UK Health Security Agency

Mpox asymptomatic and pre-symptomatic transmission

A rapid evidence summary

Contents

Main messages

1. This rapid evidence summary (search up to 29 August 2024) identified and summarised evidence relating to asymptomatic and pre-symptomatic transmission of mpox infection in humans.

2. Seven studies were included (1 to 7), of which 3 were prospective cohort studies (2, 5, 7), 3 were retrospective cohort studies (1, 3, 6), and one was a case-control study (4). Five of the included studies report detection of the virus in asymptomatic or pre-symptomatic cases rather than evidence of confirmed transmission.

3. Two studies reported on mpox clade IIb (1, 2), 5 studies did not report mpox clade (3 to 7). All studies were conducted between May 2022 and June 2023, in Asia, Europe and North America. It is likely that studies which did not report mpox clade were mostly describing mpox clade IIb, given the countries and timeframes. However, as this was not confirmed the results have been reported separately in this review.

4. One study demonstrated detectable viral load of mpox clade IIb in asymptomatic cases. The study reported that viral load was slightly lower in rectal and perianal samples from asymptomatic cases than in samples from symptomatic cases. However, this finding was only from 2 samples (from 2 out of 4 asymptomatic cases) and was close to the range of values from symptomatic cases (33 cases). Throat samples showed no difference in viral load. In this study, 19 cases (51.4%) were living with Human Immunodeficiency Virus (HIV), of which 11 were receiving regular antiretroviral treatment. Three cases had Cluster of Differentiation 4 (CD4) counts between 300 to 400 per millimetre cubed [mm^3], 6 had counts above 500 cells per mm^3, and CD4 counts were not reported for the remaining cases living with HIV (1).

5. A second study reported pre-symptomatic detection of mpox clade IIb, by viral positivity in samples from 5 cases at one to 4 days before symptom onset. HIV status of these cases was not reported (2).

6. Two studies reported asymptomatic and pre-symptomatic transmission of mpox (clade not reported) (3, 4). One study (HIV status not reported) reported pre-symptomatic transmission in 5 cases, with the contacts developing symptoms 0 to 4 days after the date of exposure (3). Another study reported that sexual transmission from asymptomatic cases was the cause of infection in 10 out of 54 cases (4). Nineteen cases (35%) were living with HIV (antiretroviral treatment status and CD4 counts not reported).

7. Three studies reported that mpox viral load (clade not reported) in asymptomatic cases was the same as, or slightly greater, than in symptomatic cases (5 to 7). However, the sample sizes of these studies were very small (4 to 9 cases). HIV status was reported in 2 of these studies (5, 6). Across the 2 studies, 6 out of the 11 cases (54%) were people

living with HIV, all of whom were receiving antiretroviral treatment. CD4 counts were only reported by one study, in which all 3 cases had counts above 350 cells per mm^3 (6).

8. Critical appraisal was not performed, which restricts the interpretation of the findings, although important limitations of the evidence have been highlighted. These include the small sample sizes of all included studies (4 to 54 cases), and discrepancy in the reporting of results by one study (1). Whether cases had symptoms or not was based on self-reporting and may be subjective. It should also be noted that most studies report viral load or viral positivity as an indicator of the likelihood of infectiousness and therefore the possibility of transmission. However, these outcomes do not inform whether transmission actually occurred. Viral load may also vary by stage of infection, but the studies did not all clearly report when samples were taken.

9. In summary, limited evidence was identified to answer the review question. There was evidence of detectable virus in asymptomatic and pre-symptomatic cases, and 2 studies suggested that transmission of mpox had occurred from asymptomatic and pre-symptomatic cases. However, the evidence doesn't enable conclusions to be made about the overall likelihood of asymptomatic and pre-symptomatic transmission. Living with HIV, HIV treatment and CD4 counts were inconsistently reported between studies, therefore It was not possible to determine whether asymptomatic and pre-symptomatic transmission was affected by HIV positivity or immune status of the cases. No evidence was identified on mpox clade I.

Purpose

The purpose of this rapid evidence summary was to identify and summarise the available evidence of asymptomatic and pre-symptomatic transmission of mpox.

The review question was:

What is the evidence for asymptomatic and pre-symptomatic transmission of mpox virus in humans?

Methods

A rapid evidence summary was conducted, following streamlined systematic methods to accelerate the review process. A literature search was undertaken to look for relevant primary studies published or available as preprint, up to 29 August 2024. A previous review on the infectious and incubation periods, and transmission of mpox completed by UKHSA in 2022 was also checked for relevant studies (8).

Any measures of transmission of mpox from cases with asymptomatic or pre-symptomatic mpox were included, including when in comparison to cases with symptomatic mpox. Studies on transmission provide the most direct evidence for the infectious period. Other studies provide evidence that indicate likelihood of transmission, such as viral load (amount of detectable virus), and viral positivity (presence of detectable virus).

The following definitions were applied in this review:

- asymptomatic cases were defined as people infected with the mpox virus who did not exhibit any noticeable symptoms of infection
- pre-symptomatic cases were defined as people infected with the mpox virus who did not have mpox symptoms at the time of testing, but eventually exhibited them
- symptomatic cases were defined as people infected with the mpox virus who exhibited recognised symptoms of the disease at the time of testing, such as a high temperature (fever), a headache, muscle aches, backache, swollen glands, shivering (chills), exhaustion, joint pains (9)

A protocol was produced before the literature search was conducted, including the review question, the eligibility criteria, and all other methods. Full details of the methodology are provided in the protocol in Annexe A.

One protocol deviation was made to amend the inclusion criteria to include evidence from laboratory confirmed mpox when clade was not reported (from any country), as well as those specified as clade Ia, Ib, IIa or IIb. This was to ensure that all information which

may inform whether there is asymptomatic or pre-symptomatic transmission of mpox was included in this review.

Screening on title and abstracts was undertaken in duplicate by 2 reviewers for 10% of eligible studies, with the remainder completed by one reviewer. Screening on full text was undertaken by one reviewer and excluded studies were checked by a second. Data extraction was performed by one reviewer and checked by a second.

Where available, smallpox vaccination history was reported, as well as whether cases were immunocompromised. For cases with Human Immunodeficiency Virus (HIV), Cluster of Differentiation 4 (CD4) count and antiretroviral treatment status was also reported.

Evidence

In total, 3,258 studies were screened at title and abstract and 63 studies were screened at full text. Of these, 7 studies met the inclusion criteria (1 to 7). No additional studies were identified from the mpox review completed by UKHSA in 2022. A PRISMA diagram showing the flow of studies through the review is shown in Annexe B, and studies excluded on full text screening are available with the reasons why in Annexe C. Study characteristics are available in Annexe D.

Three studies were prospective cohort studies (2, 5, 7), 3 were retrospective cohort studies (1, 3, 6), and one was a case-control study (4). All studies were conducted between May 2022 and June 2023. Two studies were conducted in Belgium (2, 6), one was conducted in China (1), one was conducted in Japan (7), one was conducted in the Netherlands (3), one was conducted in Spain (5) and one was conducted in the USA (4).

Two studies reported transmission from asymptomatic and pre-symptomatic cases (3, 4). One study suggested possibility of transmission by measuring viral positivity (2) and 4 measured viral load (1, 5 to 7). Viral load is defined as the quantity of virus present in a sample, using a polymerase chain reaction (PCR) test and reported as cycle threshold (Ct) values. Lower Ct values reflect a higher viral load.

Two studies specified the clade of mpox as IIb (1, 2), 5 did not report the clade (3 to 7).

