	• 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	Published 8 July 2022 (pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		• 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 Source	
	• Epidemiology (including transmission)	• 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: o 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 o The estimated probability of 100 to 1000 deaths was 0.59, with a 0·23 probability on 1000 or more deaths o Probabilities for 10 to 100 cases by 1 July 2022 was 0.56 and 0.51 for USA and Canada, respectively o 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 Source	Published 7 July 2022
	• Epidemiology (including transmission) •	• 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	Published 5 July 2022 (pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		• 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 Source	
	• Epidemiology (including transmission) • Clinical presentation	• 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 • The study identified the following demographic characteristics of the 54 confirmed cases: o All patients identified as men who have sex with other men (MSM) o A median age of 41 years o 38 of 54 individuals were White and born in the UK o 13 of 54 individuals were living with HIV • The clinical characteristics included: o 36 of 54 individuals reported fatigue o 31 individuals reported fever o 10 individuals had no prodromal symptoms o All patients presented with skin lesions o 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 Source	Published 1 July 2022
	• Epidemiology (including transmission) • Clinical presentation	• 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	Published 6 July 2022 (pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		○ 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 outside of Africa, and that rapid field diagnostics are needed to optimize worldwide early detection and surveillance of monkeypox Source	
	• Epidemiology (including transmission)	• 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 Source	Published 1 July 2022
	• Epidemiology (including transmission)	• 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	Published 1 July 2022

Type of document	Relevance to question	Key findings	Recency or status
		• 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 Source	
	• Epidemiology (including transmission)	• This study built dynamic models to mimic the spread of the monkeypox virus (MPX) as an emerging zoonosis in a hypothetical metropolitan area, including high- and low-risk transmission among humans and animals to humans • 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 MPX 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 MPX 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 Source	Published 29 June 2022
	• Biology	• 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	Published 24 June 2022

Type of document	Relevance to question	Key findings	Recency or status
		• A mutational analysis shows signs of potential monkeypox human adaptation in ongoing microevolution Source	
	• Epidemiology (including transmission)	• 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 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 Source	Published 23 June 2022
	• Epidemiology (including transmission)	• 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	Published 23 June 2022

Type of document	Relevance to question	Key findings	Recency or status
		• 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 Source	
	• Diagnosis	• 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 Source	Last updated 23 June 2022 (Pre-print)
	• Prevention and control	• This study estimated the incubation period of the monkeypox virus (MPX) using United States data from 22 probable and confirmed patient cases reported from 17 May 2022 to 6 June 2022 • 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 Source	Published 21 June 2022
	• Prevention and control • Clinical presentation	• 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 (MPX) • 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	Published 16 June 2022 (pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		monitoring at Massachusetts General Hospital's special pathogens unit and treatment facilities: 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 MPX exposure, the next step was to conduct risk assessment and classification o Healthcare personnel were presented with a series of exposure scenarios and asked to identify which ones applied to their interactions with the index patient o 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 MPX, with the full suite in production within 4 days of confirmation of the diagnosis of MPX Source	
	• Clinical presentation	• 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	Published 14 June 2022

Type of document	Relevance to question	Key findings	Recency or status
		clinicians should be cognizant of exclusive genital lesions to offer timely ring vaccination Source	
	• Epidemiology (including transmission)	• 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) o The 18 cases used for data collection were all men that identified themselves as men who have sex with men (MSM) • 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 Source	Published 13 June 2022 (pre-print)
	• Epidemiology (including transmission)	• 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 MSM population (despite the absence of such patterns in past outbreaks) • It is plausible that monkeypox had a large transmission potential in the MSM 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 (R_0) for monkeypox over the MSM sexual contact network may be substantially larger than 1	Last updated 13 June 2022 (pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		• It was inferred that the non-sexually associated R_0 for monkeypox would be substantially lower than the R_0 for the MSM sexual network if the proportion of non-sexually associated cases remained low in the future; however, the authors warned that the R_0 may still be >1 if the R_0 for the MSM sexual network is high • It was recommended that ongoing support and public health messaging facilitates prevention and early detection among MSM with a large number of partners Source	
	• Epidemiology	• The Lancet correspondence describes the case of two white British men with reported MPX • 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 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 Source	Published 31 May 2022
	• Epidemiology (including transmission)	• This study assessed the effect of an enhanced surveillance approach to detect monkeypox virus (MPX) cases and measure the cumulate incidence of MPX 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	Published 25 May 2022

