McMaster University | Health Forum

Living evidence profile appendices

Best-available evidence related to the mpox outbreak

27 February 2025

[MHF product code: LEP 6.14]

Appendices

Appendix 1: Methodological details

We use a standard protocol for preparing living evidence profiles (LEP) to ensure that our approach to identifying research evidence is as systematic and transparent as possible in the time we were given to prepare the profile.

Identifying research evidence

For this LEP, we searched PubMed for:
1) evidence syntheses
2) single studies

To identify any new evidence syntheses, we conducted our PubMed search on 4 September 2024, 1 October 2024, 5 November 2024, 22 January 2025, and 3 February 2025 using an open text search for: (Monkeypox[All Fields] OR Monkeypox*[All Fields] OR "Monkey pox"[All Fields] OR "Monkey orthopox"[All Fields] OR Simianpox[All Fields] OR "Simian pox"[All Fields] OR "Simian orthopox"[All Fields] OR MPXV[All Fields] OR Monkeypox[MeSH Terms] OR Monkeypox virus[MeSH Terms] OR "Variole du singe"[All Fields] OR "orthopoxvirose simienne"[All Fields] OR "Variole simienne"[All Fields] OR "mpox" [All Fields]). We selected the following filters on PubMed: Meta-Analysis, Review, Systematic Review, and only those from 2022 – 2025.

To identify new single studies about clade I since the last version (6.13b), we searched PubMed on 22 January 2025 and 3 February 2025 using an open text search for: (((Monkeypox[All Fields] OR Monkeypox*[All Fields] OR "Monkey pox"[All Fields] OR MPXV[All Fields] OR Monkeypox[MeSH Terms] OR Monkeypox virus[MeSH Terms] OR "Variole du singe"[All Fields] OR "mpox" [All Fields])) AND ((clade* 1) OR ("clade* I") OR ("I clade"))) OR ("Congo Basin clade" OR ("Central Africa clade") OR ("CA clade"))

Evidence documents from the systematic searches were uploaded into Covidence (a software to support conducting evidence syntheses), where staff undertook title and abstract screening followed by full-text review. Documents were screened by two reviewers. Any conflicts were resolved by the lead author.

For the 4 September and 1 October 2024 searches, we screened 741 evidence syntheses (including 19 duplicates). Of these, 147 went to full-text review, from which 32 were excluded because they were descriptive articles that did not contain methods sections (n= 20), they were identified in previous versions (n= 10), they did not relate to mpox (n= 1), or the full-text was unavailable (n= 1). In addition, we hand-searched the documents included in the two previous LEPs (6.11 and 6.12) and included 22 documents. Finally, we reviewed 31 protocols that were identified in LEP 6.11 to capture in this LEP those evidence syntheses that have been since published. From these, 18 were discontinued or have not been published to date, 12 have been captured as published evidence syntheses in this LEP, and one was published beyond the 1 October 2024 search (but was captured in the 5 November 2024 search).

For the 5 November 2024 search (including single studies and evidence syntheses), we screened 47 documents, of which 38 went to full-text review. 12 documents were deemed relevant (7 single studies and four new evidence syntheses). Finally, to bridge all the versions (1 to 13), we reviewed and verified the complete list of evidence documents in its entirety to identify any remaining duplicate evidence documents. We removed six evidence documents (including a pre-print, where we instead included the published article).

For the 22 January 2025 and 3 February 2025 searches, we screened 50 evidence documents, of which 34 went to full-text review. From these, 20 evidence documents (13 evidence syntheses and seven single studies) were deemed relevant for version 14.

In total, versions 1 to 14 include 192 evidence documents (153 evidence syntheses, 38 single studies, and one set of slides from a global conference).

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, Portuguese 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. We excluded documents that did not directly address the research questions and the relevant organizing framework.

Assessing relevance and quality of evidence

Relevance was determined by the team member who completed the data extraction and then reviewed by the lead author. An evidence document is considered ‘high relevance’ if it directly addresses the research question. An evidence document is deemed ‘low relevance’ if it indirectly addresses the research question but still holds value to include in the LEP.

Two reviewers independently appraise the methodological quality of evidence syntheses that are deemed to be highly relevant using the first version of the AMSTAR tool. Two reviewers independently appraise each synthesis, and 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 evidence syntheses are those with scores of eight or higher out of a possible 11, medium-quality evidence syntheses are those with scores between four and seven, and low-quality evidence syntheses are those with scores less than four. It is important to note that the AMSTAR tool was developed to assess evidence syntheses focused on clinical interventions, so not all criteria apply to those pertaining to health-system arrangements or implementation strategies. Furthermore, we apply the AMSTAR criteria to evidence syntheses addressing all types of questions, not just those addressing questions about effectiveness, and some of these evidence syntheses addressing other types of questions are syntheses of qualitative studies. While AMSTAR does not account for some of the key attributes of syntheses of qualitative studies, such as whether and how citizens and subject-matter experts were involved, researchers’ competency, and how reflexivity was approached, it remains the best general quality-assessment tool of which we’re aware. 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, an evidence synthesis that scores

8/11 is generally of comparable quality to another scoring 11/11; both ratings are considered 'high scores.' A high score signals that readers of the evidence synthesis can have a high level of confidence in its findings. A low score, on the other hand, does not mean that the evidence synthesis should be discarded, merely that less confidence can be placed in its findings and that it 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 cited in the reference list at the end of the LEP. For this version, the research team reviewed the full text of each evidence synthesis and single study, tagged each synthesis according to the organizing framework, and extracted the key findings. We then drafted a summary that highlights the key areas of research and gaps in the evidence that were identified.

Upon completion, the LEP is sent to a subject matter expert and citizen partners.

Appendix 2a: Overview of included high-quality evidence syntheses (on all clades) and all single studies (on clade I) as of 3 February 2025

	Biology	Epidemiology	High-risk populations	Prevention and control	Diagnosis	Clinical presentation	Prognosis	Treatment
High-quality evidence syntheses on all clades (N = 26)	**10**	**14**	**9**	**11**	**6**	**11**	**7**	**5**
Single studies on clade I (N = 38)	**33**	**28**	**16**	**12**	**10**	**5**	**8**	**1**

*Some documents were tagged in more than one category so the column total does not match the total number of documents in Appendix 2 and the number of key findings in Appendix 3

Appendix 2b: All included evidence syntheses on mpox with unspecified clade (N = 95, tagged only once based on the synthesis's primary objective)

	Quality of the evidence synthesis		
Organizing framework	**High** *(AMSTAR score: ≥ 8 / 11)* N = 17	**Medium** *(AMSTAR score: 4 – 7 / 11)* N = 54	**Low** *(AMSTAR score: < 4 / 11)* N = 24
Biology	1	0	0
Epidemiology	1	8	7
High-risk populations	2	3	0
Prevention and control	4	25	8
Diagnosis	0	1	0
Clinical presentation	6	12	8
Prognosis	2	1	1
Treatment	1	4	0

Appendix 2c: All included evidence syntheses that described clade I and/or clade II (N = 57, tagged only once based on synthesis's primary objective)

	Quality of the evidence synthesis		
Organizing framework	**High** *(AMSTAR score: ≥ 8 / 11)* N = 7	**Medium** *(AMSTAR score: 4 – 7 / 11)* N = 26	**Low** *(AMSTAR score: < 4 / 11)* N = 24
Biology	0	2	2
Epidemiology	3	9	12
High-risk populations	2	2	1
Prevention and control	0	3	1
Diagnosis	0	0	1
Clinical presentation	1	5	3
Prognosis	0	2	2
Treatment	1	3	2

Appendix 3: Key findings from evidence syntheses (N = 13) with high relevance and newly identified single studies (N = 7) according to the organizing framework (clade type specified where identified by the literature)

Organizing framework	Key findings
Biology	• The first detection of the mpox virus clade Ib variant in China, with the complete genome sequence of the strain designated as hMpxV/China/JXHY/2024/12; phylogenetic analysis showed its close relationship with MPXV clade Ib strains from African countries, as well as international regions like the UK and Thailand (Last year literature searched 2025) – **clade I** • This review did not identify any information on the viral period of clade I, nor the overall impacts of either clade for high-risk population; however, the incubation period of clade I was an estimated seven days (3/9 AMSTAR rating; last year literature searched 2023) – **clade I**
Epidemiology	• Since 2022, large-scale outbreaks of both clade I and clade II of the mpox virus have occurred, with distinct transmission patterns and clinical characteristics, influenced by factors such as clade type, route of exposure, infectious dose, and host immune response (2/9 AMSTAR rating; last year literature searched October 2022) – **clade I & clade II** • Primarily transmitted through animal-to-human and human-to-human transmission, mpox presents with fever, painful lesions, and lymphadenopathy, with Clade I causing more severe disease; while typically self-limiting, it poses greater risks for high-risk groups (1/9 AMSTAR rating; last year literature searched January 2025) – **clade I & clade II** • The ongoing mpox outbreak in the Democratic Republic of Congo has spread widely across multiple provinces, with significant impacts on rural areas, a notable rise in sexual transmission, and challenges in controlling the epidemic due to resource limitations (1/9 AMSTAR rating; last year literature searched December 2024) • The most common self-reported route of transmission of clade I was sexual conduct and person-to-person contact (5/9 AMSTAR rating; last year literature searched 2024) – **clade I** • Pooled estimates of key epidemiologic parameters from the 2022–2023 global mpox outbreak indicate that the disease's transmissibility is characterized by a pooled incubation period of 7.60 days and a pooled serial interval of 8.30 days (10/11 AMSTAR rating; last year literature searched September 2023) – **clade I** • During the clade Ib outbreak, mpox primarily spread through close contact, with sexual transmission as the main route in adults, causing mild genitourinary symptoms, while children, though less affected, predominantly developed extragenital lesions and faced higher mortality risks, particularly those under five (Last year literature searched 2025) – **clade I** • The 2023 mpox outbreak in Katako-Kombe, Democratic Republic of the Congo, found an attack rate of 2.15 per 1,000 population, a case fatality rate (CFR) of 4.6%, and a reproduction rate (R0) of 1.29, indicating sustained human-to-human transmission (Last year literature searched 2025) – **clade I**
High-risk populations	• People living with HIV have a statistically significantly increased pooled risk of hospitalization from mpox; however, the authors indicate that the results should be interpreted with caution given the substantial heterogeneity in the meta-analysis (6/11 AMSTAR rating; last year literature searched 2024
Prevention and control	• Majority (61.2%) of the analyzed sequences were fully homologous to both mpox clades, highlighting the potential of peptide-based vaccines, which could expand eligibility, enhance effectiveness, and improve accessibility in regions lacking cold-chain infrastructure (Last year literature searched 2025) – **clade I & clade II**

Organizing framework	Key findings
	• Examples of efforts to address mpox may include raising public awareness on immunization and sexual health (particularly among high-risk populations) and potentially investigating the use of monoclonal antibodies and artificial intelligence in infectious disease management (3/9 AMSTAR rating; last year literature searched 2024) • Prevention and control measures include deploying medical and healthcare resources and vaccinating high-risk groups (0/9 AMSTAR rating; last year literature searched December 2024) • There were no studies in the review that reported on the barriers and facilitators to the adherence of mpox guidance; however, it was reported that the bay, bisexual and men who have sex with men (gbMSM) community from the United States and the Netherlands were more frequently willing to receive a vaccination and reduce their number of sexual partners and encounters if recommended by their healthcare providers (5/9 AMSTAR rating; last year literature searched 2022) – **clade II** • The United States Centers for Disease Control and Prevention has become a key player in advancing mpox research, focusing on areas like epidemiology, outbreaks, surveillance, diagnostics, vaccination, and molecular docking, highlighting the global and collaborative effort needed to address infectious diseases (Last year literature searched 2025)
Diagnosis	• PCR has proven to be an accurate tool for detecting mpox infections in humans, demonstrating high sensitivity and specificity across diverse study settings, and ensuring excellent diagnostic accuracy for clinical and public health responses during outbreak (6/11 AMSTAR rating; last year literature searched December 2024) • LAMP-1 assay targets clade I, offering dual-readout capabilities (fluorescence and colorimetric) with detection within 30 minutes, while the LAMP-2 assay focuses on clade II, utilizing a novel R-Duplex DARQ probe for fluorescence-based detection within 40 minutes (Last year literature searched 2025) – **clade I & clade II** • The development of multiplex real-time PCR assay is capable of simultaneously detecting and differentiating mpox virus (MPXV) clades I and II, as well as goatpox virus (GTPV), with high sensitivity and specificity (Last year literature searched 2024) – **clade I & clade II**
Clinical presentation	• A high degree of diagnostic suspicion (e.g., when individuals present with cutaneous lesions) and familiarity with atypical clinical presentations are crucial for identifying any suspected cases of mpox (2/9 AMSTAR rating; last year literature searched October 2024)
Prognosis	• No new evidence document identified that focused on prognosis
Treatment	• Tecovirimat was linked to faster lesion healing, symptom relief, and reduced viral shedding in some mpox patients (i.e., those with mild to moderate illness), but its effectiveness in severe cases (e.g., those requiring hospitalization) and its role in complete viral clearance remain unclear due to limited data and study design limitations (6/10 AMSTAR rating; last year literature searched 2024) – **clade I**

Appendix 4a: Details about each identified high-quality evidence synthesis

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations

• Biology
  ○ Clade I
• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
• Prognosis (e.g., clinical severity, including morbidity and mortality)
	Pooled estimates of key epidemiologic parameters from the 2022–2023 global mpox outbreak indicate that the disease's transmissibility is characterized by a pooled incubation period of 7.60 days and a pooled serial interval of 8.30 days; regarding severity, the pooled case fatality rate (CFR) varies by continent, with 0.19% in the Americas and 0.33% in Europe
	• The slightly larger pooled serial interval compared to pooled incubation period suggests that the transmission primarily occurs after the symptom onset, although presymptomatic transmission can also occur
	• CFR estimates varied by geographical region, but were higher in Africa, in countries linked with clade I
		High	No	10/11	September 2023	No	None identified

• Biology
  ○ Clade II
• Prevention and control
  ○ Non-pharmaceutical measures to control the spread of infections
• Diagnosis
• Clinical presentation
  ○ Symptom onset and duration
	Oral lesions were found to be among the first clinical signs of mpox, and ulcers on the dorsal surface of the tongue and lips were found to be the most commonly affected areas
	• Greater efforts to recognize and identify oral lesions in mpox patients may help provide more effective care and help prevent cross-infection between patients and medical staff
		High	No	8/11	March 2024	No	None identified