It is likely that studies which did not report mpox clade were mostly describing mpox clade IIb, given the countries and timeframes. However, as this was not confirmed the results have been reported separately in this review.

Mpox clade IIb

Two studies reported on the possibility of asymptomatic or pre-symptomatic transmission of laboratory confirmed mpox clade IIb (1, 2).

Viral load

Dou and others conducted a retrospective study of 37 men infected with confirmed mpox clade IIb (median age 30 years, IQR: 26.5 to 34.5 years) between 31 May to 21 June 2023, in China (1). Of the total cohort, 33 cases were symptomatic and 4 were asymptomatic. Nineteen cases (51.4%) were living with HIV, with antiretroviral treatment status reported for 12 cases. Eleven were receiving regular antiretroviral treatment, and one was receiving irregular antiretroviral treatment. Three cases had CD4 counts between 300 to 400 mm^3, 6 had counts above 500 cells per mm^3, and CD4 counts were not reported for the remaining HIV positive cases.

There were 4 positive samples from asymptomatic cases. Two of the positive samples from rectal or perianal samples had Ct values of 36 and 37, median (calculated) as 36.25 (IQR: 36.25 to 36.75), and 2 positive throat samples had Ct values of 24 and 37, median (calculated) as 30.5 (IQR: 27.25 to 33.75). In the symptomatic cases, rectal or perianal samples had a median Ct value of 30 (IQR: 17 to 36, 5 positive samples) and throat samples had a median Ct value of 30 (IQR: 27 to 34, 25 positive samples). The study did not report the HIV status of the cases in which viral load was estimated.

Viral positivity

Brosius and others conducted a prospective study of 25 contacts of 23 confirmed mpox clade IIb cases (median age: 43 years, interquartile range [IQR]: 36 to 51 years) between 24 June and 31 July 2022, in Belgium (2). Five contacts (20%) were living with HIV (treatment status and CD4 counts not reported), 5 (20%) received post exposure vaccination for mpox, and 6 (24%) had received childhood smallpox vaccination. Contacts were followed up for a median of 16 days (IQR: 14 to 26 days) after their last exposure to an individual infected with mpox. Mpox testing was performed in blood samples, throat swabs, genital swabs, anorectal swabs, and skin lesion swabs, but the study did not report results by sample type.

Of the 25 contacts, 8 had confirmed mpox infection, 5 of which had mpox detected when they were pre-symptomatic. This occurred one day before symptom onset in 3 cases, and 4 days before symptom onset in 2 cases. The study did not report whether these 5 contacts were the same as the 5 contacts who were HIV positive. Viral culture was also attempted on samples from the pre-symptomatic cases with confirmed mpox infection (4 anorectal and one saliva sample). Of these, 3 anorectal samples tested positive, one had insufficient sample volume to be cultured and the saliva sample tested negative.

Mpox clade not reported

Five studies did not report mpox clade (3 to 7).

Transmission

Miura and others conducted a retrospective study of 109 mpox cases and confirmed contact pairs in the Netherlands, between May to September 2022 (3). Age, HIV positivity, and smallpox vaccination status were not reported. Further information on transmission was reported for a subset of 18 case and contact pairs. Of these, 5 (28%) were confirmed as pre-symptomatic transmission, 8 (44%) were confirmed as symptomatic transmission, and 5 (28%) had unknown exposure. Transmission was reported from 4 days before to 8 days after symptom onset.

Snyder and others conducted a case-control study which included 54 mpox cases (88.9% men, 5.6% women, 3.7% transgender men, and 1.9% transgender women) and 117 controls negative for mpox, in the USA, between November 2022 to June 2023 (4). Nineteen cases were living with HIV (treatment status and CD4 counts not reported). Eight cases had previously received one dose of smallpox vaccination and 12 had received 2 doses of smallpox vaccination. Asymptomatic sexual transmission was reported in 10 cases (18.5%), of which 5 (9.3%) reported sexual contact with a confirmed asymptomatic mpox case, and 5 (9.3%) reported sexual contact with a suspected asymptomatic mpox case. The study did not report the HIV status of the cases in which transmission was reported.

Viral load

Agusti and others conducted a prospective cohort study in highly exposed MSM and transgender women attending a community clinic, which included 7 MSM with laboratory confirmed mpox (median age 37 years [IQR: 34 to 48.5 years]), in Spain between August and October 2022 (5). Of these, 3 were living with HIV, all of which were receiving pre-exposure prophylaxis, CD4 counts not reported, 3 cases had HIV negative status and one had unknown HIV status. Two cases had previously received smallpox vaccination, 4 had not received smallpox vaccination and smallpox vaccination status was unknown for one case. Two cases were asymptomatic, one individual was pre-symptomatic and 3 were symptomatic.

Ct values from throat samples of the 2 cases who were asymptomatic were 34.9 and 36.99 (Ct values not reported for anal samples). The pre-symptomatic case throat sample had a Ct value of 30.1 (anal sample Ct value not reported). Ct values in cases who reported symptoms ranged from 24.85 to 36.79 for throat samples and 35.35 to 38.06 for anal samples. The study did not report the HIV status of the cases in which viral load was estimated.

De Baetselier and others conducted a retrospective study which included 4 men with laboratory confirmed mpox, in Belgium, May 2022 (6). Of these, 3 cases were asymptomatic (age range: 30 to 50 years, no smallpox vaccine received) and one case reported symptoms (age and smallpox vaccine status not reported). The 3 asymptomatic cases were living with HIV,

receiving antiretroviral treatment, CD4 counts above 350 per µL). Asymptomatic cases showed Ct values ranging from 17.16 to 26.69. In all asymptomatic cases, there were no symptoms reported or detectable viral material upon retesting (21 to 37 days after the initial sample). While all asymptomatic cases reported sexual intercourse with at least one male partner within a few days to one month before testing, no sexual contacts were reported to be symptomatic for mpox. The symptomatic case had a Ct value of 27.38 and no follow-up test was conducted. Although it is possible the higher viral load observed in asymptomatic cases compared to the symptomatic case could be due to immunosuppression in the asymptomatic cases, the very small sample size of the study mean that firm conclusions cannot be made.

Mizushima and others conducted a prospective cohort study in highly exposed MSM, which included 9 MSM with laboratory confirmed mpox (age not reported), in Japan, between January to March 2023 (7). Four cases were living with HIV, (all receiving antiretroviral treatment, CD4 count above 500 cells per mL). Of these, 3 (33.3%) were asymptomatic (including one case living with HIV) and 6 (66.7%) were symptomatic (including 3 cases living with HIV). In asymptomatic cases Ct values ranged from 20.8 to 28.4. In symptomatic cases Ct values ranged from 28.8 to 31.

Health inequalities

Many of the studies included people who were living with HIV, however their antiretroviral treatment status or CD4 counts was not consistently reported, and it was unclear if they were immunocompromised. The studies also did not often compare asymptomatic and pre-symptomatic transmission in cases who were more likely to be immunocompromised (living with HIV, no treatment, low CD4 count) to those who were less likely to be immunocompromised.

Additionally, many of the studies included MSM or transgender people. While a difference in asymptomatic or pre-symptomatic transmission would not be expected in these groups, they may still be more at risk of experiencing health inequalities.

No evidence was identified in pregnant people, in children, or other vulnerable groups. This rapid evidence summary therefore is unable to provide further information on health inequalities with respect to this review question.

Limitations

This rapid evidence summary used streamlined systematic methods to accelerate the review process. Sources of evidence searched included databases of peer-reviewed and preprint research, but an extensive search of other sources was not conducted and most article screening was completed without duplication, so it is possible relevant evidence may have been missed.