Type of document	Relevance to question	Key findings	Recency or status
		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 MPX were identified • The study showed that enhanced surveillance improved reporting of MPX in hotspots of LGAs across the priority states Source	
	• Clinical Presentation • Diagnosis • Prognosis • Treatment	• 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 • 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 Source	Published 24 May 2022
	• Clinical presentation	• A prospective observational study in the Democratic Republic of Congo reported 216 patients who were positive for monkeypox virus o The study reported three deaths, in addition to fetal death occurring in four of five patients who were pregnant at admission o Patients with fatal disease had higher viral DNA in blood, maximum lesion count, and on day of admission	Last updated May 29 2022 (Pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		○ 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 MPX rash (99.5%), and lymphadenopathy (98.6%) ○ 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 Source	
	• Epidemiology • Prevention and control	• 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 ○ 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 ○ Rapid field diagnostics should be adopted to optimize worldwide early detection and surveillance of monkeypox Source	Last updated 5 June 2022 (Pre-print)
	• Epidemiology (including transmission) • Prevention and Control • Clinical Presentation	• 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 ○ 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	Published 21 August 2021

Type of document	Relevance to question	Key findings	Recency or status
		• Contacts of Case 1 included household contacts, healthcare workers, hospital laundry workers, and members of the public ○ 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 Source	

	• Epidemiology (including transmission)
	• Clinical presentation
	• Diagnosis
		• 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
		• A confirmed monkeypox case requires detection of Orthopoxvirus or MPXV DNA with real-time polymerase chain reaction (PCR) or isolation of MPXV 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:
		  ○ 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
			Published 4 June 2021

Type of document	Relevance to question	Key findings	Recency or status
		○ 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 Source	
	• Clinical presentation • Prognosis	• 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 • 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 Source	Published 15 October 2020
	• Epidemiology (including transmission)	• 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	Published 8 July 2020

Type of document	Relevance to question	Key findings	Recency or status

		• 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:
		  ○ Frequent outbreaks with R<1 may occur due to involuntary human contact with animal reservoirs
		  ○ 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
		Source	

	• Epidemiology (including transmission)	• 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	Published April 2020

Type of document	Relevance to question	Key findings	Recency or status
		• 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 Source	
	• Clinical presentation • Prognosis	• 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 Source	Published 24 December 2019
	• Epidemiology (including transmission) • Clinical presentation	• 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	Published 25 November 2019

Type of document	Relevance to question	Key findings	Recency or status
		• 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 orhtorpoxvirus (which was most likely monkeypox) in human populations Source	
	• Epidemiology (including transmission) • Clinical presentation	• 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 Source	Published August 2019
	• Epidemiology (including transmission) • Prevention and control	• 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	Published 17 April 2019

Type of document	Relevance to question	Key findings	Recency or status
		• 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 Source	
	• Biology • Epidemiology (including transmission)	• 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	Published February 2019

Type of document	Relevance to question	Key findings	Recency or status
		well-functioning cold chain, that would have resulted in inconsistent and incomplete reporting Source	
	• Epidemiology (including transmission) • Prevention and control	• 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 • 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 Source	Published 20 December 2018
	• Treatment	• While smallpox was eradicated in 1980, the variola virus (VARV) causing smallpox, still exists ○ 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 Source	Published 5 July 2018

Type of document	Relevance to question	Key findings	Recency or status

	• Epidemiology (including transmission)
	• Prevention and Control
		• 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
		• Robust disease surveillance systems with initial and long-term financial and human resource investment are required to stop the further spread of monkeypox
		  ○ 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
		Source
			Published 16 March 2018