• Clinical presentation ○ Variability in clinical presentation	The symptoms observed in patients with mpox have become more varied over a 53-year span, leading to a stronger correlation between them; while the prevalence of rash has remained consistent, the occurrence of other symptoms has declined • The meta-analysis aimed to investigate the changing clinical symptoms associated with mpox from 1970 to 2023 and explore their interrelations • The meta-analysis included 61 studies that reported 21 symptoms in 720 patients from period 1, 39 symptoms in 1756	High	No	8/11	February 2024	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
	patients from period 2, and 37 symptoms in 12,277 patients from period 3 • The most common symptom among patients from all 3 periods was rash followed by lymphadenopathy						

• Biology
  ○ Clade II
  ▪ Sub-clade IIb
• Epidemiology
  ○ Transmissibility
  ○ Protective immunity
• Prevention and control
  ○ Pharmaceutical measures
	MVA-BN vaccine is highly effective in preventing mpox, with vaccine effectiveness (VE) estimated at 76% for one dose and 82% for two doses, and it reduces hospitalization risk by 67%, although post-exposure prophylaxis (PEP) shows limited effectiveness at 20%, influenced by timing and exposure conditions
	• Limited real-world data on the effectiveness of LC16m8 and OrthopoxVac, with the analysis primarily focusing on MVA-BN to assess its ability to prevent infection, hospitalization, and death
	• The VE estimates were derived from 35 studies involving 110,914 participants, with 35,738 reported cases of clade IIb MPXV
		High	No	10/11	January 2024	No	None identified

• Prevention and control ○ Pharmaceutical measures used as part of public health strategies	Limited evidence exists on the effectiveness of interventions to prevent sexual transmission of mpox, as well as qualitative evidence about values and preferences that might influence intervention acceptability • A total of 16 included studies (1 on contact-tracing,2 on sexual behaviour, and 13 on asymptomatic testing) provided insufficient evidence to fully evaluate asymptomatic testing • Four qualitative studies revealed that preferences about preventative interventions were influenced by mpox information, accessibility and quality of mpox testing and care, diversity of sexual practices, and perceived cost to wellbeing	High	No	8/10	January 2024	No	None identified

• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
	The pooled prevalence of HIV infection among individuals with mpox was 41%; a relatively lower prevalence of HIV was observed in Africa, whereas a higher prevalence of HIV was found among nonendemic countries
	• Studies from Europe and North America reported a high prevalence of HIV infection among individuals with mpox- 41% and 52%, respectively, while studies from Nigeria, Africa reported a relatively low prevalence of HIV infection of 21%
		High	No	9/11	September 2023	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations

• Biology
  ○ Clade I
  ○ Clade II
  ▪ Sub-clade IIb
• High-risk populations
  ○ Children
  ○ Pregnant People
• Diagnosis
• Clinical Presentation
  ○ Complications
  ○ Variability in Clinical Presentation
• Prognosis
• Treatment
	Paediatric mpox case fatality rate was 11% including both clades, with higher mortality in children aged 0–4 years (15%) versus 5–9 years (8%), and a 50% foetal death rate among pregnant individuals; there is limited data on treatments, including tecovirimat use, highlight research gaps, especially in endemic regions
	• The review of 61 studies, covering 2123 paediatric and 32 maternal or congenital cases, reviewed transmission, diagnosis, clinical presentation, prognosis and treatment
	• Rash, fever, and lymphadenopathy as common symptoms in children, with secondary bacterial infections causing most complications, while pregnant individuals universally experienced rash
	• Tecovirimat was used in 21 paediatric and 12 maternal cases, but no randomized trials exist to confirm its efficacy or safety.
		High	No	8/11	April 2023	No	Gender/sex

• Prevention and control ○ Pharmaceutical measures used as part of public health strategies	Considerable variation exists in mpox vaccine acceptance across different populations, with higher prevalence of acceptance in Asian and African countries compared to those in North America and Europe • A review of 10 studies found that the prevalence of mpox vaccine acceptance was 58.5% overall, with African and Asian countries estimated at 68% and North American and European countries estimated at 44.3%	High	No	8/11	March 2023	No	None identified

• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
• High-risk populations
  ○ 2SLGBTQI+
  ○ Children
  ○ People who are immunocompromised
• Prevention and control
  ○ Information and education (e.g., including risk communication)
	The mpox virus can lead to serious eye complications, with a range of symptoms (e.g., conjunctivitis, eyelid lesions, and in severe cases, corneal opacity that can cause blindness), stressing the importance of antiviral treatments (e.g., tecovirimat) and the need for more precise data on these symptoms to guide effective care	High	No	9/11	February 2023	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
○ Pharmaceutical measures used as part of public health strategies • Clinical presentation ○ Symptom onset and duration ○ Complications ○ Variability in clinical presentation • Prognosis (e.g., clinical severity, including morbidity and mortality) • Treatment							
• Treatment	In the context of mpox, tecovirimat is the most commonly used treatment and has shown significant benefits in managing severe cases, with no major safety concerns identified • This systematic review compiles all evidence of various antivirals used on their efficacy and safety • Tecovirimat was used in 61 individuals, followed by cidofovir in seven and brincidofovir in three individuals • Of the total cases, 59 reported complete resolution of symptoms, one experienced fluctuating symptoms, one had died, and the remaining cases were in the process of symptom resolution • PLATINUM-CAN seeks to assess tecovirimat in MPXV infection in Canada and is expected to start recruiting soon	High	No	8/10	February 2023	No	None identified
• Biology ○ Clade I ○ Clade II • Epidemiology ○ Transmissibility ○ Geographic Spread ○ Protective Immunity • High-risk populations ○ 2SLGBTQI+ ○ Other	Mpox transmission patterns have shifted from 61.64% animal-to-human transmission in pre-2022 African outbreaks to 93.5% human-to-human transmission, primarily through sexual contact among MSM, in post-2022 outbreaks with global spread to non-endemic regions like Europe, Asia, and the Americas. • The systematic review compiles evidence on the epidemiologic, demographic, and clinical characteristics of monkeypox (mpox) cases before and after the 2022 outbreak, analyzing 98 studies to identify changes in transmission	High	No	8/11	February 2023	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations

• Diagnosis
• Clinical Presentation
  ○ Complications
  ○ Variability in Clinical Presentation
	patterns, affected populations, clinical presentations, and diagnostic practices
	• Diagnostic practices evolved from lesion-based RT-PCR tests to include anal and oropharyngeal swabs with the West African strain
	• Clinically, rashes and lymphadenopathy persisted, but novel symptoms like proctalgia (16.6%) and anal lesions (39.8%) emerged in the 2022 outbreak, alongside milder disease and lower mortality rates
	• Post-2022 outbreaks primarily involved 93.5% MSM, with a median patient age increasing from 10 years (pre-2022) to 35 years (post-2022)						

• Epidemiology • High-risk populations ○ Other	Mpox cases among women represent a considerable percentage of all mpox cases, with mpox among women being significantly greater in endemic regions of the world, and reported in higher prevalence prior to 2022 • The review estimated the pooled prevalence of mpox among women across 47,407 mpox cases to be 17.22% • The pooled proportion of mpox cases among women in endemic regions was almost ten times greater than in non-endemic regions • Mpox cases in women were 20 times higher prior to 2022 than in studies published after 2022	High	No	8/11	4 January 2023	No	Gender/sex
• Epidemiology ○ Geographic spread	The 2022 multi-country mpox outbreak involved higher average ages and comorbidity rates compared to previous years; cases correlated with 2020 international arrivals across 55 countries, emphasizing the need for urgent response and global cooperation to address its spread and impact • The average age of mpox cases was 21.05 years • Study estimated that the proportion of male patients was 57.9%, and it was higher in the European region • Up to now, the 2022 Mpox Outbreak Global Map shows that the top three countries are the United Kingdom, Germany, and Spain • The average duration of mpox symptoms was 11.41 days, with shorter durations observed in high-income regions and the Americas compared to low-income regions and Africa	High	No	8/11	January 2023	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
• Treatment	While this Cochrane review of therapeutics for treating monkeypox (mpox) in humans did not identify any evidence from randomized controlled trials (RCTs) about the efficacy and safety of therapeutics for mpox, very low-certainty evidence reported no serious safety signals from the use of tecovirimat for people with mpox infection; however, there was a safety signal raised from very low-certainty evidence that brincidofovir may cause liver injury • In the three included non-randomized studies that assessed safety of mpox treatment (355 received tecovirimat, three received brincidofovir), all of the participants who received brincidofovir reported an increase in the liver enzyme alanine transaminase (ALT), which led to their treatment being discontinued	High	No	9/10	January 2023	No	None identified

• Epidemiology
  ○ Transmissibility
• Clinical presentation
  ○ Symptom onset and duration
	Skin legions act a reservoir of mpox viral DNA, subsequently contributing to high infectivity risk
	• Pooled skin sample positive rate was 98.77% (CI: 94.74%–99.72%)
	• No significant moderators were identified
		High	No	9/11	January 2023	No	None identified

• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
• High-risk populations
  ○ 2SLGBTQI+
• Prevention and control
  ○ Information and education (e.g., including risk communication)
  ○ Non-pharmaceutical measures to control the spread of infections
  ○ Surveillance and reporting
• Diagnosis
	There is an urgent need for targeted health measures to manage and contain the spread of mpox, given that mpox skin lesions have very high viral loads, which makes them a significant source of infection that can drive rapid transmission, especially during direct skin-to-skin contact (i.e., in close social or physical settings)	High	No	9/11	January 2023	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations

• Clinical presentation
  ○ Symptom onset and duration
  ○ Complications							

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
  ○ Protective immunity
• High-risk populations
  ○ Children
  ○ Healthcare workers
• Prevention and control
  ○ Information and education (e.g., including risk communication)
  ○ Surveillance and reporting
• Clinical presentation
  ○ Symptom onset and duration
  ○ Complications
  ○ Variability in clinical presentation
• Prognosis (e.g., clinical severity, including morbidity and mortality)
• Treatment
	Eye-related symptoms in mpox patients (e.g., conjunctivitis, photophobia), affect about 9% of cases globally but are significantly more common in Africa, where nearly 27% of patients experience these issues, highlighting the need for healthcare workers in endemic regions to prioritize early detection and treatment to prevent severe complications like vision loss	High	No	9/11	December 2022	No	None identified

• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
• High-risk populations
  ○ 2SLGBTQI+
	The 2022 mpox outbreak primarily affected men who have sex with men, with most cases showing a range of symptoms (e.g., skin lesions especially anogenital, fever, and inguinal lymphadenopathy), and nearly half of the patients were also living with HIV, highlighting an urgent need to update guidelines for	High	No	8/11	November 2022	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
○ People who are immunocompromised • Prevention and control ○ Information and education (e.g., including risk communication) ○ Surveillance and reporting • Clinical presentation ○ Symptom onset and duration ○ Variability in clinical presentation • Prognosis (e.g., clinical severity, including morbidity and mortality)	these high-risk groups and include the unique symptom patterns seen in this outbreak						
• Biology ○ Clade II ▪ Subclade IIb • Epidemiology ○ Transmissibility • High-risk populations ○ 2SLGBTQI+	Six Spanish and English studies including 541 male mpox patients during the 2022 global outbreak found that 214 (40%) had HIV and 255 (43%) had other STIs	High	No	8/11	September 2022	No	Personal characteristics associated with discrimination
• Prevention and control ○ Pharmaceutical measures used as part of public health strategies	A total of 11 studies including 8045 participants found a pooled prevalence of mpox vaccination acceptance of 56%, with Asian countries estimated at 50% and European countries estimated at 70% • Subgroup analyses revealed that vaccine acceptance was 43% in the general population, 63% among healthcare workers, and 84% in the LGBTI community across studies	High	No	8/11	September 2022	No	Personal characteristics associated with discrimination
• Biology ○ Clade I ○ Clade II • Clinical presentation	Headache, sore throat, cough, and cervical lymphadenopathy were found to be the most prevalent otolaryngologic symptoms of mpox	High	No	8/11	August 2022	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
○ Symptom onset and duration	• Across 38 studies, headache occurred in approximately 31% of cases, while sore throat, cough, and cervical lymphadenopathy occurred at 22%, 16%, and 10%, respectively. • Cough, oral ulcers, and the presence of tonsillar signs were more common in endemic areas compared to non-endemic areas						
• Epidemiology ○ Transmissibility • High-risk populations ○ Pregnant people • Prevention and control ○ Pharmaceutical measures used as part of public health strategies ○ Surveillance and reporting • Diagnosis • Clinical presentation ○ Complications	Monkeypox infection in pregnancy is linked to high rates of miscarriage (39%), intrauterine fetal death (23%), and significant perinatal loss (77%), and with a 62% chance of vertical transmission, highlighting the need for vigilant maternal and fetal monitoring	High	No	9/11	June 2022	No	None identified
• Biology ○ Clade I ○ Clade II • Epidemiology ○ Transmissibility • Prevention and control ○ Non-pharmaceutical measures to prevent infection ○ Non-pharmaceutical measures to control the spread of infections	A recent scoping review identified that there is currently a lack of understanding on how the virus alters the host physiology and/or biochemistry, a lack of mpox virus-specific rapid diagnostic kit, limited number of national and/or international frameworks and policies for controlling mpox, and the limited information on the socio-ecological, economic, and psychological consequences of this disease • A homolog of the vaccinia virus complement control is present in clade I and is absent in the clade II, which may contribute to the reduced virulence of the latter • Most studies reported that humans and animals as the host of mpox, while the authors noted that there are additional reservoirs for mpox infections such as monkeys, Gambian pouched rats, squirrels, elephant shrews, gazelle, and pig • Clade II is the most documented strain in Africa	High	No	9/10	May 2022	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
• Diagnosis • Clinical presentation ○ Symptom onset and duration • Prognosis (e.g., clinical severity, including morbidity and mortality) • Treatment	• Transmission occurred from human-animal-environmental interactions, human-to-human, zoonotic, and cross-species • The clinical signs and symptoms of mpox in humans include fever, headache, night sweats, myalgia, coryzal illness, peripheral lymphadenopathy (a defining feature when compared to smallpox), and after one to two days there could be lesions on the mucosal surfaces and skin (specifically in the face, scalp, trunk, limbs) • Over the course of two to four weeks, the rash may progress from raised lesions to pustules with fevers, chills, enlarged lymph nodes, headaches, muscle aches • Majority of the human cases in Africa have been mild disease and recover within a few weeks; higher risk of mortality include children, young adults and those immunocompromised • Mpox is believed to be self-limiting and recovery can occur without treatment • The authors reported that antiviral medications (e.g., Tecovirimat, Brincidofovirmay be used in combination with vaccines • Additional measures could include the use of personal protective equipment (especially for clinical settings involving patients with mpox), rehydration therapy and nutritional support can support management therapy for individuals with mpox • The authors identified gaps in research such as the lack of understanding on how the virus alters the host physiology and/or biochemistry, lack of mpox virus-specific rapid diagnostic kit, limited number of national and/or international frameworks and policies for controlling mpox, and the lack of data on? socio-ecological, economic, and psychological consequences of this disease						