Critical appraisal was not performed due to the rapid completion of this work. This restricts the interpretation of the findings, although important limitations of the evidence have been highlighted in this report.
Sample sizes were small in most of the included studies which may affect generalisability of the conclusions. Whether cases had symptoms or not was based on self-report and may be subjective.

Five out of the 7 included studies only reported viral load or viral positivity. Viral load and viral positivity are indirect measures of transmission, where higher viral loads or a positive test may indicate more likelihood of transmission, but this may not be true for all cases. Ct values may also be influenced by stage of infection (high viral load is usually detected at the early stage of infection and decreases as the infection progresses), however stage of infection was not consistently reported between studies.

The limitations identified in this review impact the level of confidence in its findings, potentially influencing the overall reliability and interpretation of the results.

Evidence gaps

Limited evidence was identified for asymptomatic and pre-symptomatic transmission as all available evidence was from a small number of cases and only 2 studies reported confirmed asymptomatic or pre-symptomatic transmission.

No evidence was identified on mpox clade I infection.

Conclusion

This rapid evidence summary identified 7 studies which reported on virus detection or transmission of mpox in asymptomatic and pre-symptomatic cases.

Two studies reported asymptomatic and pre-symptomatic transmission of mpox clade IIb. Mpox clade IIb was detected one day before symptom onset in 3 cases, and 4 days before symptom onset in 2 cases. The second study of mpox clade IIb did not suggest a clear difference in viral load between asymptomatic and symptomatic cases.

Five studies investigated asymptomatic and pre-symptomatic mpox cases but did not report mpox clade. It is likely that studies which did not report mpox clade were mostly describing mpox clade IIb, given the countries and timeframes. One study reported sexual transmission from asymptomatic cases in 10 cases, and sexual transmission from symptomatic cases in 3 cases. Another reported pre-symptomatic transmission in 5 cases, with cases developing symptoms 0 to 4 days after the date of exposure. Three studies with very small sample sizes

reported no clear difference in viral load of mpox (clade not reported) between asymptomatic cases and symptomatic cases.

No evidence was identified on mpox clade I.

Critical appraisal was not performed which restricts the interpretation of the findings, although important limitations of the evidence have been highlighted in this rapid evidence summary. The studies had small sample sizes. Whether cases had symptoms or not was based on self-report and may be subjective. Additionally, viral load and viral positivity are indirect measures of transmission, where higher viral loads or positive tests may indicate more likelihood of transmission, but this may not be true for all cases. Viral load may also vary by stage of infection, which was not clearly reported in all studies. HIV positivity, treatment and CD4 counts were inconsistently reported between studies, therefore it was not possible to determine from the evidence whether asymptomatic and pre-symptomatic transmission was affected by HIV positivity or immune status of the cases.

Acknowledgments

This review was completed by the All Hazards Public Health Response evidence review team.

We would like to thank colleagues within the All Hazards Public Health Response division who either reviewed or input into aspects of the review.

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- use accelerated methods and may not be representative of the whole body of evidence publicly available
- have undergone an internal independent peer review but not an external peer review
- are only valid as of the date stated on the review

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References

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2. Brosius I and others. 'Presymptomatic viral shedding in high-risk mpox contacts: A prospective cohort study' Journal of Medical Virology 2023: volume 95, issue 5, page e28769
3. Miura F and others. 'Time scales of human mpox transmission in The Netherlands' The Journal of Infectious Diseases 2024: volume 229, issue 3, pages 800 to 804
4. Snyder RE and others. 'Sexual exposures associated with mpox infection: California, November 2022 to June 2023' Journal of Infectious Diseases 2024: volume 229, pages S188 to S196
5. Agusti C and others. 'Self-sampling monkeypox virus testing in high-risk populations, asymptomatic or with unrecognized Mpox, in Spain' Nature Communications 2023: volume 14, issue 1, page 5,998
6. De Baetselier I and others. 'Retrospective detection of asymptomatic monkeypox virus infections among male sexual health clinic attendees in Belgium' Nature Medicine 2022: volume 28, issue 11, pages 2,288 to 2,292
7. Mizushima D and others. 'Prevalence of asymptomatic Mpox among men who have sex with men, Japan, January to March 2023' Emerging Infectious Diseases 2023: volume 29, issue 9, pages 1,872 to 1,876
8. UKHSA. 'Mpox (monkeypox) transmission, and mpox infectious and incubation periods' 2022
9. UKHSA. 'Mpox: background information' 2024

Annexe A. Protocol

The review question is:

What is the evidence for asymptomatic and pre-symptomatic transmission of mpox infection (clade Ia, Ib, IIa, IIb) in humans?

A search for primary evidence to answer this review question will be conducted up to 29 August 2024.

Eligibility criteria

Table A.1 Inclusion and exclusion criteria

	Included	Excluded
Population	Humans (any age) Children (aged up to and including 16 years) Adults	Animals
Settings	Any	
Intervention or exposure	Laboratory-confirmed infection with any clade of mpox (clade Ia, Ib, IIa, IIb) Or: Clinically suspected or laboratory-confirmed infection with mpox (clade Ia, Ib, IIa, IIb, or unspecified) in clade I outbreak countries (DRC, Republic of Congo, Central African Republic, Burundi, Rwanda, Uganda, Kenya, Cameroon, Gabon) since 1 January 2023	
Outcomes	Any measure of human-to-human transmission of mpox from cases with asymptomatic or pre-symptomatic mpox, compared to symptomatic or no transmission Viral load in cases who are asymptomatic or pre-symptomatic, compared to viral load in those who are symptomatic or not infected	Animal-to-human transmission
Language	English	Any other language

	Included	Excluded
Date of publication	Up to 29 August 2024	
Study design	Observational studies: cross-sectional, case-control, and cohort studies	Experimental studies (randomised-controlled trials, quasi-experimental studies, cross-over designs, before-and-after studies) Systematic or narrative reviews Modelling studies Case reports Case series
Publication type	Peer-reviewed published research Preprints	• editorials • letters • news articles • grey literature • conference abstracts

Identification of studies

The following databases will be searched for studies published up to 29 August 2024: Ovid Medline, Embase, and Web of Science Preprint Citation Index. The search strategy is presented below.

A previous review on the infectious and incubation periods, and transmission of mpox was completed in 2022 (8). This will be checked for relevant studies.

Screening

Title and abstract screening will be undertaken in duplicate by 2 reviewers for at least 10% of the eligible studies, with the remainder completed by one reviewer. Disagreement will be resolved by discussion or with involvement of a third reviewer where necessary.

Screening on full text will be undertaken by one reviewer and checked by a second.

Data extraction

Summary information for each study will be extracted and reported in tabular form. Information to be extracted will include country, study period, study design, participants, results, and any relevant contextual data. This will be undertaken by one reviewer and checked by a second.

Risk of bias assessment

Risk of bias of included studies will not be assessed in this rapid evidence summary due to time constraints.

Synthesis

Where studies are similar enough to combine and present data in a consistent format, a narrative synthesis will be produced to interpret the findings. The number of studies, the number of participants in each study, effect size and variance and a summary of study limitations across studies reporting each outcome will be summarised and presented. Alternatively, if studies present methodological differences that would make synthesis inappropriate, a narrative summary of each study will be provided.

Health inequalities

Variations across the following populations and subgroups will be considered, where evidence is available: those who may be at high risk from mpox including pregnant women, children, and those who are immunocompromised.

