UK Health Security Agency

Mpox (monkeypox) transmission, and mpox infectious and incubation periods

A rapid review

Search to 15 August 2022

Contents

Main messages

1. This review (search up to 15 August 2022) identifies and summarises evidence relating to monkeypox (mpox) (clade II) transmission (one review for pre-2022 outbreaks, 30 studies from 2022), and mpox infectious and incubation periods (0 studies for infectious period, 8 studies for incubation period, 21 studies for whether environmental or individual samples contained mpox DNA or live monkeypox virus from 2022).
2. All studies were observational, typically case series and cross-sectional studies, describing mpox cases from the 2022 outbreak, mainly across Europe and North America.
3. Evidence from the 30 studies from 2022 consistently suggested that, up to August 2022, transmission of mpox was mostly from sexual contact, with the vast majority of cases being gay, bisexual, or other men who have sex with men, most commonly between 30 and 50 years of age, reporting multiple sexual partners (often 5 or more within the last 3 months), previous or current sexually transmitted infections (including HIV), and use of HIV pre-exposure prophylaxis (GRADE assessment: low certainty of evidence).
4. There was some evidence of transmission from non-sexual contact, but no evidence of transmission through the air, although the transmission route remains unknown for some cases. Healthcare associated infection was confirmed in 3 cases.
5. Evidence from 8 studies suggested a median or mean incubation period ranging from 6 to 10 days in 2022, shorter than the 12 days estimated in the 2003 outbreak (GRADE assessment: very low certainty of evidence).
6. Evidence from 16 individual sample studies suggested mpox DNA was present in lesion, anorectal, and nasopharyngeal swabs, and in serum, plasma, blood, saliva, faeces, urine, and semen and seminal fluid samples taken from mpox cases (GRADE assessment: very low certainty of evidence). Live virus was isolated from semen in one study, and from a skin lesion in another study, although the remaining studies did not report testing for live virus. Detection of viral DNA does not necessarily indicate infectious virus.
7. Evidence from 6 environmental sample studies suggested the presence of mpox DNA in a high proportion of surface and air samples taken from the residences and hospital rooms of mpox cases, and that many of these samples contained live virus.
8. No studies reported directly on the infectious period of mpox.
9. The included studies describe mpox cases up to August 2022, and the demographics of cases and transmission routes may change over time, especially if mpox begins circulating in different groups.

Purpose

To identify and summarise evidence relating to mpox (clade II) transmission, and mpox infectious and incubation periods.

Methods

A rapid review was conducted, following streamlined systematic methodologies to accelerate the review process (1). A literature search was undertaken to look for primary studies related to mpox transmission, and mpox infectious and incubation periods, published (or available prior to peer review as a preprint) up to 15 August 2022. Only studies including the clade II of mpox were considered, as this is the clade circulating in the 2022 global outbreak, including in the UK.

Ten percent of the screening on title and abstract was screened in duplicate, while full text screening and data extraction were performed by one reviewer and checked by another. Risk of bias assessment using the quality criteria checklist (QCC) (2) was planned for this review, but as the studies included in this review were almost all descriptive rather than analytical, risk of bias assessments were not performed. GRADE assessment was performed for 3 mpox outcomes: transmission, incubation period, and individual and environmental sampling. Full details on the methodology are provided in Annexe A.

Evidence

In total, 49 observational studies were included in this report (7 preprints (3 to 9)). Nine studies reported on transmission of clade II mpox in outbreaks before 2022 (10 to 18). As these outbreaks were included in a systematic review by Bunge and others (19), the review is summarised here rather than the individual studies.

Of the remaining 40 studies, 30 reported on transmission or the demographics of mpox cases in the 2022 outbreak (4,5,7,9,20 to 46), 8 studies reported on incubation period (4,21,33,36,42,47,48) (44), and 21 studies reported on whether environmental or individual samples contained mpox DNA or were infectious for mpox (3,5,6,8,20,24,25,28,31,32,34,36,37,41,42,45,49 to 53) (some studies contributed information to more than one outcome). All 40 studies were conducted between January and July 2022 (mostly in May and June), except Atkinson and others (49), which reported on infectious sampling of a single mpox case in the UK in December 2019, and Huhn and others (47), which reported the incubation period of mpox in an outbreak in the US in 2003. Table 1 gives study characteristics of the 40 included studies.