	• Diagnosis
	• Prevention and Control
	• Prognosis
	• Treatment
		• 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:
		  ○ 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:
		  ○ During hospitalization, pregnant women received antibiotics (amoxicillin, chloramphenicol via eye drops, and erythromycin, as well as gentamycin, if necessary) for
			Published 17 October 2017

Type of document	Relevance to question	Key findings	Recency or status
		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 MPXV infection experienced fetal demise • Findings of this study confirm that maternal MPXV infection may have adverse consequences for the fetus without apparent correlation with severity of maternal disease • Further studies should focus on the relatively high risk of fetal demise among pregnant women with MPXV Source	
	• Clinical presentation • Diagnosis	• 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 zoter 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 Source	Published 11 September 2017

Type of document	Relevance to question	Key findings	Recency or status
	• Biology • Clinical presentation • Diagnosis	• 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 morbidity, with clinical signs including pox lesions in the skin, eyes, mouth and nose • 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 Source	Published 21 August 2017
	• Biology	• This study evaluates the performance and added value of the MinION real-time TGS sequencing device for sequencing the complete genome of a MPXV 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 Source	Published 24 June 2022
	• Epidemiology (including transmission) • Prevention and control	• 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	Last updated 31 May 2022 (pre-print)

Type of document	Relevance to question	Key findings	Recency or status
		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" Source	
	• Epidemiology (including transmission)	• 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 Source	Published 28 May 2022
	• Epidemiology (including transmission) • Prevention and control • Treatment	• Imported monkeypox from international traveller, Maryland, U.S., 2021 Source	Published May 2022
	• Epidemiology (including transmission)	• Exportation of monkeypox virus from the African continent Source	Published 19 April 2022
	• Biology • Epidemiology (including transmission) • Prevention and control	• Monkeypox in a traveller returning from Nigeria - Dallas, Texas, July 2021 Source	Published 8 April 2022
	• Treatment	• New methylene blue derivatives suggest novel anti-orthopoxviral strategies Source	Published July 2021
	• Biology	• Genomic history of human monkey pox infections in the Central African Republic from 2001 to 2018 Source	Published 22 June 2021
	• Epidemiology (including transmission)	• Re-emergence of human monkeypox and declining population immunity in the context of urbanization, Nigeria, 2017-20 Source	Published April 2021
	• Epidemiology (including transmission) • Clinical presentation • Diagnosis • Prognosis • Treatment	• Human monkeypox virus infection in plateau state, north central Nigeria: a report of two cases Source	Published 30 December 2021
	• Diagnosis	• CRISPR/Cas9 as an antiviral against orthopoxviruses using an AAV vector	Published 9 November 2020

Type of document	Relevance to question	Key findings	Recency or status
		Source	
	• Prevention and control	• Imported monkeypox, Singapore Source	Published August 2020
	• Prevention and control	• Assessment of media reportage of monkeypox in southern Nigeria Source	Published January 2020
	• Biology • Epidemiology (including transmission) • Clinical presentation	• Monkeypox virus emergence in wild chimpanzees reveals distinct clinical outcomes and viral diversity Source	Published July 2020
	• Biology	• Comparison of multiplexed immunofluorescence imaging to chromogenic immunohistochemistry of skin biomarkers in response to monkeypox virus infection	Published 23 July 2020
	• Prevention and control	• Confidence in managing human monkeypox cases in Asia: A cross-sectional survey among general practitioners in Indonesia Source	Published June 2020
	• Prevention and control	• Knowledge of human monkeypox viral infection among general practitioners: a cross-sectional study in Indonesia Source	Published March 2020
	• Prevention and control	• Use of surveillance outbreak response management and analysis system for human monkeypox outbreak, Nigeria, 2017-19 Source	Published February 2020
	• Prevention and control	• 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
	• Epidemiology (including transmission)	• Do monkeypox exposures vary by ethnicity? Comparison of Aka and Bantu suspected monkeypox cases Source	Published January 2020
	• Epidemiology (including transmission)	• Temporal and spatial dynamics of monkeypox in democratic republic of Congo, 2000-2015 Source	Published September 2019
	• Epidemiology (including transmission) • Clinical presentation • Diagnosis	• Human monkeypox in Sierra Leone after 44-year absence of reported cases Source	Published May 2019