Search strategy

Ovid MEDLINE(R) ALL (1946 to 29 August 2024)

1. "Mpox (monkeypox)"/ (2754)
2. Monkeypox virus/ (1420)
3. Poxviridae Infections/ or Poxviridae/ (3692)
4. monkeypox.tw,kf. (4185)
5. monkey pox.tw,kf. (124)
6. mpox*.tw,kf. (1730)
7. monkeypoxvir*.tw,kf. (13)
8. hMPXV*.tw,kf. (28)
9. MPXV*.tw,kf. (855)
10. MPX*.tw,kf. (1398)
11. chimpanzeepox.tw,kf. (1)
12. chimpanzee pox.tw,kf. (0)
13. or/1-12 (8882)
14. Virus Shedding/ (4315)
15. cycl* threshold*.tw,kf. (3012)
16. CT value*.tw,kf. (5782)
17. Viral Load/ (40004)
18. transmi*.tw,kf. (677847)

19. (latent or latency).tw,kf. (201774)
20. Latent Infection/ (228)
21. (generation adj3 time).tw,kf. (5951)
22. ((viral or virus) adj load*).tw,kf. (46144)
23. ((viral or virus) adj concentration*).tw,kf. (1866)
24. ((viral or virus) adj burden).tw,kf. (1437)
25. ((viral or virus) adj level*).tw,kf. (1001)
26. (shed*1 or shedding).tw,kf. (142348)
27. cytopath* effect*.tw,kf. (9101)
28. exp Disease Transmission, Infectious/ (83190)
29. Cytopathogenic Effect, Viral/ (9614)
30. asymptomatic*.tw,kf. (199908)
31. symptomatic*.tw,kf. (236887)
32. pre-symptomatic.tw,kf. (2161)
33. non-symptomatic.tw,kf. (1100)
34. (symptom free or symptom-free).tw,kf. (9480)
35. no symptom*.tw,kf. (12417)
36. with* symptom*.tw,kf. (87756)
37. symptomless.tw,kf. (3267)
38. symptom* status.tw,kf. (1749)
39. exp Asymptomatic Diseases/ (10307)
40. Carrier State/ (22638)
41. ((prior or before) adj3 symptom*).tw,kf. (17540)
42. carrier state.tw,kf. (3843)
43. or/14-42 (1600049)
44. 13 and 43 (2108)

Embase (1974 to 30 August 2024)

1. monkeypox/ (4620)
2. monkeypox virus/ (2351)
3. poxvirus infection/ (1435)
4. poxviridae/ (1156)
5. monkeypox.tw,kf. (4673)
6. monkey pox.tw,kf. (133)
7. mpox*.tw,kf. (1963)
8. monkeypoxvir*.tw,kf. (20)
9. hMPXV*.tw,kf. (36)
10. MPXV*.tw,kf. (969)
11. MPX*.tw,kf. (1867)
12. chimpanzeepox.tw,kf. (1)
13. chimpanzee pox.tw,kf. (0)
14. or/1-13 (9085)
15. virus shedding/ (11231)

16. cycl* threshold*.tw,kf. (4004)
17. CT value*.tw,kf. (9141)
18. exp virus load/ (117210)
19. transmi*.tw,kf. (766157)
20. (latent or latency).tw,kf. (251764)
21. latent infection/ or latent virus infection/ (3820)
22. (generation adj3 time).tw,kf. (6527)
23. ((viral or virus) adj load*).tw,kf. (71104)
24. ((viral or virus) adj concentration*).tw,kf. (2029)
25. ((viral or virus) adj burden).tw,kf. (1839)
26. ((viral or virus) adj level*).tw,kf. (1268)
27. (shed*1 or shedding).tw,kf. (164382)
28. cytopath* effect*.tw,kf. (9984)
29. exp disease transmission/ (256831)
30. cytopathogenic effect/ (12016)
31. asymptomatic*.tw,kf. (293515)
32. symptomatic*.tw,kf. (366756)
33. pre-symptomatic.tw,kf. (3658)
34. non-symptomatic.tw,kf. (1733)
35. (symptom free or symptom-free).tw,kf. (13069)
36. no symptom*.tw,kf. (18810)
37. with* symptom*.tw,kf. (135315)
38. symptomless.tw,kf. (2908)
39. symptom* status.tw,kf. (2750)
40. exp asymptomatic disease/ (34495)
41. asymptomatic carrier/ (1874)
42. asymptomatic transmission/ (153)
43. ((prior or before) adj3 symptom*).tw,kf. (29485)
44. carrier state.tw,kf. (3992)
45. or/15-44 (2106403)
46. 14 and 45 (3393)
47. limit 46 to (conference abstract or editorial or letter) (820)
48. 46 not 47 (2573)

Web of Science Preprint Citation Index (1990 to current)

TS=(monkeypox) OR TS=("monkey pox") OR TS=(mpox*) OR TS=(monkeypoxvir*) OR TS=(hMPXV*) OR TS=(MPXV*) OR TS=(MPX*) OR TS=(chimpanzeepox) OR TS=("chimpanzee pox")

And:

TS=("cycl* threshold*") OR TS=("CT value*") OR TS=(transmi*) OR TS=((latent or latency)) OR TS=((generation NEAR/2 time)) OR TS=(((viral or virus) NEAR/0 load*)) OR TS=(((viral or virus)

NEAR/0 concentration*)) OR TS=(((viral or virus) NEAR/0 burden)) OR TS=(((viral or virus) NEAR/0 level*)) OR TS=((shed*1 or shedding)) OR TS=("cytopath* effect*") OR TS=(asymptomatic*) OR TS=(symptomatic*) OR TS=(pre-symptomatic) OR TS=(non-symptomatic) OR TS=(("symptom free" or symptom-free)) OR TS=("no symptom*") OR TS=("with* symptom*") OR TS=(symptomless) OR TS=("symptom* status") OR TS=(((prior or before) NEAR/2 symptom*)) OR TS=("carrier state")

129 results

Protocol deviations

There has been one protocol deviation.

The inclusion criteria for exposure were amended to include unspecified clade as follows:

“Laboratory-confirmed infection with any clade of mpox (clade 1a, 1b, 2a, 2b **or unspecified clade)**