Eighteen of these 40 studies were case series and reports (3,20,23 to 25,28,30 to 32,34,36,38,41,43,45,49,50,52) (7 studies reported on a single case (3,24,25,41,43,49,50)), 19 were cross-sectional studies (4 to 6,8,21,22,26,27,29,33,35,37,39,40,44,46 to 48,51,53), one

was a prospective cohort study (42), one was a retrospective cohort study (9), and one was an observational study following patients vaccinated against mpox following exposure (7). Nine studies provided data from the UK (3,6,22,23,30,37 to 39,46,49), 21 from Europe (5,7,20,21,25,26,28,29,31 to 35,42 to 45,48,51 to 53), 5 from the US (8,27,41,47,50), one from South Korea (24), one from Israel (9), and 3 from multiple countries (4,36,40).

Transmission

Evidence from before the 2022 outbreak

Bunge and others conducted a systematic review of mpox, and reported the mode of transmission for all outbreaks up to 2020 (when known) (19). Although the mpox clade was not reported in many of the included studies, the authors considered outbreaks in the US (2003), the UK (2018), Nigeria (starting in 2017), Sierra Leone (1970, 2014 and 2017), Israel (2018), and Singapore (2019) to be of the clade II (West African clade).

Many outbreaks were likely as a result of contact with animals with mpox:

- in the US all 47 cases reported exposure to ill or infected prairie dogs
- one case of 3 in the UK reported consumption of bush meat during his visit to a rural area in Nigeria
- 10 of 122 cases in Nigeria reported contact with animals
- 2 cases in Sierra Leone had likely animal exposure from preparing and cooking meat from wild animals
- the only case in Israel reported he disposed of 2 rat carcasses at his residence
- the only case in Singapore reported ingestion of bush meat

There was also evidence of human-to-human transmission: in the UK, one of the 3 cases had contact with the case who ate bush meat, and the other case changed their potentially contaminated bedding, and 36 of the 122 cases in Nigeria were linked with people who had similar lesions prior to developing mpox themselves. There was no evidence of human-to-human transmission in the other outbreak detailed above.

Evidence from the 2022 outbreak

In total, 30 studies reported on transmission or the demographics of mpox cases in the 2022 outbreak (4,5,7,9,20 to 46). Of these, the World Health Organization (WHO) (40) and UK Health Security Agency (UKHSA) (46) provide ongoing situation reports or technical briefings covering large numbers of mpox cases both globally and in the UK. Zucker and others (9) conducted large cohort study in Israel that reported on differences between people who were and were not infected with mpox, and Rodriguez and others (33) reported on a large number of mpox cases in Spain. These studies will be individually summarised in detail. The remaining 27 studies typically reported on few cases (19 studies had fewer than 100 cases) and will be jointly summarised.

WHO external situation reports

The WHO external situation reports provide comprehensive overviews of the 2022 mpox outbreak (40). The latest report, from 24 August 2022, includes data for 41,664 confirmed mpox cases in 96 countries diagnosed between 1 January 2022 and 22 August 2022. The vast majority of cases were from Europe (n=20,652) and the Americas (n=20,438).

Of those with available data, 98.2% of cases (n=20,138 of 20,500) were male, with a median age of 36 years (interquartile range [IQR]: 30 to 43 years) and less than 1% of cases (n=140 of 23,626) were under 18 years of age. In total, 95.8% of cases (n=9,484 of 9,899) identified as men who have sex with men, 45% of cases (n=4,501 of 10,036) were HIV positive, and 82.1% of cases (n=5,954 of 7,250) reported a sexual encounter as the mode of transmission. Most cases (60.6%, n=2,204 of 3,639) were likely exposed at a party setting with sexual contacts. Only a small proportion of cases (5.2%, n=256) were healthcare workers, and reportedly most of these cases were infected in the community rather than through occupational exposure, with the remainder of cases under further investigation.

