

Living Evidence Profile #6.10 (interim update)
(29 September 2022)

Question

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

What we found

In this interim update to the full living evidence profile, we conducted an update search to identify new evidence documents. Experiences from 11 countries (Australia, Belgium, France, Germany, Italy, Netherlands, Portugal, Spain, Sweden, United Kingdom (U.K.), and the United States (U.S.), and from all Canadian provinces and territories will be updated in the next full version of the living evidence profile along with a more fulsome summary of key findings from the highly relevant evidence documents. Box 1 provides a description of our approach. 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)
- Diagnosis
- Prevention and control
- Clinical presentation
- Prognosis
- Treatment

Evidence documents identified

We identified 38 new evidence documents since the last update of this LEP, of which 18 were deemed highly relevant. The newly added highly relevant evidence documents include:

- three full systematic reviews;
- two rapid reviews;
- six protocols for systematic reviews; and
- seven single studies.

Box 1: Our approach

We identified evidence published from 2017 onwards (to capture any evidence related to recent outbreaks outside Africa) addressing the question by searching Health Systems Evidence (HSE), Health Evidence, ACCESSSS, PROSPERO (review protocols and registered titles), PubMed and MedRxiv on 28 September 2022. 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. Experiences from these jurisdictions will be updated in the next full version of the living evidence profile.

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 interim update to the living evidence profile was prepared in the equivalent of a one-day ‘full-court press’ by all involved staff.

For this interim update, we provide a list of the highly relevant documents in Table 1 according to the organizing framework, which is accompanied by the evidence documents assessed as medium or low relevance in Table 2. A detailed summary of our methods is provided in Appendix 1, and the hyperlinks to excluded documents (at the final stage of reviewing) in Appendix 2.

Table 1: New highly relevant evidence documents

Framework category	Evidence documents identified
Biology	<p><i>Full systematic reviews</i></p> <ul style="list-style-type: none"> • Serial intervals and incubation periods of the monkeypox virus clades (5/11 AMSTAR rating; literature last searched 26 August 2022)
Epidemiology (including transmission)	<p><i>Full systematic reviews</i></p> <ul style="list-style-type: none"> • Multi-country monkeypox outbreak: A quantitative evidence synthesis on clinical characteristics, potential transmission routes, and risk factors (4/10 AMSTAR rating; literature last searched 21 August 2022) <p><i>Rapid reviews</i></p> <ul style="list-style-type: none"> • Is monkeypox a new, emerging sexually transmitted disease? A rapid review of the literature (1/9 AMSTAR rating; literature last searched – Not stated) <p><i>Single studies</i></p> <ul style="list-style-type: none"> • Health care personnel exposures to subsequently laboratory-confirmed monkeypox patients — Colorado, 2022 (published 23 September 2022) • Short-term forecasts of Monkeypox cases in multiple countries: Keep calm and don't panic (published 19 September 2022) • Impact of airline travel network on the global importation risk of monkeypox, 2022 (pre-print; posted 18 September 2022)
Prevention and control	<p><i>Rapid reviews</i></p> <ul style="list-style-type: none"> • Prevention of monkeypox with vaccines: A rapid review (3/9 AMSTAR rating; literature last searched 8 August 2022) <p><i>Protocols for reviews underway</i></p> <ul style="list-style-type: none"> • The role of vaccination and treatment in monkey pox: A systematic review (anticipated completion 12 October 2022) <p><i>Single studies</i></p> <ul style="list-style-type: none"> • Findings on the monkeypox exposure mitigation strategies employed by men who have sex with men and transgender women in the United States (published 14 September 2022)
Diagnosis	<p><i>Protocols for reviews underway</i></p> <ul style="list-style-type: none"> • Diagnostic accuracy of PCR and ELISA for monkeypox infection: A systematic review and meta-analysis (anticipated completion 6 October 2022) <p><i>Single studies</i></p> <ul style="list-style-type: none"> • Evaluating the accuracy of self-collected swabs for the diagnosis of monkeypox (pre-print; posted 20 September 2022) • Clinical performance and trends during the first two months of monkeypox virus PCR testing at two United States reference labs (pre-print; posted 21 September 2022)
Clinical presentation	<p><i>Full systematic reviews</i></p> <ul style="list-style-type: none"> • The clinical manifestations and severity of the 2022 monkeypox outbreak among 4,080 patients (3/11 AMSTAR rating; literature last searched 2 September 2022) • Multi-country monkeypox outbreak: A quantitative evidence synthesis on clinical characteristics, potential transmission routes, and risk factors (4/10 AMSTAR rating; literature last searched 21 August 2022) <p><i>Protocols for reviews underway</i></p>