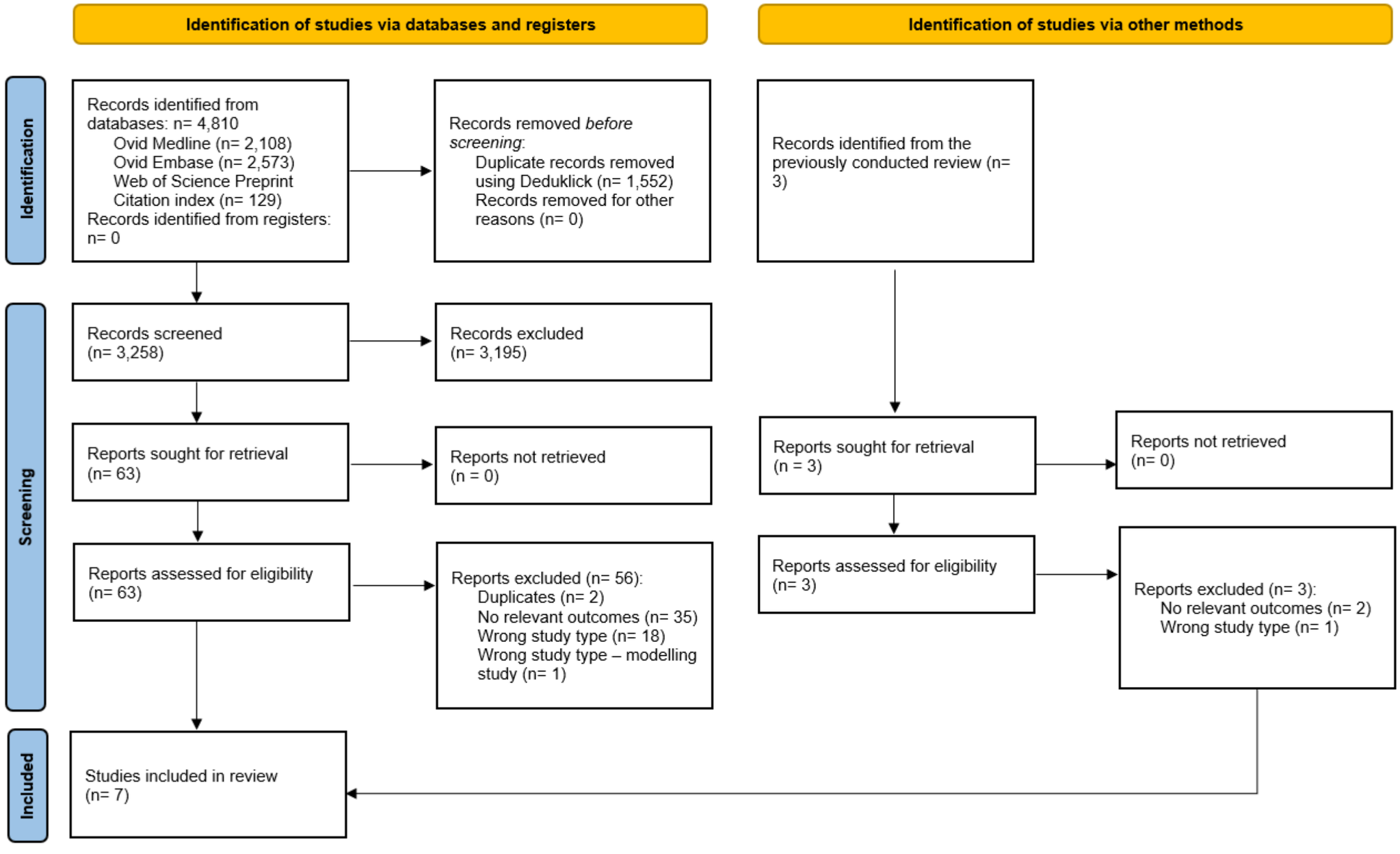
Or:

Clinically-suspected or laboratory-confirmed infection with mpox (clade 1a, 1b, 2a, 2b, or unspecified clade) in clade 1 outbreak countries (DRC, Republic of Congo, Central African Republic, Burundi, Rwanda, Uganda, Kenya, Cameroon, Gabon) since 1 January 2023”

This is to ensure that all information that may inform whether there is asymptomatic or pre-symptomatic transmission of mpox was included in this review.

Annexe B. Study selection flowchart

Figure B.1. PRISMA diagram



Text version of Figure B.1. PRISMA diagram

A PRISMA diagram showing the flow of studies through this review, ultimately including 7 studies.

From identification of studies via databases and registers, n= 4,810 records identified from databases:

- Ovid Medline (n= 2,108)
- Ovid Embase (n= 2,573)
- Web of Science (n= 129)

From these, records removed before screening:

- duplicate records removed using Daedalic (n= 1,552)
- records removed for other reasons (n= 0)

n= 3,258 records screened, of which n= 3,195 were excluded, leaving n= 63 papers sought for retrieval, all were retrieved.

n= 41 additional studies were identified from the previously conducted review, of which 3 were retrieved and all were excluded.

Of the n= 66 papers assessed for eligibility; n= 59 reports were excluded:

- duplicates (n= 2)
- no relevant outcomes (n= 37)
- wrong study type (n= 19)
- wrong study type – modelling study (n= 1)

n= 7 studies included in the review.

Annexe C. Excluded full texts

Duplicates (2 studies)

Agusti and others . 'Asymptomatic Monkey Pox Virus Infection: A Self-Sampling Screening Intervention Addressed to Gay, Bisexual and Other Men Who Have Sex with Men and Trans Women in Spain' medRxiv 2023: volume 22

Brosius and others. 'Pre- and asymptomatic viral shedding in high-risk contacts of monkeypox cases: A prospective cohort study' medRxiv 2022: volume 27

No relevant outcomes (37 studies)

Angelo and others. 'Epidemiological and clinical characteristics of patients with monkeypox in the GeoSentinel Network: a cross-sectional study' The Lancet Infectious Diseases 2023: volume 23, issue 2, pages 196 to 206

Bailey and others. 'Healthcare personnel with laboratory-confirmed mpox in California during the 2022 outbreak' Infection Control and Hospital Epidemiology 2024: pages 1 to 3

Caldeira and others. 'Demographic and Clinical Characteristics of Mpox Patients Attending an STD Clinic in Lisbon' International Journal of Environmental Research and Public Health [Electronic Resource] 2023: volume 20, issue 19, page 22

Candela and others. 'Mpox DNA clearance in semen over 6-month follow-up' Journal of Medical Virology 2023: volume 95, issue 12, page e29259

Chin and others. 'Clinical presentation, viral shedding, and neutralizing antibody responses of mpox cases in South Korea: Single center experience' Journal of Clinical Virology 2024: volume 173, page 105,692

Damhorst and others. 'Multisite Mpox Infection and Viral Dynamics Among Persons With HIV in Metro Atlanta' Journal of Infectious Diseases 2024: volume 229, pages S213 to S218

Essajee and others. 'Characteristics of Mpox Infections in Louisiana in the 2022 Outbreak' AIDS Research and Human Retroviruses 2023: volume 39, issue 11, pages 587 to 592

Fahrni and others. 'Possibility of vertical transmission of the human monkeypox virus' International Journal Of Surgery 2022: volume 105, page 106,832

Ferré and others. 'Detection of Monkeypox Virus in Anorectal Swabs From Asymptomatic Men Who Have Sex With Men in a Sexually Transmitted Infection Screening Program in Paris, France' Annals of Internal Medicine 2022: volume 175, issue 10, pages 1,491 to 1,492

Fleischauer and others. 'Evaluation of human-to-human transmission of monkeypox from infected patients to health care workers' Clinical Infectious Diseases 2005: volume 40, issue 5, pages 689 to 694

Formenty and others. 'Human monkeypox outbreak caused by novel virus belonging to Congo Basin clade, Sudan, 2005' Emerging Infectious Diseases 2010: volume 16, issue 10, pages 1,539 to 1,545

Garba-Ouangole and others. 'Laboratory Diagnosis of Mpox, Central African Republic, 2016-2022' Emerging Infectious Diseases 2023: volume 29, issue 9, pages 1,846 to 1,849

Girometti and others. 'Demographic and clinical characteristics of confirmed human monkeypox virus cases in individuals attending a sexual health centre in London, UK: an observational analysis' The Lancet Infectious Diseases 2022: volume 22, issue 9, pages 1,321 to 13,28

Golden and others. 'Asymptomatic and Subclinical Mpox: An Association With Modified Vaccinia Ankara Vaccine' Sexually Transmitted Diseases 2024: volume 51, issue 5, pages 342 to 347

Kibungu and others. 'Clade I-Associated Mpox Cases Associated with Sexual Contact, the Democratic Republic of the Congo' Emerging Infectious Diseases 2024: volume 30, issue 1, pages 172 to 176