Cases reported by other studies may have been included in the WHO external situation reports, since the latest report stated the WHO receive case reporting forms for 90% of total confirmed cases (40), although the exact degree of overlap is unknown.

UKHSA technical briefings

The UKHSA technical briefings provide comprehensive information about the 2022 mpox outbreak in the UK (37,46). The latest briefing, from 19 August 2022, includes data for 3,195 mpox cases diagnosed between 6 May 2022 and 15 August 2022. Most cases were in England (95%, n=3,050 of 3,195).

Of those with available data, 99% of cases (n=2,989 of 3,025) were male, with a median age of 36 years (IQR: 31 to 44 years) and only one case was under 16 years of age. In total, 917 cases (30%) completed an enhanced surveillance questionnaire (and may not be representative of all cases in the UK). Of these, most respondents were white (76%, n=701 of 917), were born in the UK (53%, n=488 of 917), were gay, bisexual, or were men who have sex with men (96.7%, n=857 of 886), had a history of a sexually transmitted infection in the last year (53.5%, n=481 of 899), had ever used HIV pre-exposure prophylaxis (78.5%, n=490 of 624), and had 4 to 9 sexual partners (34.5%, n=312 of 904) or 10+ sexual partners (29.5%, n=267 of 904) in the last 3 months. In total, 26.3% of respondents (n=228 of 867) were living with HIV. In England, 14% of cases (n=442) travelled internationally within 21 days prior to symptom onset, with most cases travelling to Europe, particularly Spain (n=204).

The primary reported transmission route across all cases was through close sexual contact, with no confirmed instances of airborne transmission. There was also evidence of limited household transmission, and a small number of cases had no identified route of transmission.

Of the 32 adult cases who were women with available information, 38% (n=12) were transgender women, and 47% (n=15) had evidence of possible transmission during sexual contact (either sex with a reported case, or high numbers of anonymous sexual partners through sex work), 25% (n=8) potentially had non-sexual routes of transmission (through household transmission, or no reported sexual activity for 21 days prior), and 28% (n=9) had unclear transmission routes. There were 20 cisgender men who reported no sexual contact with another man 21 days prior, and of these, a small number had evidence of possible transmission during sexual contact with cisgender women.

Cases reported by other studies in the UK were almost certainly included in the UKHSA technical briefings, and there is therefore a high chance of overlap.

Large studies

A retrospective cohort study by Zucker and others compared men at high of mpox infection who were and who were not infected with mpox in Israel between June and July 2022 (9). The included men were members of the Clalit Health Services, and had at least one of the following:

- at least one rectal or pharyngeal polymerase chain reaction (PCR) test for sexually transmitted infection (STI) since 1 January 2021
- were on HIV pre-exposure prophylaxis
- aged 25 to 46 years and received the human papilloma virus vaccine (designated primarily for men who have sex with men in this age group)
- were HIV positive

In total, 8,089 men were included, of which 51 (0.6%) tested positive for mpox. The study performed a multivariable logistic regression to find risk factors for mpox infection. The results suggested that being born after 1980, living in Tel-Aviv, receiving HIV pre-exposure prophylaxis, having a positive rectal STI PCR test, and having erectile dysfunction treatment were all risk factors for mpox infection, and being HIV positive may be a risk factor, but the results were imprecise. Specifically, the associations between each risk factor and mpox infection were:

- year of birth 1980 or later: Hazard ratio (HR) = 3.49 (95% confidence interval [CI]: 1.43 to 8.54, p = 0.006)
- Tel-Aviv district: HR = 3.44 (95% CI: 1.56 to 7.59, p=0.002)
- HIV-positive: HR = 2.32 (95% CI: 0.97 to 5.55, p=0.059)
- HIV pre-exposure prophylaxis: HR = 4.99 (95% CI: 2.51 to 9.93, p<0.001)
- positive rectal STI on PCR: HR = 3.79 (95% CI: 1.93 to 7.42, p<0.001)
- positive pharyngeal STI on PCR: HR = 0.77 (95% CI: 0.31 to 1.91, p=0.58)
- erectile dysfunction treatment: HR = 2.94 (95% CI: 1.62 to 5.32, p<0.001)

A cross-sectional study by Rodriguez and others reported the demographics and transmission of 1,182 mpox cases in Spain between May and July 2022 (33). In total, 98.9% of cases (n=1,242 of 1,256) were in men, the median age of cases was 37 years and all but one case

were adults, and 14.1% of cases (n=62 of 440) reported travelling to countries reporting mpox cases during their incubation periods. Of those with available information, the reported most likely type of transmission was intimate and prolonged contact during sex for 85.8% of cases (n=332 of 387), then close contact unrelated to sex (8.0% of cases, n=31 of 387), and information was pending for 6.2% of cases (n=24 of 387). Of the 332 cases where transmission was likely through sexual contact, 87.3% of cases (n=290) were men who have sex with men, 1.8% of cases (n=6) had heterosexual sexual contact, and information was pending 10.8% of cases (n=36). In total, 39% of cases (n=163 of 413) attended a mass gathering before symptoms onset. Of the 14 women with mpox, 50% (n=7) reported sexual contact with men, 14% (n=2) had close family contacts with mpox, and information was pending for 36% of women (n=5).

Remaining studies

The remaining studies looking at demographics and transmission all had fewer than 600 cases, and may have substantial overlap in cases with the studies above, particularly those conducted in the UK and Spain (4,5,7,20 to 32,34 to 36,38,39,41 to 45).

The demographics of cases included in these studies were very similar to the studies above, where cases were typically:

- gay, bisexual, or other men who have sex with men
- often between 30 and 50 years of age (usual mean or median age of around 37 to 40 years)
- reporting multiple sexual partners (5 or more within the last 3 months)
- previous or current sexually transmitted infections (including HIV)
- use of HIV pre-exposure prophylaxis
- unprotected sexual contact as the likely transmission route

Multiple studies reported that a relatively large proportion of cases had travelled (nationally or internationally) in their incubation period (travel to Gran Canaria was specifically noted in multiple studies) (4,7,20 to 22,24 to 28,30,31,35,36,39,41,42,44), although Selb and others noted a decrease in the proportion of new cases related to travel in Germany between May and June 2022 (35). No studies reported on cases that differed substantially from the above.

A study by Thy and others reported on the proportion of people developing mpox who were exposed to a confirmed mpox case and subsequently received a smallpox vaccination (IMVANEX®) in France between May and July 2022 (7). In total, 276 people (91% male, median age: 19 years, IQR: 14 to 25 years) received one dose of vaccine a median of 11 days (IQR: 8 to 14 days) after exposure to a mpox case (mode of exposure: droplets in 91% of cases, indirect contact in 71% of cases, and unprotected sex in 54% of cases). Of these, 12 people (4%) developed mpox (median age: 24 years, IQR: 16 to 27 years), none of which had a severe infection: 10 cases developed an infection within 5 days following vaccination, and 2 had infections at 22 and 25 days after vaccination.

In addition to transmission between humans, there was evidence from a study by Seang and others of transmission from 2 cases to their dog, with whom they co-slept, in France in June 2022 (34).

Summary

Before the 2022 mpox outbreak, there was evidence from one review that transmission of mpox occurred both from animals and between humans. However, evidence from 30 studies of the 2022 outbreak suggested that most mpox transmission was between humans from sexual contact. The vast majority of cases in 2022 were gay, bisexual, or other men who have sex with men, most commonly between 30 and 50 years of age, reporting multiple sexual partners (often 5 or more within the last 3 months), previous or current sexually transmitted infections (including HIV), and use of HIV pre-exposure prophylaxis. There was some evidence of transmission from non-sexual contact, but no evidence of transmission through the air, although the transmission route remains unknown for some cases. From the WHO external situation reports, healthcare associated infection has only been confirmed in 3 cases.