• Biology
  ○ Clade I
  ○ Clade II
• Clinical Presentation
  ○ Complications
	Neurological and psychiatric symptoms such as encephalitis, confusion, and seizures occurred in approximately 2–3% of monkeypox cases, with headache, myalgia, and fatigue also reported
	• The analysis included 19 eligible studies with 1512 participants, of whom 1031 had confirmed monkeypox
		High	No	9/11	May 2022	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
○ Variability in Clinical Presentation	• The pooled prevalence estimates for these symptoms varied, and there is a lack of data on the long-term neuropsychiatric impacts of monkeypox						
• Biology ○ Clade I ○ Clade II • Clinical presentation ○ Symptom onset and duration ○ Complications • Prognosis (e.g., clinical severity, including morbidity and mortality)	Mpox is spreading quickly, with about 35% of cases resulting in hospitalization, and 5% resulting in fatal outcomes • Across 19 studies, rash (93%), fever (72%), pruritus (65%), and lymphadenopathy (62%) were the most common manifestations of mpox	High	No	8/11	Published 2022	No	None identified

Appendix 4b: Details about each identified medium and low-quality evidence synthesis in version 14

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
• Epidemiology ○ Transmissibility • High-risk populations ○ People who are immuno-compromised • Prevention and control ○ Surveillance and reporting • Diagnosis • Clinical presentation ○ Complications ○ Variability in clinical presentation	People living with HIV have a significantly higher risk of hospitalization from mpox (pooled risk ratio: 1.566); however, the results should be interpreted with caution given the variability across the included studies • The substantial heterogeneity indicate that the pooled estimate of risk may not accurately reflect specific subgroups or regions • The findings highlighted the need for integrated care approaches, enhanced surveillance, and targeted public health interventions • The authors reported that future research could further explore the mechanisms linking HIV and mpox severity (i.e., immune dysfunction, antiretroviral therapy adherence) to improve outbreak preparedness and patient outcomes, in addition to investigating the trajectory of mpox over time through the conduct of longitudinal studies	High	No	6/11	2024	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
• Prognosis (e.g., clinical severity, including morbidity and mortality) • Treatment							
• Diagnosis	PCR has proven to be an accurate tool for detecting mpox infections in humans, demonstrating high sensitivity and specificity across diverse study settings, and ensuring excellent diagnostic accuracy for clinical and public health responses during outbreak • Evaluated diagnostic accuracy of PCR in detecting mpox infection • PCR test demonstrated a strong diagnostic performance of the test with a pooled sensitivity of 0.99 (95% CI [0.95, 1.00]) and a specificity of 1 (95% CI [0.96, 1.00])	High	No	6/11	Published December 2024	No	None identified
• Biology ○ Clade I ▪ Subclade Ia ▪ Subclade Ib • Clinical presentation ○ Symptom onset and duration • Prognosis (e.g., clinical severity, including morbidity and mortality) • Treatment	Tecovirimat was linked to faster lesion healing, symptom relief, and reduced viral shedding in some mpox patients (i.e., those with mild to moderate illness), but its effectiveness in severe cases (e.g., those requiring hospitalization) and its role in complete viral clearance remain unclear due to limited data and study design limitations • The findings highlighted that observational studies show mixed outcomes regarding viral clearance, delayed treatment effects, and adverse reactions in vulnerable groups	High	No	6/10	2024	No	None identified
• Biology ○ Clade I ▪ Subclade Ia ▪ Subclade Ib ○ Clade II ▪ Subclade IIa ▪ Subclade IIb • Epidemiology ○ Transmissibility • High-risk populations ○ Children	The most common self-reported route of transmission of clade I were sexual conduct and person-to-person contact • The purpose of this review was to summarize evidence of routes of transmission in humans • A total of two explored the route of transmission of clade I ○ A total of six individuals were infected through heterosexual sexual conduct ○ A total of one individual was infected through an infected medical item ○ A total of two individuals had nonsexual conduct with an index case ○ A total of one individual was undefined	High	No	5/9	2024	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
	○ All, but three cases were laboratory confirmed ○ One study reported that 16.4% of their cases were from sexual conduct • Route of transmission was often self-reported and may be subject to recall bias • Across clades possible routes of transmission include sexual conduct, meal sharing, hospital visits, and living in the same household • Across age groups (besides children) and clades, sexual conduct was the most common route of transmission • In children, the most common route of transmission was person to person contract • The authors concluded that no information was provided for pregnant people, children, and other vulnerable groups						
• Biology ○ Clade II ▪ Subclade IIa ▪ Subclade IIb • Epidemiology ○ Transmissibility • High-risk populations ○ 2SLGBTQI+ • Prevention and control ○ Non-pharmaceutical measures to prevent infection ○ Non-pharmaceutical measures to control the spread of infections ○ Pharmaceutical measures used as part of public health strategies	There were no studies in the review that reported on the barriers and facilitators to the adherence of mpox guidance; however, it was reported that gbMSM community from the United States and the Netherlands were more frequently willing to receive a vaccination and reduce their number of sexual partners and encounters if recommended by their healthcare providers • The purpose of this study was to summarize evidence regarding adherence and barriers to isolation guidance for clade II • The results of Malik et al included the following: ○ One study identified that 47% of participants self-reported poor knowledge of the mpox outbreak ○ Approximately 80% of participants used isolation and handwashing to prevent spread of mpox ○ Only 46% of participants felt confident in receiving an mpox vaccine; persons vaccinated with COVID were more likely to want to be vaccinated (odds ratio [OR]: 32.1, 95% CI: 16.7 to 61.7) as well as women (OR = 0.6, 95% CI: 0.4 to 0.8) • The results of Wang et al included the following: ○ All participants were men who identified as having sex with other men	High	No	5/9	2022	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
	○ Approximately 69% of participants reduced their number of sexual encounters to avoid the spread ○ A total of 70% of participants felt comfortable receiving an mpox vaccination ○ Men who were single or dating or in an open relationship were more likely to want a vaccination ○ Approximately 44% of participants were willing to self-isolate to reduce the spread, this was more likely in retired men than unemployed men and less likely in men with bachelor/master's degrees						
• Biology ○ Clade I ▪ Subclade Ia ▪ Subclade Ib ○ Clade II ▪ Subclade IIa ▪ Subclade IIb • Prevention and control ○ Surveillance and reporting • Clinical presentation ○ Symptom onset and duration	This review did not identify any information on the viral period of clade I, nor the overall impacts of either clade for high-risk populations; however, the incubation period of clade I was an estimated seven days • The purpose of this review was to summarize information on the incubation period and infectious periods of mpox • The incubation period of clade I was estimated to be 7 days (range 0–17 days, IQR: 1–13 days) • The incubation period of clade II was estimated to be 9.1 days (95% CI 6.5–10.9 days) • The median viral clearance of clade II was 10.5 days (IQR: 7–33 days) • Viral positivity varied per date range: ○ one to five days: 67% ○ 6 to 10 days: 71% ○ 11 to 15 days: 55% ○ 16 to 20 days: 30% ○ 21 to 25 days: 24% ○ more than 25 days: 9% • No evidence on the infectious period of clade I was provided • The authors concluded that no information was provided for pregnant people, children, and other vulnerable groups	High	No	3/10	2023	No	None identified
• Epidemiology ○ Transmissibility ○ Geographic spread • High-risk populations	Examples of efforts to address mpox may include raising public awareness on immunization and sexual health (particularly among high-risk populations) and potentially investigating the use of	High	No	3/9	2024	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
○ 2SLGBTQI+ • Prevention and control ○ Information and education (e.g., including risk communication) ○ Non-pharmaceutical measures to prevent infection ○ Non-pharmaceutical measures to control the spread of infections ○ Pharmaceutical measures used as part of public health strategies ○ Strategies grounded in behavioural science • Treatment	monoclonal antibodies and artificial intelligence in infectious disease management • The evidence synthesis provided a comprehensive overview of what is currently known about mpox in terms of its epidemiology, diagnosis, treatment, vaccination, and deep learning applications • There was limited information reported in the review about how artificial intelligence can support the management of mpox, except for a brief description in its potential use in drug discovery and treatment						
• Biology ○ Clade I ▪ Subclade Ia ▪ Subclade Ib ○ Clade II ▪ Subclade IIb • Epidemiology ○ Transmissibility • Clinical presentation ○ Variability in clinical presentation	Since 2022, large-scale outbreaks of both clade I and clade II of the mpox virus have occurred, with distinct transmission patterns and clinical characteristics, influenced by factors such as clade type, route of exposure, infectious dose, and host immune response • Examined the concurrent outbreaks of mpox in Africa, focusing on clade Ia, the newly emerged clade Ib, and clade IIb lineage A, and how they differ from the 2022 global outbreak caused by clade IIb lineage B.1 • For clades Ia and IIa, zoonotic transmission plays a key role, whereas clades Ib and IIb spread through sustained human-to-human transmission without zoonotic exposure	High	No	2/9	October 2022	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
• Prognosis (e.g., clinical severity, including morbidity and mortality)	• Lesion distribution varies, with clades Ia and IIa presenting a generalized centrifugal distribution, while clade IIb lesions are mainly localized to the anogenital area • Disease severity is highest for clade Ia, with a case fatality rate of up to 12%, whereas other clades have lower fatality rates ranging from 0% to 3.6%						

• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
• Prognosis (e.g., clinical severity, including morbidity and mortality)
	The ongoing mpox outbreak in the Democratic Republic of Congo has spread widely across multiple provinces, with significant impacts on rural areas, a notable rise in sexual transmission, and challenges in controlling the epidemic due to resource limitations
	• This review provides an analysis of the current mpox outbreak in the Democratic Republic of Congo
	• Approximately 12,569 suspected mpox cases have been reported, with 581 fatalities, resulting in a case fatality rate of 4.6%
	• These cases have been documented across 156 health sectors in 22 out of 26 provinces, representing the highest recorded number of cases to date
	• The epidemic has also spread into previously unaffected regions, indicating that the virus is not confined to its original areas and is impacting new areas that were not previously exposed to mpox
	• Hospitalization rates for affected individuals have varied between 4% and 10%, indicating a moderate level of severity among cases, with a significant portion of the cases linked to sexual transmission
	• Over 70% of cases are being reported from rural areas
		High	No	1/9	Published December 2024	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations

• Clinical presentation
  ○ Symptom onset and duration
  ○ Complications
  ○ Variability in clinical presentation
	A high degree of diagnostic suspicion (e.g., when individuals present with cutaneous lesions) and familiarity with atypical clinical presentations are crucial for identifying any suspected cases of mpox
	• Reported the typical mucocutaneous manifestations of mpox and those that differ from the usual clinical course of infection
	• Mpox primarily affects men who have sex with men
	• After an incubation period of four to 10 days, it manifests with mucocutaneous lesions and systemic symptoms
	• Certain anatomical sites exhibit distinct clinical features, with genital edema being a potentially serious complication
	• The ocular and ear/nose/throat areas are also uncommon sites with specific manifestations
		High	No	2/9	October 2024	No	None identified

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
  ○ Transmissibility
• High-risk populations
  ○ 2SLGBTQI+
  ○ Children
  ○ Pregnant people
  ○ People who are immunocompromised
  ○ Healthcare workers
• Prevention and control
  ○ Information and education (e.g., including risk communication)
  ○ Non-pharmaceutical measures to control the spread of infections
	Primarily transmitted through animal-to-human and human-to-human transmission, mpox presents with fever, painful lesions, and lymphadenopathy, with clade I causing more severe disease; while typically self-limiting, it poses greater risks for high-risk groups
	• Clade I has been associated to a higher rate of severe disease compared to clade II
	  ○ Sporadic mpox cases were reported outside Africa, including in the U.K., U.S., Singapore, and Israel, primarily linked to travel history or contact with infected individuals, often involving imported animals from endemic regions
	  ○ Mpox spreads from animals to humans through body fluids, bites, scratches, or contaminated meat, while human-to-human transmission occurs via skin contact, respiratory droplets, sexual contact, or fomites, with higher risk for immunocompromised individuals, pregnant women, and newborns
	• Prevention and control
	  ○ Standard mpox care includes testing and risk assessment to determine hospitalization needs; if not, home isolation will be adequate
	  ○ Screening for STIs, including HIV, along with health education and improved access to care, is essential
		High	No	1/9	January 2025	No	• Gender/Sex
							• Personal characteristic

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
○ Pharmaceutical measures used as part of public health strategies ○ Surveillance and reporting • Diagnosis • Clinical presentation • Prognosis (e.g., clinical severity, including morbidity and mortality) • Treatment	○ Mpox vaccination is recommended for at-risk groups, including the unvaccinated, pregnant women, neonates, those with skin infections, and immunocompromised individuals ○ Key strategies involve strengthening surveillance, multisector partnerships, prophylactic measures, healthcare capacity, and equitable vaccine access while reducing stigma; public health measures focus on isolation, monitoring high-risk individuals, and effective vaccination programs • Diagnosis ○ Suspected mpox cases require immediate testing, with PCR as the preferred confirmatory method, considering clinical and epidemiological factors • Clinical presentation ○ After incubation, the virus replicates at the inoculation site, spreading to lymph nodes and causing early symptoms like painful lesions, fever, chills, and lymphadenopathy for one to four days • While typically self-limiting, mpox can lead to severe multisystem complications, especially in high-risk groups, including immunocompromised individuals, those with eczema, children, people with HIV, and men who have sex with men • No approved treatment for mpox exists, but the antiviral tecovirimat (Tpoxx), FDA-approved for smallpox, was used successfully during the 2022 outbreak • Brincidofovir, a cidofovir prodrug, is used for severe smallpox and shows to be effective against mpox, recommended for severe cases, immunodeficient patients, or those unresponsive to tecovirimat						
• Biology ○ Clade I ▪ Subclade Ib • Epidemiology ○ Transmissibility • High-risk populations	Understanding mpox transmission dynamics, risk factors, social and behavioural influences, and disease progression is crucial; prevention and control measures include deploying medical and healthcare resources and vaccinating high-risk groups • Sexual contact is the most frequently reported mode of transmission and accounts for 95.6% of transmissions	High	No	0/9	Published December 2024	No	• Personal characteristic

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
○ Children ○ Pregnant people ○ People who are immunocompromised • Prevention and control ○ Non-pharmaceutical measures to control the spread of infections ○ Pharmaceutical measures used as part of public health strategies • Clinical presentation	• The new mpox virus strain (clade Ib), which emerged and rapidly spread in the Democratic Republic of the Congo, is transmitted through sexual contact • Most mpox cases in current outbreaks (since 2022) are mild, but severe illness can occur in young children, pregnant women, and immunocompromised individuals • Control measures include deploying healthcare resources, establishing treatment centres, contact tracing, and isolation • Vaccination is recommended for high-risk individuals, and treatment focuses on managing rash, pain, and complications • Rash (systemic, oral, genital, or of unknown origin) is the most common symptom, appearing in 89% of cases						