Type of document	Relevance to question	Key findings	Recency or status
	• Epidemiology (including transmission) • Treatment	• Intrafamily transmission of monkeypox virus, Central African Republic, 2018 Source	Published August 2019
	• Diagnosis	• Recombinase polymerase amplification assay for rapid detection of Monkeypox virus Source	Published September 2019
	• Biology • Diagnosis	• Molecular evidence of human monkeypox virus infection, Sierra Leone Source	Published June 2019
	• Biology • Epidemiology (including transmission) • Clinical presentation	• Diagnosis of imported monkeypox, Israel, 2018 Source	Published May 2019
	• Diagnosis	• Preliminary screening and in vitro confirmation of orthopoxvirus antivirals Source	Published 2019
	• Epidemiology (including transmission) • Prevention and control	• Two cases of monkeypox imported to the United Kingdom, September 2018 Source	Published September 2018
	• Epidemiology (including transmission)	• Investigation of an outbreak of monkeypox in an area occupied by armed groups, Central African Republic Source	Published June 2018
	• Diagnosis	• Intranasal monkeypox marmoset model: Prophylactic antibody treatment provides benefit against severe monkeypox virus disease Source	Published 21 June 2018
	• Biology	• Genomic characterization of human monkeypox virus in Nigeria Source	Published March 2018
	• Clinical presentation	• 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
	• Diagnosis	• Validation of a pan-orthopox real-time PCR assay for the detection and quantification of viral genomes from non-human primate blood Source	Published 3 November 2017

Type of document	Relevance to question	Key findings	Recency or status
	• Biology • Epidemiology (including transmission)	• Assessing monkeypox virus prevalence in small mammals at the human-animal interface in the Democratic Republic of the Congo Source	Published 3 October 2017
	• Epidemiology (including transmission)	• Varicella co-infection in patients with active monkeypox in the Democratic Republic of the Congo Source	Published September 2017
	• Prevention and control	• A single vaccination of non-human primates with highly attenuated smallpox vaccine, lc16m8, provides long-term protection against monkeypox Source	Published 24 July 2017
	• Biology	• Monkeypox virus host factor screen using haploid cells identifies essential role of GARP complex in extracellular virus formation Source	Published 12 May 2017
	• Epidemiology (including transmission)	• Presumptive risk factors for monkeypox in rural communities in the Democratic Republic of the Congo Source	Published 13 February 2017
	• Treatment	• Pharmacokinetics and efficacy of a potential smallpox therapeutic, Brincidofovir, in a lethal monkeypox virus animal model Source	Published 3 February 2021
	• Epidemiology (including transmission) • Clinical presentation	• A tale of two viruses: co-infections of monkeypox and varicella zosvter virus in the Democratic Republic of Congo Source	Published 7 December 2020
	• Prevention and control	• 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
	• Biology	• Analgesia during monkeypox virus experimental challenge studies in prairie dogs (Cynomys ludovicianus) Source	Published 1 July 2019
	• Biology	• Characterization of monkeypox virus dissemination in the black-tailed prairie dog (Cynomys ludovicianus) through in vivo bioluminescent imaging Source	Published 26 September 2019

Type of document	Relevance to question	Key findings	Recency or status
	• Biology	• Monkeypox virus phylogenetic similarities between a human case detected in Cameroon in 2018 and the 2017-18 outbreak in Nigeria Source	Published April 2019
	• Treatment	• Effects of treatment delay on efficacy of Tecovirimat following lethal aerosol monkeypox virus challenge in cynomolgus macaques Source	Published 22 September 2022
	• Diagnosis	• Evaluation of the GeneXpert for human monkeypox diagnosis Source	Published 8 February 2017
	• Treatment	• 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	
Rapid reviews	
Non-systematic reviews	
Protocols for reviews that are already underway	
Titles and questions for reviews being planned	
Single studies	Monkeypox - a description of the clinical progression of skin lesions: a case report from Colorado, USA The first monkeypox virus infection detected in Taiwan-the awareness and preparation Antivirals with Activity Against Monkeypox: A Clinically Oriented Review Monkeypox Virus Containment: The Application of Ring Vaccination and Possible Challenges
Other types of documents	Monkeypox Virus Infection in Humans across 16 Countries - April-June 2022