GRADE assessment: low certainty of evidence.

Infectious and incubation periods

Eight studies reported the incubation period of mpox cases, 7 studies in 2022 (4,21,33,36,42,44,48) and one study in 2003 (47). No studies reported directly on the infectious period of mpox cases.

Thornhill and others reported a median incubation period of 7 days (range: 3 to 20 days) in 23 mpox cases with a clear exposure history across 16 countries in April to June 2022 (36). These cases may overlap with other studies.

Three studies reported on mpox cases in Spain, and it is unclear whether there is overlap in cases between studies (21,33,42). Catala and others reported a median incubation period of 6 days (interquartile range [IQR]: 4 to 9 days) in 118 cases in May to July 2022 (21). Rodriguez and others reported an average incubation period of 7 to 9.6 days in 45 cases in May to June 2022 (33). Tarin-Vicente and others reported a median incubation period of 7.0 days (IQR: 5.0 to 10.0 days, range: 1.0 to 19.0 days) in 181 cases in May to July 2022, and that the incubation period did not differ between cases who were or were not HIV positive, or between cases who did or did not receive a smallpox vaccination (42).

Charniga and others reported a median incubation period of 6.4 days (95% credible interval: 5.1 to 7.9 days) and a mean incubation period of 7.6 days (95% credible interval: 6.2 to 9.7 days, standard deviation: 1.8 days) in 22 cases in May to June 2022 in the US and 18 cases in the Netherlands (4). Additionally, the reported median time from exposure to rash onset was 7.8 days (95% credible interval: 5.9 to 10.0 days), and the reported mean time was 8.7 days (95%

credible interval 6.9 to 11.7 days, standard deviation: 1.6 days). Miura and others included only the 18 cases from the Netherlands, and so their results are not reported separately (48).

Guzzetta and others reported a mean incubation period of 9.1 days (95% CI: 6.5 to 10.9 days, 5th and 95th percentiles of the distribution: 2 and 20 days) in 30 cases in May to June 2022 in Italy (44).

Huhn and others reported a median incubation period of 12 days (interquartile range: 11 to 18 days) in 29 cases after initial animal exposure in the 2003 outbreak in the US (47).

Summary

Eight studies reported the incubation period of mpox cases, with estimates of the median or mean incubation period ranging from 6 to 10 days in 2022, shorter than the 12 days estimated in the 2003 outbreak.

No studies reported directly on the infectious period of mpox cases.

GRADE assessment: very low certainty of evidence.

Infectious sampling

Twenty-one studies reported on whether environmental or individual samples contained either live monkeypox virus, or evidence of monkeypox virus on RT-PCR (reverse transcriptase polymerase chain reaction) in 2022 (3,5,6,8,20,24,25,28,31,32,34,36,37,41,45,51 to 53), 2021 (50) and 2019 (49). The range, mean, or median of reported Ct (cycle threshold) values are presented here, where a lower Ct value indicates a higher viral load.

Note that the presence of mpox DNA, as indicated using RT-PCR, does not necessarily indicate the presence of live virus capable of infecting others. Studies that looked specifically for live virus, for example through looking for cytopathic effects, are reported as such.

Individual sampling

Antinori and others collected serum, plasma, genital or rectal lesions, nasopharyngeal, skin lesions, seminal fluid, scab, faeces, and saliva samples from 4 cases in hospitals in Italy in May 2022 (20). The analysis of samples was reported to be ongoing, but a sample from at least one case was positive on RT-PCR for each of the different types of sample collected (Ct values: serum: 29.7, plasma: 30.2, genital or rectal lesions: 15.7 to 17.5, nasopharyngeal swab: 27.6 to 30.4, skin lesions: 17.6 to 30.4, seminal fluid: 27.7 to 30.1, scabs: 13.1 to 20.0, faeces: 22.6 to 26.1, saliva: 27.1).