Appendix 5: Details about each identified single study about clade I

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations

• Biology
  ○ Clade I
  ▪ Subclade Ib
• Epidemiology
  ○ Transmissibility
• High-risk populations
  ○ Children
  ○ Pregnant people
• Clinical presentation
	During the clade Ib outbreak, mpox primarily spread through close contact, with sexual transmission as the main route in adults, causing mild genitourinary symptoms, while children, though less affected, predominantly developed extragenital lesions and faced higher mortality risks, particularly those under five
	• Clade Ib infections in Kamituga exhibited unique clinical characteristics compared to clade Ia outbreaks in other regions of the country and the global clade IIb outbreak
	• Most cases (58%) involved contact with a suspected or confirmed mpox case, primarily colleagues, spouses, or sexual partners in adults and parents or siblings in children
	• Sexual transmission was the main driver among adults
	• Household transmission raises concerns for severe disease in young children.
	• Mpox appears teratogenic, as 67% (4 out of 6) of documented pregnancies resulted in fetal loss
	• In adults, 89% developed genital skin lesions, with the highest lesion density observed in the genital region
	• In children, who accounted for a minority of cases, extragenital lesions were most common, with all reported fatalities occurring in those under five
	• Post-discharge complications, aside from scarring, were uncommon
		High	Publication Date: 2025
			
			Jurisdiction studied: Democratic Republic of the Congo
			
			Methods used: Prospective observational cohort
				• Personal character-istics

• Biology
  ○ Clade I
  ○ Clade II
• Prevention and control
  ○ Pharmaceutical measures used as part of public health strategies
	Majority (61.2%) of the analyzed sequences were fully homologous to both mpox clades, highlighting the potential of peptide-based vaccines, which could expand eligibility, enhance effectiveness, and improve accessibility in regions lacking cold-chain infrastructure
	• Among the sequences analyzed, 61.2% were fully homologous to both mpox clades (I and II), indicating immunologic cross-reactivity due to sequence homology between poxviruses
	• The findings support the potential use of VACV-derived peptides in developing an mpox peptide-based vaccine; peptide-based vaccines could offer significant advantages over existing options, including stability, lower manufacturing costs, and no reliance on cold-chain storage
		High	Publication Date: 2025
			
			Jurisdiction studied: United States
			
			Methods used: Analysis of vaccinia-derived peptide sequences by mass spectrometry; please note that the authors disclosed potential conflicts, including one's roles with multiple vaccine developers and others holding patents and
				None identified

			receiving funding for peptide-based vaccine research	
• Prevention and control ○ Surveillance and reporting	The United States Centers for Disease Control and Prevention has become a key player in advancing mpox research, focusing on areas like epidemiology, outbreaks, surveillance, diagnostics, vaccination, and molecular docking, highlighting the global and collaborative effort needed to address infectious diseases • The article examined the hotspots and development patterns of mpox research using bibliometric analysis by identifying trends in the number of publications over time, highlighting the increase in mpox-related research following outbreaks • Initial mpox outbreaks were observed in Africa; however, developed nations have taken the lead in research because of their advanced laboratory facilities, economic resources, and concerns regarding biological threats	Low	Publication date: January 2025 Jurisdiction studied: Global Methods used: Citation analysis	None identified

• Biology
  ○ Clade I
  ○ Clade II
• Diagnosis
	Two highly sensitive and specific LAMP (loop-mediated isothermal amplification) based diagnostic assays created to differentiate between Monkeypox Virus Clades I and II; the LAMP-1 assay targets clade I, offering dual-readout capabilities (fluorescence and colorimetric) with detection within 30 minutes, while the LAMP-2 assay focuses on clade II, utilizing a novel R-Duplex DARQ probe for fluorescence-based detection within 40 minutes
	• Designed for point-of-care applications, these assays provide rapid, portable, and cost-effective tools for accurate clade differentiation, ensuring enhanced diagnostic utility
	• By simplifying the diagnostic process in terms of speed, the LAMP-based diagnostic assays are a quicker alternative compared to qPCR (quantitative polymerase chain reaction)
		High	Publication Date: 2025
			
			Jurisdiction studied: Turkey
			
			Methods used: Methodological study
				None identified

• Biology
  ○ Clade I
  ▪ Subclade Ia
  ▪ Subclade Ib
• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
• Prevention and control
  ○ Surveillance and reporting
	The first detection of the mpox virus clade Ib variant in China, with the complete genome sequence of the strain designated as hMpxV/China/JXHY/2024/12; phylogenetic analysis showed its close relationship with MPXV clade Ib strains from African countries, as well as international regions like the UK and Thailand
	• The strain exhibited 127 nucleotide mutations and 57 amino acid mutations, potentially impacting virulence, immune evasion, and transmissibility
	• Among 13 biological samples collected from the patient, 12 tested positive for MPXV
	• The highest viral loads were found in herpes fluid from the back and lower limbs (Ct values ~18–20), while the lowest viral loads were in blood (Ct = 34.08)
	• The MPXV clade Ib genome obtained from the case was 195,405 base pairs long, with a 99.978% similarity to a U.K. strain (hMpxV/UnitedKingdom/UKHSA-0072/2024)
		High	Publication Date: 2025
			
			Jurisdiction studied: China
			
			Methods used: Genomic and epidemiological study
				None identified

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
  ○ Transmissibility
• Prevention and control
  ○ Non-pharmaceutical measures to control the spread of infections
  ○ Surveillance and reporting
	The development of multiplex real-time PCR assay is capable of simultaneously detecting and differentiating monkeypox virus (MPXV) clades I and II, as well as goatpox virus (GTPV), with high sensitivity and specificity
	• The study designed and validated a novel PCR assay that simultaneously detects and differentiates monkeypox virus (MPXV) clade I, clade II, and goatpox virus (GTPV) using specific genetic markers: D14L for clade I, D18L for clade II, and RPO30 for GTPV
	• The assay demonstrated limits of detection of 207.83 copies/reaction for clade I, 252.07 copies/reaction for clade II, and 208.72 copies/reaction for GTPV; it showed no cross-reactivity with other poxviruses or pathogens, ensuring accurate identification
	• The multiplex PCR assay outperformed existing methods in speed, precision, and repeatability, offering a significant improvement over previously published assays
		High	Publication Date: 2024
			
			Jurisdiction studied: China
			
			Methods used: Methodological study
				None identified

• Epidemiology
  ○ Transmissibility
• Clinical presentation
  ○ Symptom onset and duration
  ○ Complications
  ○ Variability in clinical presentation
• Prognosis (e.g., clinical severity, including morbidity and mortality)
	The 2023 mpox outbreak in Katako-Kombe, Democratic Republic of the Congo, found an attack rate of 2.15 per 1,000 population, a case fatality rate (CFR) of 4.6%, and a reproduction rate (R0) of 1.29, indicating sustained human-to-human transmission
	• Delayed medical care significantly increased complications, with encephalitis (14% CFR), pulmonary complications (23.68% CFR), and anemia (18.03% CFR) being the most severe
	• 100% of cases had a rash, 86% had swollen lymph nodes, and 66.9% had genital or perianal lesions; complications such as encephalitis (14% CFR) and pulmonary complications (23.68% CFR) increased mortality
	• Limited PCR testing (only 10 samples tested, eight positive) forced reliance on clinical diagnosis, while poor healthcare infrastructure and lack of PPE hindered response efforts
	• Early medical intervention led to a 100% survival rate, while delayed care increased fatalities to 12.79%, with higher rates of complications
		High	Publication Date: 2024
			
			Jurisdiction studied: Democratic Republic of the Congo
			
			Methods used: Retrospective observational and descriptive study
				None identified

• Biology
  ○ Clade I
  ▪ Subclade Ia
  ▪ Subclade Ib
  ○ Clade II
  ▪ Subclade IIb
• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
• High-risk populations
  ○ Children
• Prevention and control
	Multiple strains of monkeypox virus were circulating in the Republic of the Congo during the 2024 outbreak, with the majority belonging to clade Ia and these strains were likely introduced through both cross-border human-to-human transmission and direct zoonotic events, with evidence of local spread in previously unaffected areas	High	Publication date: November 2024
			
			Jurisdiction studied: Republic of the Congo
			
			Methods used: Pathogen sequencing, phylogenetic analysis, and epidemiological data collection
				None identified

○ Information and education (e.g., including risk communication) ○ Surveillance and reporting • Diagnosis • Clinical presentation ○ Complications ○ Variability in clinical presentation • Prognosis (e.g., clinical severity, including morbidity and mortality)				
• Biology ○ Clade I ▪ Subclade Ia ▪ Subclade Ib ○ Clade II ▪ Subclade IIa ▪ Subclade IIb • Epidemiology ○ Geographic spread	A global genomic analysis of 10,670 sequences collected from 65 countries (including Canada) reported that most of the genetic sequences come from outbreaks between 2022 and 2024, where they found that clade I remains circulating in Central Africa whereas clade IIb have shown wider geographical human-to-human spread • Majority of the sequences were collected from 2022 to 2024, with limited to no historical surveillance between 1958 and 2015 ○ Subclade IIa and clade I were first detected in 1958 and 1970 respectively ○ Clade I continued to be detected in the Democratic Republic of the Congo and Sudan between 2022 and 2024, with a novel divergent lineage showing human-to-human transmission within South Kivu in 2024 ▪ Majority of clade I sequences have been sampled in humans, with some also found in captive chimpanzees, wild shrew and rope squirrel ○ Clade IIa has not been observed since 2018 ▪ Most of these have been isolated in chimpanzees, with some isolated in wild sooty mangabey, imported cynomolgus monkeys, and a prairie dog ○ Clade IIb A was first detected in Nigeria in 2017 and continued circulating through human-to-human transmission to at least 2023, while descendent lineage B.1 was detected in 2022 • The authors reported transmission of clade I within nations and interprovincial in parts of Eastern Africa and inferred transmission of clade IIb A in the Eastern Mediterranean • The authors concluded that clade I were mostly sampled from humans and clade IIb from animals, suggesting possible distinct abilities to infect humans, differential disease severity in humans and/or animals, different contacts between animals and reservoirs, and different surveillance or sampling strategies	High	Publication date: 23 October 2024 Jurisdiction studied: Global (65 countries, including Canada) Methods used: Genomic analysis from 10,670 sequences from 65 countries collected between 1958 and 2024	None identified

	• The authors indicate that mpox surveillance programs are integral to understanding and characterizing the evolution and genetic diversity of the virus • The analysis included information provided Public Health Agency of Canada, National Microbiology Laboratory			

• Biology
  ○ Clade I
  ▪ Subclade Ib
• Epidemiology
  ○ Geographic spread
• Prevention and control
  ○ Surveillance and reporting
• Diagnosis
• Prognosis (e.g., clinical severity, including morbidity and mortality)
	The novel sub-lineage (clade Ib) was identified in Kamituga, Democratic Republic of the Congo, where a genomic analysis of the laboratory-confirmed cases imply recent sustained human-to-human transmission and the potential role of sexual transmission;
	• The study included patients from General Hospital of Kamituga in the Democratic Republic of the Congo with 241 suspected mpox cases (i.e., patients who have vesicular or pustular rash with deep-seated firm pustules and more than one of other symptoms such as fever preceding eruption, lymphadenopathy, pustule or crusts on hand palms or foot soles)
	• Among the suspected mpox cases, 108 patients had laboratory-confirmed mpox, of which 51.9% female, median age of 22 years, and were not vaccinated against mpox
	• 28.7% of the confirmed cases indicated that sex work was their profession
	• Two of the laboratory-confirmed patients died in the hospital, suggesting a higher case fatality rate than clade IIb but lower than the current Ia outbreak
	• Near-full-length mpox virus genomic analysis indicated that these strains clustered tightly with each other on a distinct lineage of clade I, which estimated that the most recent common ancestor of the Kamituga genomes existed around mid-September 2023.
	• The authors concluded that a novel clade I lineage is linked to sustained human-to-human transmission in eastern Democratic Republic of the Congo, which is bolstered by the identification of the APOBEC3-related mutations, a hallmark of human-to-human transmission
	• Additional data is needed to assess clade Ib infection severity in addition to intensified local surveillance, enhanced community engagement and case management, and targeted mpox vaccination for individuals
	• The authors established an African-led consortium with key research priorities include further characterization of clade Ib, transmission modes and disease severity, evaluation of point-of-care rapid diagnostic tests, and prevention and treatment strategies
		High	Publication date: 13 June 2024
			
			Jurisdiction studied: Democratic Republic of the Congo
			
			Methods used: Combination of diagnostic samples from the national mpox program or provincial health authorities and data from outbreak response surveys and retrospective medical chart reviews
				None identified

• Biology
  ○ Clade I
  ▪ Subclade Ib
• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
	Mpox clade I shows slower transmission dynamics compared to clade IIb in the Democratic Republic of Congo, however, the newly identified subclade Ib shows sustained human-to-human transmission and reproductive numbers exceeding the epidemic threshold in the South Kivu Province, indicating concerns about viral spread and adaptation	High	Publication Date: 2024
			
			Jurisdiction studied: Democratic Republic of Congo
				None Identified

	• The estimated mean incubation period of mpox clade I was 9.9 days, with generation time between 11.3-17.2 days, suggesting slower transmission dynamics for clade I compared to clade IIb in the Democratic Republic of Congo • Presymptomatic transmission was minimal in clade I, accounting for only 17-20% of cases, which differs from clade IIb where significant presymptomatic transmission has been reported • The reproduction number for clade I was below the epidemic threshold for most of the Democratic Republic of Congo, except in the South Kivu Province, where human-to-human transmission resulted in reproductive numbers exceeding the threshold, suggesting active local spread		Methods used: Retrospective modelling and epidemiological data analysis	

• Biology
  ○ Clade I
  ▪ Subclade Ib
• Epidemiology
  ○ Geographic spread
	A genomic surveillance study analysing all data belonging to Clade I shows a clear monophyletic clade, representing Clade Ib, which seems to be evolving more rapidly than other clusters and be present in DRC and other countries.
	• Clade Ib appears to evolve more rapidly than other clusters
	• Clade Ib needed an evolutionary shift for successful dispersion, which allows its presence not only in DRC, but also in Sweden Thailand, Kenya and Uganda
	• Although clade Ib has shown better fitness than previous clusters, it has not yet been strong enough to replate ancestral lineage
		High	Publication date: 2024
			