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	**Biology** • The government of Australia characterizes monkeypox as a viral zoonotic self-limited disease with symptoms lasting two to four weeks **Epidemiology** (including transmission) • As of 28 July 2022, the government of Australia has reported 45 confirmed cases of monkeypox, including 25 in New South Wales, 16 in Victoria, two in the Australian Capital Territory, one in Queensland and one 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 o 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 **Prevention and control** • Two vaccines are available in Australia for the prevention of monkeypox, which are the 3rd generation JYNNEOS and the 2nd generation ACAM2000 o Limited supplies of the 3rd generation JYNNEOS have been secured by the Commonwealth and some States and Territories o JYNNEOS is administered in a 2-dose schedule by subcutaneous injection with a minimum dose interval between doses of 28 days o JYNNEOS is associated with fewer potential adverse events and is safe to use in people with immunocompromise or atopic dermatitis o JYNNEOS may also be used in children or during pregnancy o 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 o ACAM2000™ (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 o Individuals who have received a smallpox vaccine in the past are not recommended to be revaccinated with ACAM2000 o 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 ○ Vaccination aftercare involves the expected reaction (e.g., papule, blister, pustule, scab, permanent pitted scar) ○ The JYNNEOS vaccine is not registered or available in Australia • 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 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 **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 ○ 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 ○ 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 **Diagnosis** • The government of Australia indicates that monkeypox is confirmed with laboratory testing and clinical assessment **Treatment**

	• 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
Belgium	**Biology** • Monkeypox is zoonotic disease caused by an orthopoxvirus **Epidemiology (including transmission)** • As of 02 August 2022, Belgium has reported a total of 482 Monkeypox cases 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 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 • The Institute of Tropical Medicine is conducting a study to investigate "asymptomatic shedding" and the risk of Monkeypox infection **Prevention and control** • Belgium was the first country to announce a mandatory 21-day quarantine period for individuals infected with Monkeypox **Clinical presentation** • 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 **Diagnosis** • The Institute for Tropical Medicine (ITM) 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 **Prognosis** • 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 **Treatment** • Currently, there are no approved treatments for Monkeypox, however, individuals typically recover on their own after a few weeks
France	**Biology** • Monkeypox is a rare viral infectious disease caused by an orthopoxvirus **Epidemiology (including transmission)** • As of 02 August 2022, there have been 2,239 confirmed cases of Monkeypox in France • 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 27 July 2022, 32,000+ doses have been delivered by the Agency to the territories
	  ○ Vaccination centers have started operating at the regional level through Regional Health Agencies, with more to open in the coming weeks
	• 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 450,000+ clicks and 375,000+ visits; this site provides guidance on what to do if Monkeypox symptoms appear as well as additional information regarding preventive measures
	• On 13 July, Public Health France and SIS-Association have launched a free information service to answer Monkeypox-related inquiries
	  ○ 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
	Clinical presentation
	• 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 **Diagnosis** • Among the new cases reported on 5 July 2022, three new Monkeypox cases were detected in females and one was reported in a child **Prognosis** • 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 **Treatment** • 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	**Biology** • Monkeypox is an infectious disease caused by the monkeypox virus Orthopoxvirus simiae **Epidemiology (including transmission)** • As of 03 August 2022, there are 2,781 confirmed cases of Monkeypox across all 16 federal states in Germany • 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 o 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 o 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 o 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 ○ 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 **Clinical presentation** • The symptoms include a fever, swollen lymph nodes, skin rashes, pain, and itching in the genital area **Diagnosis** • The virus can be detected using polymerase chain reaction (PCR) and the particles can further be detected through an electron microscope **Prognosis** • The incubation period is normally between six and 13 days but it can range anywhere from five to 21 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 **Treatment** • Tecovirimat was recently approved in the European Union to help treat Monkeypox infections (however its availability is currently limited)