Framework category	Evidence documents identified
	<ul style="list-style-type: none"> • Spectrum of ocular manifestations and its treatment in monkeypox virus infection worldwide: Systematic review (anticipated completion 8 October 2022) • ENT manifestations in Monkeypox patients: A systematic review and meta-analysis (anticipated completion 15 October 2022) • Oral manifestations of human monkeypox (HMPX) infection: Systematic review and meta-analysis (anticipated completion 30 November 2022)
Prognosis	<i>No highly relevant evidence documents identified</i>
Treatment	<p><i>Protocols for reviews underway</i></p> <ul style="list-style-type: none"> • Spectrum of ocular manifestations and its treatment in monkeypox virus infection worldwide: Systematic review (anticipated completion 8 October 2022) • The role of vaccination and treatment in monkey pox: A systematic review (anticipated completion 12 October 2022) • Clinical outcomes of established and promising treatment modalities of monkeypox- A systematic review of case reports (anticipated completion 11 December 2022) <p><i>Single studies</i></p> <ul style="list-style-type: none"> • Clinical use of Tecovirimat (Tpoxx) for treatment of monkeypox under an investigational new drug protocol — United States, May–August 2022 (published 16 September 2022)

Table 2: Newly identified evidence documents rated as medium or low relevance

Framework category	Evidence documents identified
Biology	<p><i>Single studies</i></p> <ul style="list-style-type: none"> • The human host response to monkeypox infection: A proteomic case series study (published 28 September 2022) • Genomic analysis of early spread of monkeypox virus in Washington State (pre-print; posted 23 September 2022) • Evolution, epidemiology, geographical distribution, and mutational landscape of newly emerging monkeypox virus (published 12 September)
Epidemiology (including transmission)	<p><i>Single studies</i></p> <ul style="list-style-type: none"> • Perceived concern and risk of getting infected with monkeypox among MSM: Evidence and perspectives from the Netherlands, July 2022 (pre-print; posted 26 September 2022) • Transmission characteristics, replication patterns and clinical manifestations of human monkeypox virus - an in-depth analysis of four cases from Germany (published 23 September 2022) • Human immunodeficiency virus infection may be a contributing factor to Monkeypox infection: Analysis of a 42-case series (published 22 September 2022) • Heavy-tailed sexual contact networks and monkeypox epidemiology in the global outbreak, 2022 (published 22 September 2022) • Spatial modeling and ecological suitability of monkeypox disease in Southern Nigeria (20 September 2022) • Wastewater based epidemiology beyond SARS-CoV-2: Spanish wastewater reveals the current spread of Monkeypox virus (pre-print; posted 19 September 2022) • Public perceptions of the emerging human monkeypox disease and vaccination in Riyadh, Saudi Arabia: A cross-sectional study (15 September 2022) • Monkeypox virus infections in southern Italy: Is there a risk for community spread? (published 17 September 2022) • Viable Monkeypox virus in the environment of a patient room (pre-print; posted 17 September 2022) • Management of contacts of the first imported monkeypox case in Korea (published 13 September 2022) • Evolution, epidemiology, geographical distribution, and mutational landscape of newly emerging monkeypox virus (published 12 September)
Prevention and control	<p><i>Single studies</i></p> <ul style="list-style-type: none"> • Community-engaged intervention mapping for CVD-prevention in Black and Latinx sexual minority men with HIV in New York City: Protocol for a web-based mixed method study (study protocol; published 21 September 2022) • An integrative reverse vaccinology, immunoinformatic, docking and simulation approaches towards designing of multi-epitopes based vaccine against monkeypox virus (published 21 September 2022) • Multi-epitope-based vaccine candidate for monkeypox: An in-silico approach (published 19 September 2022) • Modelling the protective effect of previous compulsory smallpox vaccination against human monkeypox infection: from hypothesis to a worst-case scenario (published 17 September 2022)
Diagnosis	<p><i>Single studies</i></p>