			Jurisdiction studied: Global
			
			Methods used: Analysis of genomic sequences databases
				None identified

• Prevention and control ○ Non-pharmaceutical measures to control the spread of infections • Diagnosis	A survey to measure capability of European Centres to detect and characterize MPXV in the European Union (EU)/European Economic Area (EEA) showed a high capability for confirming cases by PCR and to identify clades and/or subclades • The survey covered all 30 countries EU/EAA countries showing that all of them had the capacity to diagnose mpox using PCR, while 28 countries had the capacity to distinguish clades • 25 countries reported having the capacity to conduct MPXV whole genomic sequencing, while 4 countries had access to this through agreement with other countries	High	Publication date: 2024 Jurisdiction studied: 30 EU/EEA countries Methods used: Cross-sectional survey	None identified

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
	A genomic surveillance study in DRC reported two patterns of MPXV transmission; one is present in the eastern South Kivu province associated with clade Ib and sustained human-to-human transmission, while the second pattern is associated with clade Ia, suggesting multiple zoonotic introductions
	• The analysis of genomic samples collected from 2018 to 2024 showed that 95% of the samples belong to clade Ia, while samples belonging to clade Ib was mainly coming from the South Kivu province in 2024
	• Some small mpox clusters from endemic areas have shown a presence of APOBEC3 mutations, which suggests the presence of human-to-human transmission
		High	Publication date: 2024
			
			Jurisdiction studied: Democratic Republic of Congo
			Methods used: Analysis of genomic sequences databases
				None identified

• Biology
  ○ Clade I
  ▪ Subclade Ib
	Clade I monkeypox virus, historically prevalent in Central Africa and associated with higher case fatality rates, has recently evolved to include a novel sub-lineage (clade Ib) in the Democratic Republic of the Congo	High	Publication date: 2024	None identified

• Epidemiology
  ○ Geographic spread
• Prevention and control
  ○ Surveillance and reporting
• Diagnosis
• Prognosis (e.g., clinical severity, including morbidity and mortality)
	• In 2023–2024, there was a surge in MPXV clade I virus cases in Africa, with over 20,000 cases and 1,000 deaths reported across 25 of 26 provinces in the Democratic Republic of the Congo (DRC) by June 2024
	• A novel monkeypox virus sub-lineage, clade Ib, emerged in South Kivu, DRC, in September 2023, primarily spreading through heterosexual transmission
	• Researchers developed and validated a new real-time PCR assay (dD14-16) that successfully identified 82 out of 92 suspected mpox cases in South Kivu as clade Ib, with whole genome sequencing confirming the results for samples with low Cq (quantification cycle) values (below 30)
			Jurisdiction studied: Democratic Republic of the Congo
			
			Methods used: Combination of laboratory techniques, clinical sample testing, and genomic analysis	

• Biology
  ○ Clade I
• Epidemiology
  ○ Geographic spread
• Prevention and control
  ○ Surveillance and reporting
• Prognosis (e.g., clinical severity, including morbidity and mortality)
	Clade I mpox, primarily circulating in Central Africa, is associated with higher morbidity, a longer incubation period (13 days, range 3–34 days), and a higher case fatality rate (approximately 11%) compared to other clades	High	Publication date: 2023
			
			Jurisdiction studied: European Union, the United Kingdom, Switzerland, and Singapore
			
			Methods used: Multi-centre, multi-country cohort
				None identified

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
  ○ High-risk populations
  ▪ Children
• Prognosis (e.g., clinical severity, including morbidity and mortality)
	Clade II monkeypox was found to have a lower case fatality rate (2.2%), compared to clade I (7–10%)
	• Mpox primarily circulates in southern, forested regions of Cameroon, with no cases reported in dry Sahelian areas, suggesting ecosystems play important roles in transmission
	• Clades I and II circulate concurrently, but are geographically segregated, possibly due to natural barriers like rivers and highlands
		High	Publication date: 2024
			
			Jurisdiction studied: Cameroon
			
			Methods used: Observational study
				Personal characteristics associated with discrimination (e.g. age, disability)

• Biology
  ○ Clade I
• Epidemiology
  ○ Transmissibility
	A cluster of clade I MPXV infections was reported in the DRC that was transmitted through sexual contact, previously only associated with clade II
	• The findings indicate that monkeypox can spread through unrecognized transmission routes, highlighting the importance of screening, including clinical, diagnostic, and surveillance approaches in both endemic and non-endemic regions
		High	Publication date: 2024
			
			Jurisdiction studied: Democratic Republic of the Congo
			
			Methods used: Descriptive study
				None identified

• Biology
  ○ Clade I
• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
	Phylogenetic analysis and genome annotation indicate that a novel lineage (termed Subgroup VI) of clade I mpox is driving a cluster of infections with a unique, pathogen-favouring mutational profile
	• The study details the genome annotation, phylogeny, and mutational profile of a novel, sustained clade I mpox outbreak in Kamituga, Eastern DRC
	• Seven proteins (C9L, I4L, L6R, A17L, A25R, A28L, and B21R) have emerged as mutation hotspots with inframe deletions, frameshift variants, synonymous variants, and amino acid substitutions
	• A deletion of the D14L (OPG032) gene was found in all samples
	• The phylogenetic analysis confirms that this cluster of mpox infections is genetically distinct from previously reported clade I outbreaks
	• This clade I outbreak shows unique characteristics, including human-to-human transmission through heterosexual and non-sexual contact (community spread), which are rarely observed in clade I outbreaks
		High	Publication date: 30 April 2024
			
			Jurisdiction studied: Kamituga, South Kivu Province, DRC
			
			Methods used: Prospective, observational cohort study
				None identified

• Treatment	A 14-day course of tecovirimat was used to treat 14 patients with mpox, of which majority identified as female with a median age of 23 years in Central African Republic; most were discharged 14 days after the start of treatment • The study focused on the outcomes of tecovirimat, an antiviral drug to combat orthopoxviruses, including mpox • 14 patients from the Central African Republic tested positive for mpox between December 2021 and February 2022 • The median age was 23 years old, of which majority were female • The median time from symptom onset to the initiation treatment was 21 days • All patients presented muscle pain, lesions (11 people had more than 100 lesions), headache, and lymphadenopathy • All patients received a 14-day oral course of tecovirimat (600mg twice daily) • By day 14, 12 patients had been discharged and were PCR-negative and recovered • The median time from the initiation of treatment until the absence of active lesions was five days	High	Publication date: 30 November 2022 Jurisdiction studied: Central African Republic Methods used: Intervention	Not reported

• Biology
  ○ Clade I
  ○ Clade II
	The study suggests that the positive selection signals represent host adaptation signatures, contributing to the differing virulence levels between clade I and II MPXV
	• Signs of positive selection were detected in genes related to immunomodulation and virulence, suggesting adaptation to host immune systems
	• Some genes showing positive selection are involved in manipulating the host's cellular pathways for sensing cytosolic DNA, while others might indicate antibody escape or immune pressures
		High	Publication date: 20 May 2023
			
			Jurisdiction studied: MPXV genomes belonging to clades I and II were retrieved from the National Center for Biotechnology Information database
				None identified

			(data primarily used from the Democratic Republic of the Congo and Central African Republic) Methods used: Observational	

• Biology
  ○ Clade I
  ▪ Subclade Ia
• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
	Monkeypox clade Ia sequences from the Republic of the Congo (RoC) had close genetic relatedness to sequences from the DRC in early 2024, indicating possible cross-border transmission between the two countries; there was also indication from phylogenetic positioning of RoC sequences that multiple strains are con-circulating in the human population
	• Samples from suspected cases of monkeypox were collected from five regions in RoC between January and 29 April 2024; a total of 31 confirmed cases were included
		High	Publication date: August 2024 (pre-print)
			
			Jurisdiction studied: Republic of the Congo, Democratic Republic from Congo
			
			Methods used: Molecular analysis of blood samples
				None identified

• Biology
  ○ Clade I
  ▪ Subclade Ia
  ▪ Subclade Ib
• Epidemiology
  ○ Geographic spread
	The epidemic in the DRC currently has zoonotic spillover involving clade Ia in traditional endemic regions, in addition to a clade Ib outbreak driven by human-to-human transmission in the eastern part of the country
	• 581 samples were collected from individuals in the DRC, where all newly generated MPXV sequences belonged to clade I
	• Majority of the samples belonged to clade Ia, whereas 17 were from clade Ib strains that came from patients infected in 2024
		High	Publication date: 22 August 2024
			
			Jurisdiction studied: Democratic Republic of the Congo
			
			Methods used: Observational
				None identified

• Biology
  ○ Clade I
• Epidemiology
  ○ Transmissibility
	The monkeypox virus isolated during this 2005 outbreak in Sudan appears to be a novel virus belonging to the Congo Basin clade
	• The hemagglutinin gene (942 bp) of the Sudan viruses was identical to that of the MPXV Congo Basin strain MPXV2003_DRC and MPXV1979_Zaire
	• Human-to-human transmission of monkeypox virus was documented for up to five generations in three chains of transmission, with 14 of 19 case-patients reporting contact with a suspected monkeypox case before onset of symptoms
	• Clade I had 6 nucleotide changes compared to the West African strains
	• The outbreak exhibited a notably low case-fatality rate, with all 19 identified monkeypox cases recovering from the illness and no deaths reported
		Medium	Publication date: 2023
			
			Jurisdiction studied: Unity State, Sudan
			
			Methods used: Retrospective epidemiological investigation cohort
				None identified

• Biology
  ○ Clade I
• Epidemiology
  ○ Geographic spread
• Prevention and control
  ○ Surveillance and reporting
	A nosocomial outbreak of monkeypox in the Central African Republic in 2015–2016, caused by a Zaire genotype strain of the Congo Basin clade, involved 10 cases and spread through familial, healthcare-related, and transport-related transmission	Medium	Publication date: 2017
			
			Jurisdiction studied: Central African Republic
			
			Methods used: Case series
				None identified

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
	Clade I monkeypox exhibited diverse subpopulations without geographic structuring in the Congo Basin, while clades 2/3 were found to be geographically structured, separated by the Dahomey Gap in West Africa	Medium	Publication date: 2023
			
			Jurisdiction studied: Central and West Africa
			
			Methods used: Retrospective analysis of MPXV genomes
				None identified

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
  ○ Transmissibility
• Diagnosis
	Approximately one-third of suspected monkeypox cases in the Central African Republic were confirmed via PCR testing as MPXV infections, with active lesions and scab specimens providing higher viral loads and better detection rates than blood samples	Medium	Publication date: 2023
			
			Jurisdiction studied: Central African Republic
			
			Methods used: Retrospective descriptive study
				None identified

• Biology
  ○ Clade I
  ○ Clade II
• Diagnosis
	The MPXV-RCC (combined recombinase polymerase amplification (RPA) with CRISPR/Cas12a-based detection) was found to be rapid and reliable as a diagnostic tool for detecting mpox within one hour, while differentiating between clades and showing no cross-reactivity with other pathogens	Medium	Publication date: 2023
			
			Jurisdiction studied: China (laboratory study)
			
			Methods used: Diagnostic tool development
				None identified

• Biology
  ○ Clade I
  ○ Clade II
• Diagnosis
	A visual assay panel was developed for detecting MPXV DNA and was found to be a highly specific tool differentiating clades and providing results within 25 minutes
	• The panel was found to be more sensitive than previous methods while showing no cross-reactivity
		Medium	Publication date: 2023
			
			Jurisdiction studied: China (laboratory study)
				None identified

			Methods used: Diagnostic tool development	

• Biology
  ○ Clade I
• Epidemiology
  ○ Transmissibility
• Clinical presentation
  ○ Symptom onset and duration
  ○ Complications
	The majority (67%) of monkeypox cases presented with mild rash, while 33% had more severe presentations most often seen in males (69.5%) and children (60% under 14 years of age) in forested areas
	• High exposure to rodents (91%) and non-human primates (77%) was common before onset of rash
		Medium	Publication date: 2020
			
			Jurisdiction studied: Democratic Republic of the Congo
			
			Methods used: Observational study
				Personal characteristics associated with discrimination (e.g. age, disability)

• Biology
  ○ Clade I
  ▪ Subclade Ia
  ▪ Subclade Ib
  ○ Clade II
  ▪ Subclade IIa
  ▪ Subclade IIb
	The heterogeneity of monkeypox 2022 genomes, including clusters in subclade I and subclade II, may prompt the viruses to frequently acquire, truncate, lose, and delete genes and require continuous surveillance of trends in virulence and transmission	Medium	Publication date: October 2022
			
			Jurisdiction studied: China
			
			Methods used: Pre-print of a bioinformatics analysis study
				None identified

• Biology
  ○ Clade I
  ○ Clade II
  ▪ Subclade IIb
	Monkeypox virus genome was sequenced; sample demonstrated close relationship to clade IIb
	• DNA purification and sequencing of a sample obtained from vesicular lesions of a male patient
	• Analysis showed a 98.77% identity to monkeypox virus (MPXV) clade I and a 99.42% identity to MPXV clade IIb
		Low	Publication date: 2022
			
			Jurisdiction studied: Colombia
			
			Methods used: MPXV genome analysis
				None identified

• Prevention and control ○ Non-pharmaceutical measures to prevent infection	The NeuMoDx MPXV assay was tested by multiple European and U.S. sites using 296 clinical samples, which found an overall analytical sensitivity of 50 copies/mL for both clades I and II as well as high sensitivity (99%) and high specificity (96%) for lesion swap samples and can differentiate clades I and II	Medium	Publication date: 2024 Jurisdiction studied: United States, Belgium, Spain Methods used: Sensitivity and reliability of a real-time PCR assay	None identified

• Biology
• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
	The samples collected in Beijing from May to July 2023 were all found to belong to the MPXV C.1 lineage, of which two were identified as imported infections from Thailand	Low	Publication date: 2023
			
			Jurisdiction studied: Beijing, China
			
			Methods used: Observational
				None identified

• Biology	DNA extracted from a lesion is enough to conduct a complete genome sequencing of MPXV strain, which is enough to understand the origin of the virus with sufficient accuracy (28) • The study evaluated MinION real-time TGS sequencing of a MPXV strain	Low	Publication date: 24 June 2022 Jurisdiction studied: Central African Republic Methods used: Observational	Not reported
• Diagnosis	The use of real-time PCR assays was found to be useful for testing suspected clinical samples of both clades with good levels of accuracy, thus these rapid diagnostic tests may be a useful approach to diagnosing cases of mpox	Low	Publication date: 23 June 2022 Jurisdiction studied: Belgium Methods used: Observational	None identified