Italy	**Biology**
	• Human monkeypox virus is a double-stranded DNA virus
	  ○ Two genetic clades have been characterized: West African and Central African
	Epidemiology (including transmission)
	• As of 02 August 2022, Italy has reported 505 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
	  ○ 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 4 cases in Italy from 17 and 22 May 2022
	  ○ All patients had travelled in the first two weeks of May, 3 participated in a mass gathering event, and 1 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
	  ○ 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
	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 **Clinical presentation** • In the rapid communications report dated 26 May 2022, lesions of the four patients appeared 1-3 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 2 weeks after symptom onset • Patient one, a male in his 30s had been treated with oral ciprofloxacin and acyclovir, and 1 single dose of benzylpenicillin for skin lesions during his travels in mid-May o At admission, multiple asynchronous deep-seated and well-circumscribed lesions with central umbilication were present on his genital area, with inguinal lymphadenopathy o 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 o 3 days later, perianal lesions appeared and presented as raised, itchy papules secreting serious, with concomitant painful inguinal lymphadenopathy o Multiple anal lesions appeared over the next 3 days, followed with lesions on the back, legs, and sole of one foot • Patient three, a male in his 30s was admitted for a 2-day fever and clustered itchy popular lesions in the anal region and single lesions on head, thorax, legs, arms, hand and penis o 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 2-day history of myalgia o Vesicular-papular genital lesions appeared, followed by further skin lesions that appeared 6 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 o 28/29 cases were males, and 16/18 reported having sex with other men o The median age of patients was 36 years o All presented with a rash, and in 18/21 cases, the rash was localized in the genital/perianal area o Fever was reported in 12/22 cases for whom information was available **Diagnosis** • 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 o Viral DNA was extracted by Qiamp Viral RNA mini kit (Qiagen) and 2 real-time PCRs using a Real-Star Orthopoxvirus PCR kit and a G2R_G assay which was used as a confirmatory PCR o Sanger sequencing was used to identify which of the 2 clades the virus belonged to **Treatment** • In the rapid communications report dated 26 May 2022, only patient 2 used anti-inflammatory and antihistaminic drugs for perianal pain and general itch

	○ The other patients recovered spontaneously, without antiviral therapy
Netherlands	**Epidemiology** (including transmission) • As of 02 August 2022, the Netherlands has reported 925 cases • Monkeypox occurs mostly in West and Central Africa, mainly infecting rodents ○ 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 ○ 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 • As of 31 May 2022, 31 cases were confirmed by PCR • As of 16 June 2022, there were 95 cases of monkeypox in the country • The National Institute for Public Helath 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 ○ 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 **Prevention and control** • 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 **Clinical presentation** • The National Institute for Public Health and the Environment report published on 30 June 2022 that 84% of patients have symptoms such as fever, tiredness, muscle pain, or swollen lymph nodes ○ 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 • Symptoms are described as mild, including fever, headache, muscle ache, swollen lymph nodes, chills, and fatigue ○ 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 ○ 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 **Diagnosis** • 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 **Treatment** • 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	**Biology** • 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 **Epidemiology** (including transmission) • As of 27 July 2022, Portugal has reported 536 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 **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 • A news report indicates that the Imvanex vaccine has been administered in Portugal since July 16 ○ 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 **Clinical presentation** • The government of Portugal indicated that individuals should seek medical attention if they have ulcerative lesions, rash, enlarged lymph nodes
Spain	**Biology** • 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 **Epidemiology** (including transmission) • As of 02 August 2022, the Public Health Agency has confirmed around 4,577 cases of MPX in Spain • Spain is the country with the most cases of monkeypox in the world • The first human cases were identified in the Democratic Republic of the Congo in 1970 ○ 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 **Prevention and control** • 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 (ERA), 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 • The Health Minister, Carolina Daria, recalled that Spain has "a significant amount" of vaccines available, 5,300 were acquired by the U.S. Authority and the EU's Health Response (HERA), and 200 from Imvanex that was purchased from another European country • 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 o Until now, in the EU it is only approved against conventional smallpox o 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 the 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
	Treatment
	• 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	**Biology** • According to the U.S. Centers for Disease Control and Prevention's 2022 Monkeypox Outbreak Global Map, Sweden has confirmed 88 cases of monkeypox as of 2 August 2022 • The clear majority of reported monkeypox cases in Sweden have been reported in Stockholm, with 65 cases • The Public Health Agency of Sweden defines monkeypox as a rare, sporadic species of the Orthopoxvirus that can be transmitted between animals and humans ○ It has previously infected people in African rainforests where the reservoirs of the virus are primarily wild monkeys **Epidemiology** (including transmission) • According to the U.S. Centers for Disease Control and Prevention's 2022 Monkeypox Outbreak Global Map, Sweden has confirmed 28 cases of monkeypox as of 6 July 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 **Prevention and Control** • 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 last week **Clinical presentation** • 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 **Diagnosis** • Sweden confirmed its first case of monkeypox on 19 May 2022, and it is unknown how the person became infected
United Kingdom (U.K.)	**Epidemiology** (including transmission) • The case count is 2,759 (2,672 confirmed and 87 highly probable) as of 01 August 2022 • The UK Health Security Agency released a technical briefing about the monkeypox outbreak in England on 19 July 2022 which places the monkeypox outbreak at level 2 of potential transmission (transmission within a defined sub-population)