	<ul style="list-style-type: none"> • Development of a loop-mediated isothermal amplification method for rapid and visual detection of monkeypox virus (published 26 September 2022) • Analysis of CNN features with multiple machine learning classifiers in diagnosis of monkeypox from digital skin images (pre-print; posted 14 September 2022) • Validation study of a direct real-time PCR protocol for detection of monkeypox virus (published 13 September 2022)
Clinical presentation	<i>Single studies</i> <ul style="list-style-type: none"> • Transmission characteristics, replication patterns and clinical manifestations of human monkeypox virus - an in-depth analysis of four cases from Germany (published 23 September 2022) • Human immunodeficiency virus infection may be a contributing factor to Monkeypox infection: Analysis of a 42-case series (published 22 September 2022)
Prognosis	<i>No evidence documents identified</i>
Treatment	<i>No evidence documents identified</i>

Wilson MG, Lavis JN. Living evidence profile #6.10 (interim update): What is the best-available evidence related to the monkeypox outbreak? Hamilton: McMaster Health Forum, 29 September 2022.

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



HEALTH FORUM

>> Contact us
 1280 Main St. West, MML 417
 Hamilton, ON, Canada L8S 4L6
 +1.905.525.9140 x 22121
 forum@mcmaster.ca

>> Find and follow us
mcmasterforum.org
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 mcmasterforum

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. The methods below are for producing the full version of the living evidence profile. This interim update only focused on identifying highly relevant evidence documents, which will be summarized in more detail in the next full version that is published.

Identifying research evidence

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

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

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

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

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

Identifying experiences from other countries and from Canadian provinces and territories

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

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

Assessing relevance and quality of evidence

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

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

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

Preparing the profile

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

Appendix 2: Documents excluded at the final stages of reviewing

Type of document	Hyperlinked title
Guidelines	
Full systematic reviews	The virology of human monkeypox virus (hMPXV): A brief overview Human monkeypox: A review of the literature Neurologic complications of smallpox and monkeypox: A review Diagnosis and management of monkeypox: A review for the emergency clinician Diagnosis of monkeypox virus – An overview
Rapid reviews	
Non-systematic reviews	
Protocols for reviews that are already underway	
Titles and questions for reviews being planned	
Single studies	The clinical spectrum of human monkeypox: An Italian single-center case series Reemergence of monkeypox: Prevention and management Orthopox viruses and the safety margins of solvent-detergent treated plasma-derived medicinal products Sexually-transmitted monkeypox: Report of two cases Global online public interest in monkeypox compared with COVID-19: Google trends in 2022 Is there any evidence for milder courses of monkeypox virus infections with childhood smallpox vaccination? Monkeypox virus transmission to healthcare worker through needlestick injury, Brazil Proposal of the French HIV Society on the CD4 threshold below which patients living with HIV who wish to be vaccinated against Monkeypox should receive a 3-dose regimen Atypical oral presentation of monkeypox virus: A report of two cases from Florence, Italy Monkeypox in patient immunized with ACAM2000 smallpox vaccine during 2022 outbreak Atypical presentation of sexually-transmitted monkeypox lesions
Other types of documents	