• Biology
  ○ Clade I
  ○ Clade II
  ▪ Subclade IIa
  ▪ Subclade IIb
• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
• Prevention and control
  ○ Information and education (e.g., including risk communication)
  ○ Surveillance and reporting
	Clinicians showed moderate accuracy but poor reliability when distinguishing clade I mpox from varicella (chickenpox) based on lesion presentation (e.g., the appearance of skin lesions) and faced challenges in consistently classifying lesion stages, especially when multiple types of lesions were present, highlighting the need for improved diagnostic resources and training in low-resource settings (i.e., areas with limited access to medical facilities and tools)
	• The study focused on evaluating the reliability and agreement among clinicians in diagnosing clade I mpox versus varicella (i.e., differentiating between two diseases) and in classifying lesion stages (e.g., identifying the progression of skin lesions) based on clinical signs and symptoms
	• This involved presenting clinicians with 17 images of clade I mpox and varicella lesions to assess their ability to diagnose and categorize lesion stages
	• The study identified moderate accuracy, poor reliability, and moderate agreement among clinicians when distinguishing between clade I mpox and varicella based on lesion presentation (e.g., visible differences in skin lesions)
		Low	Publication date: 2024
			
			Jurisdiction studied: Democratic Republic of the Congo, Central African Republic, France, Belgium, Switzerland, United Kingdom, and Nigeria
			
			Methods used: An inter-rater reliability and agreement study using a questionnaire
				None identified

• Diagnosis • Clinical presentation ○ Variability in clinical presentation • Prognosis (e.g., clinical severity, including morbidity and mortality)				

• Biology
  ○ Clade I
  ○ Clade II
  ▪ Subclade IIa
  ▪ Subclade IIb
• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
• High-risk populations
  ▪ Children
	In the Central African Republic, outbreaks since 2018 have primarily affected forested regions and younger populations, with children under 16 being particularly vulnerable	High	Publication date: 2022
			
			Jurisdiction studied: Central African Republic
			
			Methods used: Statistical analyses on surveillance data
				None identified

Appendix 6a: Identified medium and low-quality evidence syntheses on mpox (unspecified clade)

	Quality of the evidence synthesis	
Organizing framework	**Medium** *(AMSTAR score: 4 – 7 / 11)* N= 54	**Low** *(AMSTAR score: < 4 / 11)* N= 24
Biology	• None identified	• None identified
Epidemiology	*General* • A global systematic evidence review with meta-analysis of the epidemiological characteristics of the 2022 mpox outbreaks (last year literature searched: 9 February 2023) *Transmissibility* • A review of evidence related to the zoonotic characteristics of the monkeypox virus. (last year literature searched: October 2022) • Monkeypox viral detection in semen specimens of confirmed cases: A systematic review and meta-analysis. (last year literature searched: 12 October 2022) • A systematic review of 5110 cases of monkeypox: What has changed between 1970 and 2022? (last year literature searched: 31 August 2022) • Reproduction number of monkeypox in the early stage of the 2022 multi-country outbreak (last year literature searched: 24 July 2022) *Geographic spread* • A systematic review on environmental perspectives of monkeypox virus (last year literature searched: October 2022) • Factors associated with geographic variations in the 2022 monkeypox outbreak; A systematic review (last year literature searched: 30 September 2022) *Protective immunity* • None identified	*General* • From outbreaks to artificial intelligence: A comprehensive review of monkeypox virus epidemiology, diagnosis, treatment, vaccination, and deep learning applications (last year literature searched: 2024) • Emergence of mpox in the post-smallpox era - A narrative review on mpox epidemiology (last year literature searched: 28 February 2023) • The 2022 monkeypox epidemic and what has led to the current state of the disease in the US: A systematic review (last year literature searched: 20 November 2022) • Outbreaks of human monkeypox during the COVID-19 pandemic: A systematic review for healthcare professionals (last year literature searched: Not reported) • Detection of monkeypox virus according to the collection site of samples from confirmed cases: A systematic review (last year literature searched: 5 October 2022) • The Historical Epidemiology of Human Monkeypox: A Review of Evidence from the 1970 Emergence to the 2022 Outbreak (last year literature searched: 30 July 2022) *Transmissibility* • Is monkeypox a new, emerging sexually transmitted disease? A rapid review of the literature (last year literature searched: 13 September 2022) *Protective immunity* • None identified
High-risk populations	• Association of HIV infection and hospitalization among mpox cases: A systematic review and meta-analysis (last year literature searched: 2024)	• None identified

	Quality of the evidence synthesis	
Organizing framework	**Medium** *(AMSTAR score: 4 – 7 / 11)* N= 54	**Low** *(AMSTAR score: < 4 / 11)* N= 24
	• Mpox reinfection: A rapid systematic review of case reports (Published March 2024) • Risk profile and mode of transmission of mpox: A rapid review and individual patient data meta-analysis of case studies (last year literature searched: 30 July 2022)	
Prevention and control	*General* • Diagnostic accuracy of polymerase chain reaction for detection of mpox in humans (last year literature searched: December 2024) • The feasibility of elimination of monkeypox virus in Nigeria: A systematic review (last year literature searched: 2024) • Ethical considerations during mpox outbreak: A scoping review (last year literature searched: 15 February 2023) • A critical review of mpox outbreaks, risk factors, and prevention efforts in Africa: Lessons learned and evolving practices (last year literature searched: 2023) • Prevention, risk exposure, and knowledge of monkeypox in occupational settings: A scoping review (last year literature searched: 8 September 2022) *Information and education* • Characteristics, influence, prevention, and control measures of the mpox infodemic: scoping review of infodemiology studies (last year literature searched: 30 April 2024) • Sources of information on monkeypox virus infection. A systematic review with meta-analysis (last year literature searched: 3 August 2023) • Global knowledge and attitudes towards mpox (monkeypox) among healthcare workers: A systematic review and meta-analysis (last year literature searched: August 2023) • Knowledge and attitude towards mpox: Systematic review and meta-analysis (last year literature searched: 25 June 2023) *Non-pharmaceutical measures to prevent infection*	*Information and education* • Social and Behavioural Change Communication Challenges, Opportunities and Lessons from Past Public Health Emergencies and Disease Outbreaks: A Scoping Review (last year literature searched: March 2024) • Monkeypox (mpox)-related knowledge and vaccination hesitancy in non-endemic countries: Concise literature review (last year literature searched: 15 November 2022) *Non-pharmaceutical measures to prevent infection* • School-based interventions on mpox: A scoping review (last year literature searched: 21 March 2023) • Application of artificial intelligence techniques for monkeypox: A systematic review (last year literature searched: 1 January 2023) *Non-pharmaceutical measures to control the spread of infections* • Useful public health countermeasures to control the current multicountry outbreak of monkeypox disease (last year literature searched: 30 June 2022) *Pharmaceutical measures used as part of public health strategies* • Prevention of monkeypox with vaccines: A rapid review (last year literature searched: 8 August 2022) • Repositioning potentials of smallpox vaccines and antiviral agents in monkeypox outbreak: A rapid review on comparative benefits and risks (last year literature searched: 23 August 2022) *Surveillance and reporting*

	Quality of the evidence synthesis	
Organizing framework	**Medium** *(AMSTAR score: 4 – 7 / 11)* N= 54	**Low** *(AMSTAR score: < 4 / 11)* N= 24
	• None identified *Non-pharmaceutical measures to control the spread of infections* • Mpox and surgery: protocols, precautions, and recommendations (last year literature searched: 15 May 2024) • Emerging challenges of mpox transmission: an in-depth scoping review and evidence mapping on breastfeeding practices in South America (last year literature searched: September 2023) • Rapid review on monkeypox policies among the G20 nations: Relevance to policy and practitioner (last year literature searched: 6 May 2022) *Pharmaceutical measures used as part of public health strategies* • The willingness of healthcare workers to be vaccinated against monkeypox and their knowledge about monkeypox: A systematic review and meta-analysis (last year literature searched: 25 May 2024) • Willingness to receive mpox vaccine among men who have sex with men: A systematic review and meta-analysis (last year literature searched: 11 May 2024) • Global perspectives on smallpox vaccine against monkeypox: A comprehensive meta-analysis and systematic review of effectiveness, protection, safety and cross-immunogenicity (last year literature searched: 10 March 2024) • MVA-BN vaccine effectiveness: a systematic review of real-world evidence in outbreak settings (last year literature searched: February 2024) • Prevalence of intentions to receive monkeypox vaccine. A systematic review and meta-analysis. (last year literature searched: 24 July 2023) • Immunogenicity and safety of modified vaccinia ankara (mva) vaccine-a systematic review and meta-analysis of randomized controlled trials. (last year literature searched: 28 June 2023)	• Monkeypox clinical disease: Literature review and a tool proposal for the monitoring of cases and contacts (last year literature searched: 1 June 2022)

	Quality of the evidence synthesis	
Organizing framework	**Medium** *(AMSTAR score: 4 – 7 / 11)* N= 54	**Low** *(AMSTAR score: < 4 / 11)* N= 24
	• Attitudes towards receiving monkeypox vaccination: A systematic review and meta-analysis (last year literature searched: June 2023) • Systematic review on the efficacy, effectiveness, safety, and immunogenicity of monkeypox vaccine (last year literature searched: 26 May 2023) • Real-world effectiveness of monkeypox vaccines: A systematic review (last year literature searched: 3 March 2023) • Global prevalence and correlates of mpox vaccine acceptance and uptake: a systematic review and meta-analysis (last year literature searched: 25 February 2023) • Mpox vaccination and treatment: A systematic review (last year literature searched: 4 February 2023) • Assessment of the knowledge, attitude, and perception of the world's population towards monkeypox and its vaccines: a systematic review and descriptive analysis of cross-sectional studies. (last year literature searched: 2 February 2023) • Safety and efficacy of post-eradication smallpox vaccine as an mpox vaccine: A systematic review with meta-analysis (last year literature searched: 7 September 2022) • Effect of prior immunisation with smallpox vaccine for protection against human mpox: A systematic review (last year literature searched: August 2022) *Surveillance and reporting* • None identified	
Diagnosis	• Laboratory validation and clinical performance of a saliva-based test for monkeypox virus (last year literature searched: 2 October 2022)	• None identified
Clinical presentation	*Symptom onset and duration* • Multi-country monkeypox outbreak: A quantitative evidence synthesis on clinical characteristics, potential transmission routes, and risk factors (last year literature searched: 21 August 2022)	*Symptom onset and duration* • None identified *Complications* • None identified *Variability in clinical presentation*

	Quality of the evidence synthesis	
Organizing framework	**Medium** *(AMSTAR score: 4 – 7 / 11)* N= 54	**Low** *(AMSTAR score: < 4 / 11)* N= 24
	• Clinical manifestations of human mpox infection: A systematic review and meta-analysis (last year literature searched: 16 September 2022) • Comparative evaluation of the clinical presentation and epidemiology of the 2022 and previous mpox outbreaks: A rapid review and meta-analysis (last year literature searched: 30 August 2022) *Complications* • A systematic review on the mental health status of patients infected with monkeypox virus (last year literature searched: March 2023) • Monkeypox-associated manifestations and complications involving the eye: A systematic review and meta-analysis of previous and current outbreaks (last year literature searched: 5 October 2022) *Variability in clinical presentation* • Multi-organ clinical manifestations of mpox: An umbrella review of systematic reviews (last year literature searched: 25 September 2023) • A systematic review to identify novel clinical characteristics of monkeypox virus infection and therapeutic and preventive strategies to combat the virus (last year literature searched: February 2023) • Can the current monkeypox affect the heart? A systematic review of case series and case report (last year literature searched: 1 December 2022) • Epidemiologic situation of HIV and monkeypox coinfection: A systematic review (last year literature searched: 1 October 2022) • Pain associated with monkeypox virus: A rapid review (last year literature searched: 19 August 2022) • Oral lesions in patients with human monkeypox: A systematic scoping review (last year literature searched: July 2022) • Potentially asymptomatic infection of monkeypox virus: A systematic review and meta-analysis (last year literature searched: Not reported)	• Atypical mucocutaneous manifestations of mpox: A systematic review (last year literature searched: October 2024) • Mpox gastrointestinal manifestations: A systematic review (last year literature searched: June 2023) • Comparison of clinical manifestations in mpox patients living with HIV versus without HIV: A systematic review and meta-analysis (last year literature searched: 7 March 2023) • Monkeypox-induced myocarditis: A systematic review (last year literature searched: 5 January 2023) • Neurological manifestations of coronavirus disease 2019 and mpox in pediatric patients and their management: A state-of-the-art systematic review. (last year literature searched: October 2022) • The clinical manifestations and severity of the 2022 monkeypox outbreak among 4080 patients (last year literature searched: 2 September 2022) • Monkeypox infections: seizures and encephalitis (last year literature searched: 8 August 2022) • Oral manifestations in monkeypox: A scoping review on implications for oral health (last year literature searched: Not reported)

	Quality of the evidence synthesis	
Organizing framework	**Medium** *(AMSTAR score: 4 – 7 / 11)* N= 54	**Low** *(AMSTAR score: < 4 / 11)* N= 24
Prognosis	• The impact of immunosuppression on the mortality and hospitalization of monkeypox: A systematic review and meta-analysis of the 2022 outbreak (last year literature searched: 15 January 2024)	• Monkeypox outbreak in the Democratic Republic of Congo: A comprehensive review of clinical outcomes, public health implications, and security measures (last year literature searched: December 2024)
Treatment	• Antiviral treatment against monkeypox: A scoping review (last year literature searched: 12 September 2022) • Lack of clinical evidence of antiviral therapy for human monkeypox: A scoping review (last year literature searched: 2 June 2022) • Availability, scope and quality of monkeypox clinical management guidelines globally: A systematic review (last year literature searched: 14 October 2021) • Prevention and treatment of monkeypox: A systematic review of preclinical studies (last year literature searched: Not reported)	• None identified

Appendix 6b: Identified medium and low-quality evidence syntheses that described mpox clade I and/or clade II

	Quality of the evidence synthesis	
Organizing framework	**Medium** *(AMSTAR: 4 – 7 / 11)* N= 26	**Low** *(AMSTAR: < 4 / 11)* N= 24
Biology	• Virus identification for monkeypox in human seminal fluid samples: A systematic review • Serial intervals and incubation periods of the monkeypox virus clades (last year literature searched: August 2022)	• Mpox incubation and infectious periods (last year literature searched: 2023) • Viral load dynamics and shedding kinetics of mpox infection: A systematic review and meta-analysis (last year literature searched: April 2023) • Emerging evidence on monkeypox: Resurgence, global burden, molecular insights, genomics and possible management (last year literature searched: 24 November 2022)
Epidemiology	*General* • Molecular epidemiology, transmission and clinical features of 2022-mpox outbreak: A systematic review (last year literature searched: 2023	*General* • Mpox virus as a global public health emergency: A scoping review (last year literature searched: January 2025)