	○ 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 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 **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 • The UK Heath 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 • 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 UK has procured 130,000 doses of the smallpox vaccine from Bavarian Nordic to offer to those eligible for vaccination • 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 **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, and confirmed cases of monkeypox

	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
	  o Those who test orthopox-positive are deemed as highly probable cases
	• The rare and imported pathogens laboratory (RIPL) at the UK Health Security Agency Porton Down has been designated as the diagnostic laboratory for monkeypox
	  o 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
	Treatment
	• 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
	  o 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.)	**Biology** • 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 **Epidemiology** • As of 02 August 2022, the U.S. has reported a total of 6,326 confirmed monkeypox cases • 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
	Prevention and control
	• 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
	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
	Diagnosis
	• 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) **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

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	**Biology** • 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 **Epidemiology** (including transmission) • The Public Health Agency of Canada (PHAC) reported a total of 890 cases of monkeypox in Canadian provinces and territories as of 03 August 2022, with 423 cases confirmed in Québec, 373 cases in Ontario, 13 cases in Alberta, 78 cases in British Columbia, two cases in Saskatchewan, and one newly reported case in Yukon • 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 • 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 o 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 • 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 o 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 o 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." **Prevention and control**

	• 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
	  o 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
	  o 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:
	  o 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
	  o PEP should not be offered to individuals who already have a monkeypox infection
	  o A second dose of Imvamune may be offered after 28 days of the first dose if continued risk of exposure is indicated
	  o 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
	• 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
	  o 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
	  o 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
	• 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:
	  o stay home and limit contact with others if they have symptoms or are recommended to do so by a healthcare provider
	  o avoid close physical contact with anyone who is infected with or may have been exposed to the monkeypox virus
	  o maintain good hand hygiene and respiratory etiquette
	  o clean and disinfect high-touch surfaces and objects in the home, especially after having visitors
	  o 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
	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 no 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 legion(s) as well as one or more of the following:
	  ○ 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
	Prognosis
	• 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
	Treatment
	• 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	**Epidemiology** (including transmission) • As of 29 July 2022, there are 61 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 **Prevention and control** • 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 *Public Health Act* • 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 o 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 **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 states that the disease generally occurs in two stages o The first stage often includes symptoms such as fever, chills, headache, swollen lymph nodes, body pain, and fatigue and lasts two to three weeks o 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 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 **Treatment** • 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

Alberta	**Epidemiology** (including transmission)
	• As of 14 June 2022, 12 case of monkeypox has 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
	  o 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
	Prevention and control
	• Currently, Alberta residents who self-identify as meeting the following criteria are eligible for vaccination:
	  o 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
	  o Sexual contacts of the above-described groups
	  o Staff and volunteers in setting, venues, or events where sexual activities between men take place
	• Currently, while vaccine supplies are limited, vaccinations are concentrated in Edmonton and Calgary
	• 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
	Diagnosis