Kile and others. 'Transmission of monkeypox among persons exposed to infected prairie dogs in Indiana in 2003' Archives of Pediatrics and Adolescent Medicine 2005: volume 159, issue 11, pages 1,022 to 1,025

Laurenson-Schafer and others. 'Description of the first global outbreak of mpox: an analysis of global surveillance data' The Lancet Global Health 2023: volume 11, issue 7, pages e1012 to e1023

Lee and others. 'Transmissibility of mpox to the general population from travellers returning to South Korea' Journal of Travel Medicine 2023: volume 30, issue 5, page 5

Lim and others. 'Clinical Features of Mpox Patients in Korea: A Multicenter Retrospective Study' Journal of Korean Medical Science 2024: volume 39, issue 4, page e19

Madewell and others. 'Serial Interval and Incubation Period Estimates of Monkeypox Virus Infection in 12 Jurisdictions, United States, May-August 2022' Emerging Infectious Diseases 2023: volume 29, issue 4, pages 818 to 821

Masirika and others. 'Epidemiology, clinical characteristics, and transmission patterns of a novel Mpox (Monkeypox) outbreak in eastern Democratic Republic of the Congo (DRC): an observational, cross-sectional cohort study' medRxiv 2024: volume 5

Mazzotta and others. 'Poor evidence for an effect of tecovirimat in shortening recovery time in hospitalized mpox cases from real-world data' medRxiv 2023: volume 10

Meschi and others. 'MPXV DNA kinetics in bloodstream and other body fluids samples' Scientific Reports 2024: volume 14, issue 1, page 13,487

Patalon and others. 'Mpox Patient Journey in Israel' Microorganisms 2023: volume 11, issue 4, page 16

Pathela and others. 'Serological Evidence of Mpox Virus Infection During Peak Mpox Transmission in New York City, July to August 2022' Journal of Infectious Diseases 2024: volume 13, page 13

Peiro-Mestres and others. 'Frequent detection of monkeypox virus DNA in saliva, semen, and other clinical samples from 12 patients, Barcelona, Spain, May to June 2022' Eurosurveillance 2022: volume 27, issue 28

Piralla and others. 'Dynamics of viral DNA shedding and culture viral DNA positivity in different clinical samples collected during the 2022 mpox outbreak in Lombardy, Italy' Travel Medicine and Infectious Disease 2024: volume 59, page 102,698

Siegenbeek van Heukelom and others. 'Characteristics of mpox positive, versus mpox negative, and mpox unsuspected clients from the Centre of Sexual Health, Public Health Service of Amsterdam, 20 May to 15 September 2022' Journal of the European Academy of Dermatology and Venereology 2023: volume 37, issue 9, pages 1,891 to 1,896

Silva and others. 'Ambulatory and hospitalized patients with suspected and confirmed mpox: an observational cohort study from Brazil' Lancet Regional Health, Americas 2023: volume 17, page 100,406

Snyder and others. 'Sexual exposures associated with mpox infection: California, November 2022 to June 2023' medRxiv 2023: volume 9

Tarin-Vicente and others. 'Clinical presentation and virological assessment of confirmed human monkeypox virus cases in Spain: a prospective observational cohort study' Lancet 2022: volume 400, issue 10,353, pages 661 to 669

Thomas and others. 'Notes from the Field: Transmission of Mpox to Nonsexual Close Contacts – Two US Jurisdictions, May 1-July 31, 2022' Morbidity and Mortality Weekly Report 2023: volume 72, issue 50, pages 1,351 to 1,352

Vallejo-Plaza and others. 'Mpox (formerly monkeypox) in women: epidemiological features and clinical characteristics of mpox cases in Spain, April to November 2022' Eurosurveillance: Bulletin Europeen sur les Maladies Transmissibles = European Communicable Disease Bulletin 2022: volume 27, issue 48, page 12

Vivancos and others. 'Community transmission of monkeypox in the United Kingdom, April to May 2022' Euro Surveillance: Bulletin Europeen sur les Maladies Transmissibles = European Communicable Disease Bulletin 2022: volume 27, issue 22, page 6

Xiu and others. 'Characteristics of the sexual networks of gay, bisexual, and other men who have sex with men in Montreal, Toronto, and Vancouver: implications for the transmission and control of mpox in Canada' medRxiv 2023: volume 1

Yang and others. 'Clinical characteristics, viral dynamics, and antibody response of monkeypox virus infections among men with and without HIV infection in Guangzhou, China' Frontiers in Cellular and Infection Microbiology 2024: volume 14, page 1,412,753

Yinka-Ogunleye and others. 'Outbreak of human monkeypox in Nigeria in 2017-18: a clinical and epidemiological report' The Lancet Infectious Diseases 2019: volume 19, issue 8, pages 872 to 879

Wrong study type (19 studies)

Accordini and others. 'People with asymptomatic or unrecognised infection potentially contribute to monkeypox virus transmission' The Lancet Microbe 2023: volume 4, issue 4, page e209

Ackerman and others. 'A history of biological disasters of animal origin in North America' Revue Scientifique et Technique 2006: volume 25, issue 1, pages 83 to 92

Acton and others. 'Nitrogen dioxide effects on alveolar macrophages' Archives of Environmental Health 1972: volume 24, issue 1, pages 48 to 52

Adler and others. 'Clinical features and management of human monkeypox: a retrospective observational study in the UK' The Lancet Infectious Diseases 2022: volume 22, issue 8, pages 1,153 to 1,162
Alarcon and others. 'Occupational Monkeypox Virus Transmission to Healthcare Worker, California, USA, 2022' Emerging Infectious Diseases 2023: volume 29, issue 2, pages 435 to 437

Anonymous. 'The dynamics of monkeypox transmission' British Medical Journal 2022: volume 379, page o2653

Anonymous. 'Human monkeypox Kasai Oriental, Zaire, 1996-1997' Morbidity and Mortality Weekly Report 1997: volume 46, issue 14, pages 304 to 307

Anonymous. 'From the Centers for Disease Control and Prevention. Multistate outbreak of monkeypox – Illinois, Indiana, and Wisconsin, 2003' Journal of the American Medical Association 2003: volume 290, pages 30 to 31

Anonymous. 'Erratum: Extended human-to-human transmission during a monkeypox outbreak in the democratic Republic of the Congo (Emerging Infectious Diseases (2016) 22, 6, 10.3201/eid2206.150579)' Emerging Infectious Diseases 2016: volume 22, page 1,862

Correia and others. 'Detection of mpox using polymerase chain reaction from the skin and oropharynx over the course of infection: A prospective study' Journal of the American Academy of Dermatology 2023: volume 89, issue 4, pages 822 to 823

Desai and others. 'Implications of the 2023-2024 MPXV clade I outbreak in the Democratic Republic of Congo to global public health' Clinical Microbiology and Infection 2024: volume 30, pages 1,092 to 1,094

Freeman and others. 'The dynamics of monkeypox transmission' British Medical Journal 2022: volume 379, page o2504

Hampel and others. 'Low prevalence of asymptomatic mpox in populations at high risk' The Lancet Microbe 2023: volume 4, issue 11, page e856

Meo and others. 'Impact of traveling on transmission trends of human monkeypox disease: worldwide data based observational analysis' Frontiers in Public Health 2023: volume 11, page 1,029,215

Moschese and others. 'Ongoing sporadic monkeypox cases: neutralising antibody detection in asymptomatic individuals' The Lancet Microbe 2023: volume 4, issue 10, page e765