	Quality of the evidence synthesis	
	• Human monkeypox: A comprehensive narrative review and analysis of the public health implications (last year literature searched: 5 July 2022) • The changing epidemiology of human monkeypox - A potential threat? A systematic review (last year literature searched: 7 September 2020) • A systematic review of the epidemiology of human monkeypox outbreaks and implications for outbreak strategy (last year literature searched: August 2018) *Transmissibility* • Mpox routes of transmission (last year literature searched: 2024) • Mpox person-to-person transmission-where have we got so far? A systematic review (last year literature searched: 15 April 2023) • Epidemiological situation of monkeypox transmission by possible sexual contact: A systematic review (last year literature searched: 18 August 2022) • Mapping global zoonotic niche and interregional transmission risk of monkeypox: a retrospective observational study (last year literature searched: 2022) *Geographic spread* • Dynamics of mpox infection in Nigeria: A systematic review and meta-analysis (last year literature searched: Not reported) *Protective immunity* • None identified	• The growing mpox infections by clade I variant in African countries Is a public health emergency of international concern: A narrative review (last year literature searched: December 2024) • Concurrent outbreaks in Africa – An update (last year literature searched: October 2022) • The re-emerging monkeypox disease. (last year literature searched: December 2022) • Relooking the monkeypox virus during this present outbreak: Epidemiology to therapeutics and vaccines (last year literature searched: 2022) • Monkeypox epidemiology, clinical presentation, and transmission: A systematic review (last year literature searched: September 2022) • Monkeypox resurgence and its implications for Dentistry - A scoping review. (last year literature searched: September 2022) • Monkeypox: A review of a zoonotic disease of global public health concern (last year literature searched: 2022) • The changing global epidemiology of re-emerging human monkeypox virus infection: A systematic review (last year literature searched: 2022) • As the world struggles with the covid-19 pandemic, another emergency threat arrives on the horizon, the monkeypox: A systematic review (last year literature searched: Not reported) • Monkeypox: A comprehensive review of virology, epidemiology, transmission, diagnosis, prevention, treatment, and artificial intelligence applications (last year literature searched: Not reported) *Transmissibility* • Monkeypox (mpox): Evolution of transmission and comprehensive review (last year literature searched: Not reported) *Geographic spread* • None identified *Protective immunity* • None identified
High-risk populations	• Meta-analysis of demographic disparities in monkeypox infections among diverse populations (last year literature searched: Not reported)	• None identified

	Quality of the evidence synthesis	
	• Clinical and epidemiological interventions for monkeypox management in children: A systematic review (last year literature searched: 1 February 2023)	
Prevention and control	*Information and education* • None identified *Non-pharmaceutical measures to prevent infection* • None identified *Non-pharmaceutical measures to control the spread of infections* • Adherence and barriers to following isolation guidance for mpox (last year literature searched: 2022) *Pharmaceutical measures used as part of public health strategies* • Effectiveness of a single dose of JYNNEOS vaccine in real world: A systematic review and meta-analysis (last year literature searched: 15 August 2023) *Surveillance and reporting* • How can imported monkeypox break the borders? A rapid systematic review (last year literature searched: 5 August 2022)	*General* • Infection prevention and control measures to reduce the transmission of mpox: A systematic review (last year literature searched: 15 December 2022) *Information and education* • None identified *Non-pharmaceutical measures to prevent infection* • None identified *Non-pharmaceutical measures to control the spread of infections* • None identified *Pharmaceutical measures used as part of public health strategies* • None identified *Surveillance and reporting* • None identified
Diagnosis	• None identified	• Overview of diagnostic methods, disease prevalence and transmission of mpox (formerly monkeypox) in humans and animal reservoirs (last year literature searched: 2 September 2022)
Clinical presentation	*Symptom onset and duration* • Mpox clinical presentation, diagnostic approaches, and treatment strategies: A review (last year literature searched: 13 September 2024) • Clinical characteristics and outcomes of patients with mpox during the 2022 mpox outbreak compared with those before the outbreak: A systematic review and meta-analysis (last year literature searched: 13 October 2022) *Complications* • None identified	*General* • Monkeypox virus: Past and present (last year literature searched: June 2022) • Human monkeypox virus: A systematic critical review during the pandemic peak (last year literature searched: July 2022) *Complications* • Neurological manifestations of an emerging zoonosis-Human monkeypox virus: A systematic review (last year literature searched: 13 April 2023) ***(clade I only)***

	Quality of the evidence synthesis	
	Variability in clinical presentation • Oral manifestation of the monkeypox virus: A systematic review and meta-analysis (last year literature searched: 15 November 2022) • Gastrointestinal symptoms of monkeypox infection: a systematic review and meta-analysis (last year literature searched: 21 October 2022) • Oral lesions in human monkeypox disease and their management - A scoping review (last year literature searched: 15 August 2022)	*Variability in clinical presentation* • None identified
Prognosis	• The effect of HIV and mpox co-infection on clinical outcomes: Systematic review and meta-analysis • Global monkeypox case hospitalisation rates: A rapid systematic review and meta-analysis (last year literature searched: August 2022)	• Symptomatology, prognosis, and clinical findings of monkeypox infected patients during COVID-19 era: A systematic-review. (last year literature searched: 14 June 2022) • Monkeypox infection 2022: An updated narrative review focusing on the neonatal and pediatric population (last year literature searched: 18 November 2022)
Treatment	• Effectiveness of Tecovirimat in mpox cases: A systematic review of current evidence (last year literature searched: 21 December 2024) • Clinical features, antiviral treatment, and patient outcomes: A systematic review and comparative analysis of the previous and the 2022 mpox outbreaks (last year literature searched: 10 January 2023) • Recent developments in mpox prevention and treatment options (last year literature searched: 2022)	• Monkeypox virus: A comprehensive overview of viral pathology, immune response, and antiviral strategies. (last year literature searched: Not reported) • Prevention and treatment of monkeypox: A step-by-step guide for healthcare professionals and general population (last year literature searched: Not reported)

Appendix 7: Full classification of identified medium and low-quality evidence syntheses from versions 1 – 13

Organizing framework	Hyperlinked title
Unspecified clade (medium-quality)	

• Epidemiology
  ○ Transmissibility
  ○ Protective immunity
• High-risk populations
• Prevention and control
  ○ Pharmaceutical measures used as part of public health strategies
	Monkeypox (Mpox): Evolution of Transmission and Comprehensive Review

• Clinical presentation
  ○ Symptom onset and duration
  ○ Complications
• Prognosis
• Treatment
	Monkeypox Virus: A Comprehensive Overview of Viral Pathology, Immune Response, and Antiviral Strategies

• Biology
• Epidemiology
  ○ Transmissibility
• Prevention and control
  ○ Pharmaceutical measures used as part of public health strategies
	Application of Artificial Intelligence Techniques for Monkeypox: A Systematic Review

• Diagnosis • Clinical presentation • Treatment	Symptomatology, prognosis, and clinical findings of Monkeypox infected patients during COVID-19 era: A systematic-review
• Epidemiology • Diagnosis • Prevention and control	Viral load dynamics and shedding kinetics of mpox infection: a systematic review and meta-analysis
• Epidemiology • Prevention and control • Treatment	School-based interventions on Mpox: A scoping review
• Prevention and control ○ Information and education (e.g., including risk communication)	Monkeypox clinical disease: Literature review and a tool proposal for the monitoring of cases and contacts

• Prevention and control
  ○ Non-pharmaceutical measures to prevent infection
  ○ Pharmaceutical measures used as part of public health strategies
	Emerging evidence on Monkeypox: resurgence, global burden, molecular insights, genomics and possible management

• Epidemiology	Oral Manifestations in Monkeypox: A Scoping Review on Implications for Oral Health

Organizing framework	Hyperlinked title
○ Transmissibility • Clinical presentation ○ Symptom onset and duration ○ Variability in clinical presentation	
• Prevention and control ○ Information and education (e.g., including risk communication) ○ Non-pharmaceutical measures to prevent infection ○ Non-pharmaceutical measures to control the spread of infections ○ Pharmaceutical measures used as part of public health strategies ○ Strategies grounded in behavioural science ○ Surveillance and reporting • Clinical presentation ○ Symptom onset and duration ○ Complications ○ Variability in clinical presentation • Prognosis (e.g., clinical severity, including morbidity and mortality)	Useful public health countermeasures to control the current multicountry outbreak of Monkeypox disease
• Epidemiology ○ Transmissibility	Overview of Diagnostic Methods, Disease Prevalence and Transmission of Mpox (Formerly Monkeypox) in Humans and Animal Reservoirs
• Clinical presentation ○ Symptom onset and duration ○ Complications ○ Variability in clinical presentation • Treatment	Neurological manifestations of an emerging zoonosis-Human monkeypox virus: A systematic review
• Prevention and control ○ Non-pharmaceutical measures to control the spread of infections • Clinical presentation ○ Symptom onset and duration ○ Complications ○ Variability in clinical presentation	Neurological Manifestations of Coronavirus Disease 2019 and Mpox in Pediatric Patients and Their Management: A State-of-the-Art Systematic Review
• Epidemiology ○ Transmissibility • Prevention and control • Clinical presentation	Detection of Monkeypox Virus according to The Collection Site of Samples from Confirmed Cases: A Systematic Review
• Clinical presentation ○ Symptom onset and duration	The Changing Global Epidemiology of Re-emerging Human Monkeypox Virus Infection: A Systematic Review
• Epidemiology ○ Transmissibility	Monkeypox Infection 2022: An Updated Narrative Review Focusing on the Neonatal and Pediatric Population

Organizing framework	Hyperlinked title

• High-risk populations
• Clinical presentation
  ○ Symptom onset and duration
  ○ Complications
  ○ Variability in clinical presentation	

• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
• High-risk populations
• Prevention and control
• Diagnosis
• Clinical presentation
  ○ Symptom onset and duration
  ○ Complications
  ○ Variability in clinical presentation
• Prognosis (e.g., clinical severity, including morbidity and mortality)
• Treatment
	Infection prevention and control measures to reduce the transmission of mpox: A systematic review

• Prevention and control • Epidemiology ○ Transmissibility	MVA-BN vaccine effectiveness: A systematic review of real-world evidence in outbreak settings
• Biology	A Review of Evidence Related to the Zoonotic Characteristics of the Monkeypox Virus
• Epidemiology • Clinical presentation	Multi-country monkeypox outbreak: A quantitative evidence synthesis on clinical characteristics, potential transmission routes, and risk factors
• Clinical presentation	The clinical manifestations and severity of the 2022 monkeypox outbreak among 4080 patients
• Diagnosis	Laboratory validation and clinical performance of a saliva-based test for monkeypox virus
• Epidemiology	Reproduction number of monkeypox in the early stage of the 2022 multi-country outbreak
Clade I and/or II (medium-quality)	

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
• Prevention and control
• Clinical presentation
• Diagnosis
	Mpox Clinical Presentation, Diagnostic Approaches, and Treatment Strategies: A Review

Organizing framework	Hyperlinked title

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
• Prevention and control
  ○ Non-pharmaceutical measures to control the spread of infections
  ○ Pharmaceutical measures used as part of public health strategies
  ○ Surveillance and reporting
	As the World Struggles With the COVID-19 Pandemic, Another Emergency Threat Arrives on the Horizon, the Monkeypox: A Systematic Review

• Biology
  ○ Clade I
  ○ Clade II
	Serial intervals and incubation periods of the monkeypox virus clades

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
  ○ Transmissibility
• Prognosis
	A systematic review of the epidemiology of human monkeypox outbreaks and implications for outbreak strategy

• Biology
  ○ Clade I
• Clinical presentation
  ○ Symptom onset and duration
• Complications
	Monkeypox: A review of a zoonotic disease of global public health concern

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
• Transmissibility
	Comparison of clinical manifestations in mpox patients living with HIV versus without HIV: A systematic review and meta-analysis

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
• Diagnosis
• Treatment
	Monkeypox resurgence and its implications for Dentistry - A scoping review

• Biology ○ Clade I	Is monkeypox a new, emerging sexually transmitted disease? A rapid review of the literature

Organizing framework	Hyperlinked title
○ Clade II	
• Biology ○ Clade I ○ Clade II • Clinical presentation ○ Symptom onset and duration • Prognosis	Mpox gastrointestinal manifestations: A systematic review
• Biology ○ Clade I ○ Clade II • Epidemiology ○ Transmissibility ○ Geographic spread • High-risk populations • Prevention and control • Treatment	Monkeypox (MPOX)-Related Knowledge and Vaccination Hesitancy in Non-Endemic Countries: Concise Literature Review
• Biology ○ Clade I ○ Clade II • Epidemiology	Outbreaks of human monkeypox during the COVID-19 pandemic: a systematic review for healthcare professionals
• Biology ○ Clade I ○ Clade II • Epidemiology ○ Transmissibility • Clinical presentation ○ Symptom onset and duration	Relooking the monkeypox virus during this present outbreak: epidemiology to therapeutics and vaccines
• Biology ○ Clade I ○ Clade II • Prevention and control ○ Pharmaceutical measures used as part of public health strategies • Treatment	Emergence of mpox in the post-smallpox era-a narrative review on mpox epidemiology
• Biology ○ Clade I ○ Clade II • Epidemiology	The 2022 Monkeypox Epidemic and What Has Led to the Current State of the Disease in the US: A Systematic Review

Organizing framework	Hyperlinked title
○ Transmissibility ○ Geographic spread ○ Protective immunity • Prevention and control ○ Pharmaceutical measures used as part of public health strategies	
• Biology ○ Clade I ○ Clade II • Epidemiology ○ Transmissibility • Prevention and control ○ Information and education (e.g., including risk communication) ○ Pharmaceutical measures used as part of public health strategies • Diagnosis • Clinical presentation ○ Symptom onset and duration • Treatment	Monkeypox epidemiology, clinical presentation, and transmission: a systematic review
• Biology ○ Clade I ○ Clade II • Epidemiology ○ Transmissibility ○ Geographic spread • High-risk populations • Protective immunity • Prevention and control ○ Non-pharmaceutical measures to prevent infection ○ Pharmaceutical measures used as part of public health strategies • Diagnosis • Clinical presentation ○ Symptom onset and duration ○ Complications ○ Variability in clinical presentation • Prognosis (e.g., clinical severity, including morbidity and mortality) • Treatment	The re-emerging monkeypox disease
• Biology ○ Clade I	Prevention and Treatment of Monkeypox: A Step-by-Step Guide for Healthcare Professionals and General Population