	• 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: o Sexual contact with a new, anonymous, or multiple partners o Sexual contact with some who had a new, anonymous, or multiple partners o Significant contact with someone who has skin lesions with no known alternate cause o Contact with a known or probable case of monkeypox • Clinicians must consult with the Virologist-on-call at the Provincial Laboratory and the local Medical Officer of Health prior to the collection of samples for monkeypox testing
Saskatchewan	**Epidemiology** (including transmission) • 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 **Prevention and Control** • 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
Manitoba	**Epidemiology (including transmission)** • Spread occurs when a person comes into close contact with an infected animal, human, or materials contaminated with the virus **Clinical presentation** • Symptoms include fever, malaise, headache, backache, chills, weakness, and swollen lymph nodes **Diagnosis** • Manitoba is actively monitoring for monkeypox cases, although none have been identified yet **Treatment** • Treatment of monkeypox is mainly supportive, but in severe cases antivirals may be considered
Ontario	**Biology** • Monkeypox is an orthopoxvirus caused by the Monkeypox virus **Epidemiology** (including transmission) • 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) o 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
	  o It is not as transmissible as COVID-19
	  o 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 July 2022, there have been 101 confirmed cases of monkeypox in Ontario, whereby 84.2% of confirmed cases were reported by Toronto Public Health and 100% of cases are male
	  o There are 8 probable cases (100% are male)
	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
	  o 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
	  o 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
	  o Healthcare works should wear a fit-tested and sealed N-95 mask, gloves, gown, and eye protection (face shield or goggles)
	  o Soiled linens should be cleaned to prevent dispersal of microorganisms
	  o Waste (dressings) should be disposed according to facility-specific guidelines for infectious waste
	  o 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
	  o Standard household cleaning disinfectants can be used to kill the virus
	  o Talking to sexual partners about sexual health and using barriers such as gloves and condoms
	  o Avoid sharing toothbrushes, sex toys, and drug use supplies
	  o Avoid prolonged face-to-fact contact, especially indoors
	  o 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 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)
	  o 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 • 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 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 probably 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 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, 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 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 **Clinical presentation** • The Ministry of Health released a fact sheet comparing monkeypox, chickenpox, and hand-food-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 noise), 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 ○ 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 **Prognosis** • 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 o 99.5% of cases are male, 0.5% are female • The most infected people will recover on their own within 2-4 weeks, and that the infection is rarely fatal **Treatment** • 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	**Epidemiology** (including transmission)
	• 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 2 August 2022, 373 cases of monkeypox have been reported in Quebec
	Clinical presentation
	• 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
	Prevention and control
	• 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 probably 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
	  o 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)
	  o If a person has symptoms of monkeypox at time of vaccination, the post-exposure vaccine may not be given
	  o 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
	  o Staff and volunteers in a social setting or event where sexual activities take place may also receive the pre-exposure vaccine
	  o 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
	Diagnosis
	• 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
	Treatment
	• Antivirals could be an option, but their clinical usefulness must be evaluated before they are recommended

New Brunswick	**Prevention and control** • 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 **Diagnosis** • New Brunswick identified a suspected case of monkeypox, but the patient was not assessed until after symptoms had passed
Nova Scotia	**Epidemiology** (including transmission) • 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 **Prevention and control** • Nova Scotia is actively monitoring the monkeypox outbreak but to date has no reported cases
Prince Edward Island	**Epidemiology** (including transmission) • Prince Edward Island is actively monitoring the monkeypox outbreak, but to date has no reported cases **Prevention and control** • As of 23 June 2022, the provincial health organization is starting to prepare for potential cases ○ 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
Newfoundland and Labrador	• 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
Yukon	**Epidemiology** (including transmission)

	• 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 **Prevention and control** • 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
Northwest Territories	**Diagnosis** • The Government of Northwest Territories released an algorithm for health professionals to identify suspect cases of monkeypox
Nunavut	**Prevention and control** • 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