Raccagni and others. 'Monkeypox infection among men who have sex with men: PCR testing on seminal fluids' Journal of Infection 2022: volume 85, issue 5, pages 573 to 607

Reda and others. 'Asymptomatic monkeypox infection: a call for greater control of infection and transmission' The Lancet Microbe 2023: volume 4, issue 1, pages e15 to e16

Valdoleiros and others. 'What you can't see can hurt you: Presymptomatic shedding of replication-competent mpox virus' Journal of Medical Virology 2023: volume 95, issue 6, page e28855

Zheng and others. 'Disparities in transmission dynamics of the 2022 mpox outbreaks between Europe and Americas' New Microbes and New Infections 2023: volume 52, page 101,111

Wrong study type – modelling study (1 study)

Nguyen and others. 'Early administration of tecovirimat shortens the time to mpox clearance in a model of human infection' Plos Biology 2023: volume 21, issue 12, page e3002249

Annexe D. Data extraction tables

Abbreviations: Ct: cycle threshold, CD4: cluster of differentiation 4, DNA: deoxyribonucleic acid, HIV: human immunodeficiency virus, IQR: interquartile range, mL: millilitre, µl: microlitre; MSM: men who have sex with men, PCR: polymerase chain reaction, PrEP: pre-exposure prophylaxis, USA: United States of America

Table D.1. Summary of asymptomatic and pre-symptomatic transmission in mpox (clade IIb)

Study	Country, time period	Population	Outcomes
Brosius and others (2)	Belgium, June 24 to July 31, 2022	25 high risk contacts of 23 confirmed mpox cases (median age 43 years [IQR: 36 to 51 years], 5 (20%) were living with HIV. HIV treatment and CD4 counts not reported. 24 (96%) identified as men who have sex with men (MSM). 18 (72%) of participants reported having sexual contact with a case and 7 (28%) had non-sexual contact with cases including 5 (20%) household contacts and 2 (10%) prolonged skin to skin contact). 5 (20%) participants received post exposure vaccination and 6 (24%) were vaccinated against smallpox during childhood. Definitions of infectious status: Definitely infected: at least one sample with PCR Ct value of less than 34 Possibly infected: at least one sample with PCR Ct value of less than or equal to 34 to less than 37 Uninfected: all PCR Ct values more than 37	Participants were followed up for a median of 16 days (IQR: 14 to 26 days) after their last high-risk contact. Asymptomatic cases (n= 9, 36%): Definitely infected: 0 (0%) Possibly infected: 2 (22.2%) Uninfected: 7 (88.8%) Samples: Blood, throat swabs, genital swabs, anorectal swabs, and swabs from skin lesions if applicable (however the study did not report Ct values by sample type). Viral culture was attempted on 4 pre-symptomatically collected anorectal samples and one saliva sample. Three out of the 4 anorectal samples tested positive for mpox. The 4th anorectal sample had insufficient sample quantity to be tested and the saliva sample tested negative. Ct values: Patients without typical symptoms (2 definitely infected, 5 possibly infected) had lower Ct values than patients with typical symptoms (median of lowest recorded Ct value 17.1 without typical symptoms compared to 34.8 with typical symptoms, Mann-Whitney p = 0.003). Symptomatic cases (n= 8, 32%): Definitely infected: 8 (100%) showed symptoms (fever, night sweats, or other symptoms). Pre-symptomatic cases: In those definitely infected and symptomatic (n= 8), 6 developed typical (such as skin lesions, proctitis, tonsillitis) mpox symptoms. Of these, 5 out of 6 (83.3%) had pre-symptomatic viral DNA detection (Ct value less than 37). The median number of days between most recent contact and first positive viral DNA detection was 5 days (IQR: 4 to 9.5 days)

Study	Country, time period	Population	Outcomes
			In those possibly infected (n= 5), the number of cases with pre-symptomatic viral DNA detection was not reported. Three (60%) reported non-typical symptoms (fever, night sweats, or other symptoms). The median number of days between most recent contact and first positive viral DNA detection was 5 days (IQR: 5 to 12 days) Among those who were definitely infected and had typical symptom presentation (n=5, 20%), DNA was detected one day before symptom onset in 3 individuals, and 4 days before symptom onset in 2 individuals.
Dou and others (1)	China, May 31 to June 21, 2023	37 confirmed mpox clade IIb cases (aged between 24 to 51 years, median age 30 years [IQR: 26.5 to 34.5 years], 16.2% aged over 40 years, 51.4% were living with HIV). 36 cases were MSM, (2 identified as bisexual, 34 identified as homosexual). Among the 36 individuals who self-identified as MSM, 32 engaged in sexual relationships with other men before contracting mpox. 3 cases (8.1%) had previously received the smallpox vaccine. 4 were asymptomatic (identified from close contacts of cases). 33 were symptomatic (rash, fever, swollen and painful lymph nodes, skin lesions). 3 asymptomatic cases were HIV-positive, and one HIV-negative case was taking HIV PrEP. Of 28 cases diagnosed at outpatient clinics, median time from symptom onset to initial consultation was 4 days (IQR 2.5 to 6.5 days, range 0 to 15 days). The median time from symptom onset to diagnosis was 6 days (IQR: 5 to 8.5 days, range 2 to 15 days). 6 cases identified through contact investigation and 3 were identified through source tracing (not defined). 19 cases had a known exposure time, with the incubation period ranging from 2 to 20 days (median of 9 days, IQR: 7 to 13 days).	Asymptomatic cases: Rectal sample or perianal sample: • 4 specimens; 2 positive (50%), Ct values: 36, 37 Oropharyngeal sample: • 4 specimens; 2 positive (50%), Ct values: 24, 37 Symptomatic cases: Vesicular or pustular fluid: • 11 specimens; 11 positive (100%), Ct value: Median 18 (IQR: 16 to 22) Skin lesion sample: • 18 specimens; 18 positive (100%), Ct value: Median 21 (IQR: 18 to 25) Scabs: • 4 Specimens; 4 positive (100%), Ct value: Median 25 (IQR: 16 to 36) Oropharyngeal sample: • 33 specimens; 25 positive (75.8%), Ct value: Median 30 (IQR: 27 to 34) Blood: • 26 specimens; 22 positive (84.6%), Ct value: Median 35 (IQR: 32 to 36) Rectal sample or perianal sample: • 6 specimens; 5 positive (83.3%), Ct value: Median 30 (IQR: 17 to 36) Overall range Ct value range regardless of sample type: 16 to 36

Table D.2. Summary of asymptomatic and pre-symptomatic transmission in mpox (clade unspecified)