Organizing framework	Hyperlinked title
○ Clade II • Prevention and control • Clinical presentation ○ Symptom onset and duration • Treatment	
Unspecified clade (low-quality)	
• Prevention and control ○ Information and education (e.g., including risk communication) ○ Strategies grounded in behavioural science	Social and Behavioural Change Communication Challenges, Opportunities and Lessons from Past Public Health Emergencies and Disease Outbreaks: A Scoping Review
• Treatment	Antiviral Treatment against Monkeypox: A Scoping Review
• Biology	Virus Identification for Monkeypox in Human Seminal Fluid Samples: A Systematic Review
• Prevention and control ○ Non-pharmaceutical measures to prevent infection ○ Pharmaceutical measures used as part of public health strategies • Treatment	Recent Developments in Mpox Prevention and Treatment Options
• Prevention and control ○ Pharmaceutical measures used as part of public health strategies • Treatment	Prevention and Treatment of Monkeypox: A Systematic Review of Preclinical Studies
• Prevention and control • Clinical presentation ○ Symptom onset and duration ○ Variability in clinical presentation	Epidemiologic Situation of HIV and Monkeypox Coinfection: A Systematic Review
• Clinical presentation ○ Symptom onset and duration • Variability in clinical presentation	Clinical manifestations of human Mpox infection: A systematic review and meta-analysis
• Prevention and control ○ Non-pharmaceutical measures to prevent infection ○ Pharmaceutical measures used as part of public health strategies	The Feasibility of Elimination of Monkeypox Virus in Nigeria: A Systematic Review
• Prevention and control ○ Pharmaceutical measures used as part of public health strategies	Systematic Review on the Efficacy, Effectiveness, Safety, and Immunogenicity of Monkeypox Vaccine
• Epidemiology ○ Transmissibility • Prevention and control ○ Non-pharmaceutical measures to prevent infection ○ Pharmaceutical measures used as part of public health strategies	A systematic review on environmental perspectives of monkeypox virus

Organizing framework	Hyperlinked title
○ Surveillance and reporting	
• Prevention and control ○ Information and education (e.g., including risk communication)	Ethical considerations during Mpox Outbreak: a scoping review
• Prevention and control ○ Pharmaceutical measures used as part of public health strategies	Global perspectives on smallpox vaccine against monkeypox: a comprehensive meta-analysis and systematic review of effectiveness, protection, safety and cross-immunogenicity
• Prevention and control ○ Information and education (e.g., including risk communication)	Attitudes towards Receiving Monkeypox Vaccination: A Systematic Review and Meta-Analysis
• Clinical presentation ○ Symptom onset and duration ○ Variability in clinical presentation • Treatment	A systematic review to identify novel clinical characteristics of monkeypox virus infection and therapeutic and preventive strategies to combat the virus
• Prevention and control ○ Information and education (e.g., including risk communication)	Knowledge and attitude towards mpox: Systematic review and meta-analysis
• Prevention and control ○ Pharmaceutical measures used as part of public health strategies • Treatment	Mpox vaccination and treatment: a systematic review
• Clinical presentation ○ Symptom onset and duration	Oral lesions in patients with human monkeypox: A systematic scoping review
• Treatment	Lack of clinical evidence of antiviral therapy for human monkeypox: A scoping review
• Prevention and control ○ Pharmaceutical measures used as part of public health strategies	Safety and Efficacy of Post-Eradication Smallpox Vaccine as an Mpox Vaccine: A Systematic Review with Meta-Analysis
• Epidemiology • Clinical presentation ○ Symptom onset and duration • Treatment	Oral lesions in human monkeypox disease and their management-a scoping review
• Epidemiology • High-risk populations • Prognosis	Mpox reinfection: A rapid systematic review of case reports
• Epidemiology • Transmissibility	Monkeypox viral detection in semen specimens of confirmed cases: A systematic review and meta-analysis
• Epidemiology ○ Transmissibility • High-risk populations • Prognosis	Risk profile and mode of transmission of Mpox: A rapid review and individual patient data meta-analysis of case studies
• Prevention and control ○ Pharmaceutical measures used as part of public health strategies	Effect of prior immunisation with smallpox vaccine for protection against human Mpox: A systematic review

Organizing framework	Hyperlinked title

• Epidemiology
• High-risk populations
• Clinical presentation
  ○ Symptom onset and duration
  ○ Variability in clinical presentation
	Comparative evaluation of the clinical presentation and epidemiology of the 2022 and previous Mpox outbreaks: a rapid review and meta-analysis

• High-risk populations • Prevention and control ○ Pharmaceutical measures used as part of public health strategies	Global prevalence and correlates of mpox vaccine acceptance and uptake: a systematic review and meta-analysis

• Prevention and control
  ○ Information and education (e.g., including risk communication)
  ○ Non-pharmaceutical measures to prevent infection
  ○ Non-pharmaceutical measures to control the spread of infections
  ○ Pharmaceutical measures used as part of public health strategies
  ○ Surveillance and reporting
• Treatment
	Rapid review on monkeypox policies among the G20 nations: relevance to policy and practitioner

• Prevention and control ○ Information and education (e.g., including risk communication)	Global knowledge and attitudes towards mpox (monkeypox) among healthcare workers: a systematic review and meta-analysis
• Prevention and control ○ Information and education (e.g., including risk communication)	Sources of information on monkeypox virus infection. A systematic review with meta-analysis
• Treatment	Availability, scope and quality of monkeypox clinical management guidelines globally: a systematic review
• Prevention and control ○ Pharmaceutical measures used as part of public health strategies	Prevalence of intentions to receive monkeypox vaccine. A systematic review and meta-analysis
• Prevention and control ○ Information and education (e.g., including risk communication)	Assessment of the knowledge, attitude, and perception of the world's population towards monkeypox and its vaccines: A systematic review and descriptive analysis of cross-sectional studies
• Clinical presentation ○ Complications	Can the current monkeypox affect the heart? A systematic review of case series and case report

• Epidemiology
  ○ Transmissibility
• High-risk populations
• Clinical presentation
  ○ Symptom onset and duration
  ○ Complications
• Prevention and control
  ○ Pharmaceutical measures used as part of public health strategies
• Prognosis
	A global systematic evidence review with meta-analysis of the epidemiological characteristics of the 2022 Mpox outbreaks

Organizing framework	Hyperlinked title
• Prevention and control ○ Information and education (e.g., including risk communication)	The willingness of healthcare workers to be vaccinated against monkeypox and their knowledge about monkeypox: A systematic review and meta-analysis
• Epidemiology ○ Transmissibility • High-risk populations • Prevention and control	Prevention, Risk Exposure, and Knowledge of Monkeypox in Occupational Settings: A Scoping Review
• Clinical presentation ○ Complications	A Systematic Review on the Mental Health Status of Patients Infected With Monkeypox Virus

• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
	Factors associated with geographic variations in the 2022 monkeypox outbreak; A systematic review

• Prevention and control ○ Pharmaceutical measures used as part of public health strategies	Real-world effectiveness of monkeypox vaccines: a systematic review

• Epidemiology
  ○ Transmissibility
• High-risk populations
• Prevention and control
  ○ Pharmaceutical measures used as part of public health strategies
• Prognosis
	A Systematic Review of 5110 Cases of Monkeypox: What Has Changed Between 1970 and 2022?

• Clinical presentation • Diagnosis	Potentially Asymptomatic Infection of Monkeypox Virus: A Systematic Review and Meta-Analysis
• Clinical presentation ○ Symptoms • Epidemiology • Prevention and control	A critical review of mpox outbreaks, risk factors, and prevention efforts in Africa: lessons learned and evolving practices
• Epidemiology • High-risk populations • Prevention and control ○ Pharmaceutical measures used as part of public health strategies	Willingness to receive mpox vaccine among men who have sex with men: a systematic review and meta-analysis

• Prevention and control
  ○ Information and education (e.g., including risk communication)
  ○ Surveillance and reporting
	Characteristics, Influence, Prevention, and Control Measures of the Mpox Infodemic: Scoping Review of Infodemiology Studies

• Clinical presentation
  ○ Symptom onset and duration
  ○ Complications
  ○ Variability in presentation
• Prognosis
	Pain Associated With Monkeypox Virus: A Rapid Review

Organizing framework	Hyperlinked title
• Treatment	
• Prevention and control ○ Pharmaceutical measures used as part of public health strategies	Immunogenicity and Safety of Modified Vaccinia Ankara (MVA) Vaccine-A Systematic Review and Meta-Analysis of Randomized Controlled Trials
• Clinical presentation ○ Symptoms • Variability in presentation	Multi-organ clinical manifestations of Mpox: an umbrella review of systematic reviews

• Prevention and control
  ○ Non-pharmaceutical measures to prevent infection
  ○ Non-pharmaceutical measures to control the spread of infections
	Mpox and Surgery: Protocols, Precautions, and Recommendations

• Epidemiology
  ○ Transmissibility
• Prevention and control
  ○ Non-pharmaceutical measures to prevent infection
	Emerging Challenges of Mpox Transmission: An In-depth Scoping Review and Evidence Mapping on Breastfeeding Practices in South America

• Epidemiology	The Historical Epidemiology of Human Monkeypox: A Review of Evidence from the 1970 Emergence to the 2022 Outbreak
• Clinical presentation	Monkeypox infections: seizures and encephalitis
Clade I and/or II (low-quality)	

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
• Prevention and control
	Monkeypox: A Comprehensive Review of Virology, Epidemiology, Transmission, Diagnosis, Prevention, Treatment, and Artificial Intelligence Applications

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
• Geographic spread
	The changing epidemiology of human monkeypox-A potential threat? A systematic review

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
  ○ Transmissibility
• High-risk populations
• Clinical presentation
  ○ Symptom onset and duration
	Epidemiological Situation of Monkeypox Transmission by Possible Sexual Contact: A Systematic Review

Organizing framework	Hyperlinked title
○ Variability in clinical presentation	
• Biology ○ Clade I ○ Clade II • Epidemiology ○ Transmissibility	Mpox Person-to-Person Transmission-Where Have We Got So Far? A Systematic Review
• Biology ○ Clade I ○ Clade II • Clinical presentation	Clinical characteristics and outcomes of patients with mpox during the 2022 mpox outbreak compared with those before the outbreak: A systematic review and meta-analysis
• Biology ○ Clade I ○ Clade II • Epidemiology • Clinical presentation ○ Symptom onset and duration ○ Variability in clinical presentation	Oral manifestation of the monkeypox virus: a systematic review and meta-analysis
• Biology ○ Clade I ○ Clade II • Clinical presentation ○ Symptom onset and duration	Gastrointestinal Symptoms of Monkeypox Infection: A systematic review and meta-analysis
• Biology ○ Clade I ○ Clade II • Prognosis	The impact of immunosuppression on the mortality and hospitalization of Monkeypox: a systematic review and meta-analysis of the 2022 outbreak
• Biology ○ Clade I ○ Clade II • High-risk populations	Meta-Analysis of Demographic Disparities in Monkeypox Infections among Diverse Populations
• Biology ○ Clade I ○ Clade II • Epidemiology ○ Transmissibility • Prevention and control ○ Surveillance and reporting	How can imported monkeypox break the borders? A rapid systematic review

Organizing framework	Hyperlinked title

• Biology
  ○ Clade I
  ○ Clade II
• Clinical presentation
  ○ Variability in clinical presentation
	Monkeypox-Associated Manifestations and Complications Involving the Eye: A Systematic Review and Meta-Analysis of Previous and Current Outbreaks

• Biology
  ○ Clade I
  ○ Clade II
• High-risk populations
• Prevention and control
  ○ Pharmaceutical measures used as part of public health strategies
• Prognosis
• Treatment
	Clinical Features, Antiviral Treatment, and Patient Outcomes: A Systematic Review and Comparative Analysis of the Previous and the 2022 Mpox Outbreaks

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
• High-risk populations
	Dynamics of Mpox infection in Nigeria: a systematic review and meta-analysis

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
  ○ Transmissibility
  ○ Geographic spread
• High-risk populations
• Clinical presentation
  ○ Symptom onset and duration
  ○ Complications
• Prevention and control
  ○ Pharmaceutical measures used as part of public health strategies
	Molecular epidemiology, transmission and clinical features of 2022-mpox outbreak: A systematic review

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
• High-risk populations
	Clinical and Epidemiological Interventions for Monkeypox Management in Children: A Systematic Review

Organizing framework	Hyperlinked title

• Clinical presentation
• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
• High-risk populations
• Prevention and control
• Diagnosis
• Treatment	

• Biology
  ○ Clade I
  ○ Clade II
• Epidemiology
• Prevention and control
  ○ Pharmaceutical measures used as part of public health strategies
• Diagnosis
• Treatment
	Human Monkeypox: A Comprehensive Narrative Review and Analysis of the Public Health Implications

• Biology
  ○ Clade I
  ○ Clade II
• High-risk populations
• Prognosis
	The effect of HIV and mpox co-infection on clinical outcomes: Systematic review and meta-analysis

• Biology
  ○ Clade I
  ○ Clade II
• Prognosis
	Global monkeypox case hospitalisation rates: A rapid systematic review and meta-analysis

• Biology
  ○ Clade I
  ○ Clade II
• Prevention and control
  ○ Pharmaceutical measures used as part of public health strategies
  ○ Surveillance and reporting
	Effectiveness of a single dose of JYNNEOS vaccine in real world: A systematic review and meta-analysis

Appendix 8: Documents excluded at the final stages of reviewing

Document type	Hyperlinked title
Other types of documents (e.g., case reports, reviews with no search strategy, commentaries, and editorials)	Mpox-induced metabolic alterations
	Update on mpox management: Epidemiology, vaccines and therapeutics, and regulatory changes
	Severe mpox requiring colostomy in a patient with advanced HIV disease: A case report and literature review
	Monkeypox (mpox): Diagnosis and emerging challenges
	Exploring the genomic basis of mpox virus-host transmission and pathogenesis
	Monkeypox: A comprehensive review on mutation, transmission, pathophysiology, and therapeutics
	Clade Ib: A new emerging threat in the mpox outbreak
	Mpox virus (MPXV): Comprehensive analysis of pandemic risks, pathophysiology, treatments, and mRNA vaccine development
	Mpox outbreak in previously non-endemic countries: A review on impact on Asia
	Immunobiology of mpox infection and its management: Experience from developing nations
	Urogenital manifestations in mpox (monkeypox) infection: A comprehensive review of epidemiology, pathogenesis, and therapeutic approaches
	The current status and future prospects of CRISPR-based detection of monkeypox virus: a review
	Transmission pathways and personal protective equipment requirement for mpox clade Ib lineage: Nothing new on this front
	Mpox clade I outbreak and the first European case ex Africa, in Sweden – a call for global health equity
	Evaluation of analytical performance of the standard(tm) m10 MPX/OPX assay for the simultaneous DNA detection and clade attribution of monkeypox virus
	Multiple introductions and sustained local transmission of monkeypox virus in southern Brazil between 2022–2023
	Repurposing drugs for synergistic combination therapies to counteract monkeypox virus tecovirimat resistance
	Case reports of human monkeypox virus infections, Uganda, 2024
	Monkeypox virus infection in pregnancy: description of two cases reported to the Colombian National Institute of Health
	Identification of potential biomarkers for 2022 mpox virus infection: a transcriptomic network analysis and machine learning approach

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