Study	Country, time period	Population	Outcomes
Agusti and others, 2023 (5)	Spain, August to October 2022	113 MSM cases recruited at a community centre in Barcelona who were asymptomatic or with mild unrecognised mpox symptoms. 7 were positive for mpox (median age 37 years [IQR: 34 to 48.5 years], 7 (100%) cis men, 7 (100%) identified as gay, 3 (42.86%) were born in Spain, 4 (57.14%) were born in other countries). 3 (42.86%) were living with HIV, all of which were receiving prophylaxis, 1 (14.29%) unknown HIV status, 3 (42.86%) had HIV negative status. CD4 counts not reported. 2 were vaccinated against smallpox (1 during childhood, and 1 in the last 12 months). One did not know their vaccination status. 4 had never received a smallpox vaccine. 3 of 7 (42.86%) mpox cases, reported contact with a confirmed mpox case in the previous 30 days.	7 individuals tested positive for mpox (PCR Ct value range: 24.85 to 38.06, viral load range: 2,674 to 8,532,000 PCR copies per mL): 2 individuals were asymptomatic (reported no symptoms prior to testing and did not report symptoms after testing) and one individual was pre-symptomatic (reported no symptoms prior to testing but after testing reported symptoms including fever, exhaustion, sore throat, and a skin lesion). 3 individuals reported symptoms including a swollen lymph node, fever, exhaustion, and skin lesions (one in the genital area). There was no symptom information available for one participant. Asymptomatic cases: Ct thresholds for individuals who were asymptomatic (n=2) ranged from 34.9 to 36.99 from throat samples (no Ct thresholds were reported for anal samples). The range of PCR copies was from 5,126 to 18,300 copies per mL (all from throat samples). Symptomatic cases: Ct thresholds for individuals who reported symptoms before testing (n=3) ranged from 24.85 to 36.79 for throat samples and from 35.35 to 38.06 for anal samples. The range of PCR copies from anal samples was from 2,674 to 13,960 copies per mL, and from throat samples was from 5,825 to 8,532,000 copies per mL. Pre-symptomatic cases: Ct threshold for the pre-symptomatic individual (n=1) was 30.1 (sample taken from throat). The number of PCR copies from the throat sample was 347,000. Anal sample Ct threshold not reported. No information on symptoms was available for one individual (n=1) who tested positive for mpox. The Ct threshold in the throat sample was 34.9, and the number of PCR copies from the throat sample was 4,827 per mL.
De Baetselier and others, 2022 (6)	Belgium, 1 May to 31 May, 2022	224 men (demographic information for total cohort not reported) were tested. 4 individuals tested positive for mpox, of which 3 were asymptomatic (between 30 to 50 years old) and one reported a vesicular perianal rash (age not reported). Participants were recruited from an HIV or and sexually transmitted infection clinic. Three asymptomatic cases were living with HIV, receiving retro antiviral treatment (HIV viral load less than 20µl, CD4 counts above 350 per µl) and were reported as well-controlled.	The 3 asymptomatic cases were recalled for further investigation 21 to 37 days after initial sampling. No symptoms of mpox were reported in asymptomatic cases 3 weeks to 2 months before initial sampling and until their return visit. Asymptomatic case 1: Initial sample: Anorectal swab had Ct value of 26.69, oropharyngeal swab was negative Follow-up sample: Negative

Study	Country, time period	Population	Outcomes
		All 3 men had sexual intercourse with at least one male partner within a few days to one month before testing. None of the 3 asymptomatic cases previously received the smallpox vaccine.	Asymptomatic case 2: Initial sample: Anorectal swab had Ct value of 20.05 Follow-up sample: Anorectal swab was negative Asymptomatic case 3: Initial sample: Anorectal swab had Ct value of 17.16 Follow-up sample: Anorectal swab was negative Asymptomatic Ct values range: 17.16 to 26.69 Symptomatic case: Initial sample: Anorectal swab had Ct value of 27.38 Follow-up sample: Not reported
Miura and others, 2024 (3)	Netherlands, May 20 to September 6, 2022	109 reported infector and infectee case pairs were collected from different regional public health services in the Netherlands. All identified as MSM. Age, ethnicity, HIV status, vaccination status not reported.	A subset of 18 pairs were further investigated, of these: • 5 pairs (28%) had the infectee report contact with a pre-symptomatic (before the infector reported symptoms) infector • 8 pairs (44%) had the infectee report contact with the infector after the infector reported symptoms • 5 pairs (28%) had the time of exposure was reported as unknown The study found transmission could occur from 4 days before to 8 days after symptom onset of the infector. Of the 5 pairs where the infectee reported contact with a pre-symptomatic infector, it took 0 to 4 days for the infector to develop symptoms after the date of exposure.
Mizushima and others, 2023 (7)	Japan, January 5 to March 20, 2023	MSM were recruited from 3 sites in Tokyo who were over 18 years of age and had sexual intercourse in the last 3 months. 1,346 were tested for mpox (median age 38 years [IQR: 31 to 47 years]), out of which 5 (0.4%) had a positive PCR test and 1,341 (99.6%) had a negative PCR test. 4 of the 1,341 who initially tested negative later developed mpox symptoms and tested positive for mpox. Of the 9 participants positive for mpox, 6 (66.7%) were symptomatic (skin lesions, fever, lymphadenopathy, and pharyngitis) and 3 (33.3%) as asymptomatic. 4 (44.4%) were living with HIV and were receiving antiretroviral therapy. CD4 count was above 500 cells per mL, viral load was undetectable.	Asymptomatic Cases (n=3): Anorectal swab Ct value: 21.2 (n=1, on PrEP) Pooled sample (anorectal swab, urine, gargle rinse) Ct values: 20.8 (n=1 living with HIV) and 28.4 (n=1, on PrEP) Overall Ct value range for asymptomatic cases: 20.8 to 28.4 Symptomatic cases (n=6): Pooled sample (anorectal swab, urine, gargle rinse) Ct value: 28.8 (n=1, living with HIV) and 31.0 (n=1, on PrEP) Skin lesion swab Ct value: Not reported (n=4)

Study	Country, time period	Population	Outcomes
		Of the 3 asymptomatic mpox cases: 1 participant was living with HIV, and 2 participants were on PrEP. Of the 6 symptomatic mpox cases: 3 participants were living with HIV, and 3 participants were on PrEP.	Overall Ct value range for symptomatic cases: 28.8 to 31.0. Some cases reported as no data. All cases with no data had only skin lesion swab taken.
Snyder and others, 2024 (4)	USA, November to June 2023	54 laboratory-confirmed cases, of which 49 (90.7%) were registered as male at birth and 5 (9.3%) were registered as female at birth. Among these, 48 (88.9%) were cisgender men, 3 (5.6%) were cisgender women, 2 (3.7%) were transgender men, and one (1.9%) was a transgender woman. 39 identified as MSM, and 15 identified as non-MSM. Vaccination History: 34 cases (63.0%) reported no vaccination, 8 (14.8%) had received one dose, and 12 (22.2%) had received 2 doses (JYNNEOS vaccination). HIV Status: 19 individuals (35.2%) were living with HIV, while 35 (64.8%) were not living with HIV. CD4 counts are not reported.	Asymptomatic cases: 10 out of 54 (18.5%) participants reported sexual exposure to a contact without apparent symptoms at the time of the encounter out of which 5 (9.3%) reported sexual exposure to a diagnosed contact and 5 (9.3%) reported exposure to suspected contact. 3 cases who did not report multiple sexual partners during the risk period, reported sexual exposure to a contact without apparent symptoms (one diagnosed case, 2 suspected cases). 7 cases reported having multiple sexual partners during the risk period and reported sexual contact with an individual without apparent symptoms (4 diagnosed cases, 3 suspected cases). Symptomatic cases: 3 out of 54 (5.6%) participants reported sexual exposure to a contact with apparent symptoms at the time of the encounter out of which one (1.9%) reported exposure to diagnosed contact and 2 (3.7%) reported exposure to suspected contact. 2 cases who did not report multiple sexual partners during the risk period reported sexual exposure to a contact with apparent symptoms (one diagnosed case, one suspected case). One case reported as having multiple sexual partners during the risk period reported sexual exposure to a contact (suspected case) with apparent symptoms.

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Authors: Katie Kerr, Aishwarya Bhatia, Jennifer Hill, Tamsyn Harris, Mikhailia McIntosh Maman and Serena Carville.

For queries relating to this document, please contact: enquiries@ukhsa.gov.uk

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