De Baeselier and others collected anorectal swabs, oropharyngeal swabs, or combined first-void urine, oropharyngeal and anorectal swabs from 224 men undergoing gonorrhoea and

chlamydia testing at a sexually transmitted infection clinic in Belgium in May 2022 (5). These samples were retrospectively tested with RT-PCR for mpox DNA. In total, 60 anorectal swabs, 2 oropharyngeal swabs, and 163 combined samples were tested. Four men tested positive for mpox: of these, one case had symptoms of mpox (painful vesicular rash) with a positive anorectal swab, the remaining 3 men were asymptomatic 2 months prior and 3 weeks after sampling, all cases with positive anorectal swabs (Ct values: 17.2 to 27.4) and one case also with a negative oropharyngeal swab. The 3 asymptomatic cases had a repeat anorectal swab at either 21, 24, or 37 days, all of which were negative.

Ferre and others collected anal swabs from 200 men who have sex with men with multiple sexual partners who are either taking HIV pre-exposure prophylaxis or living with HIV and receiving antiretroviral treatment as part of a screening program for gonorrhoea and chlamydia in France in May and June 2022 (52). All men were asymptomatic for mpox, and negative for gonorrhoea and chlamydia. In total, 13 men were positive for mpox on RT-PCR, 2 of which later developed symptoms (Ct values for these 2 cases: 20.7 when asymptomatic, 33.0 after 7 days, 38.2 when asymptomatic, 24.0 after 9 days [pharyngeal swab]).

Gould and others collected throat, lesion and plasma samples from 5 hospitalised cases in the UK in May and June 2022 (6). The cases had variable times since disease onset (6 to 30 days) and admission (2 to 18 days). Nonetheless, on RT-PCR, 4 of 5 cases (80%) had positive throat samples (Ct values: 22 to 37), all cases had positive lesion samples (Ct values: 22 to 31), and 4 of 5 cases (80%) had positive plasma samples (Ct values: 31 to 35).

Jang and others collected lesion, oropharyngeal, and nasopharyngeal samples from a single case in South Korea in June 2022 (24). All samples were positive on RT-PCR (Ct values [RNaseP[c]]: skin lesions: 30.0 to 32.2, crust: 27.3 to 29.3, pharyngeal swabs: 23.8 to 25.0, blood: 21.7).

Karan and others collected a saliva sample, and conjunctival, rectal and nasopharyngeal swabs from a single case in the US in 2022 (41). All samples and swabs were positive on RT-PCR for mpox, and the authors noted that the case did not have respiratory symptoms or visible anal lesions (Ct values not reported).

Lapa and others collected plasma, urine, semen and skin lesion samples from a single case with HIV over 19 days after symptom onset in Italy in May 2022 (25). Plasma samples were only positive on RT-PCR on day 8 (Ct value: 34.5), urine samples were all negative, all semen samples were positive (last sample on day 19, lowest Ct value on day 7 [27.8], highest Ct value on day 19 [40.6]), and skin lesion samples were positive up to day 17 (negative on day 19, Ct values not reported). Clear cytopathic effects were observed from a semen sample on day 6 (Ct value: 29.3). The authors also reported 11 of 14 cases (79%) had positive semen samples, and live virus was isolated from a seminal fluid of a second case with HIV (Ct value: 22.7).

Noe and others collected lesion, throat, skin, blood, urine and semen samples from 2 cases in hospital in Germany in May 2022 (28). All samples were positive on RT-PCR (Ct values:

lesions: 17.4 to 38.5, skin: 13.0 to 32.8, blood: 27.2 to 44.2, semen: 28.2 to 45.0), except for urine. One lesion swab showed cytopathic effects (Ct value: 27.2), while all 9 other tested samples showed no growth.

Norz and others collected lesion and throat samples in 2 hospital cases in Germany in May 2022 (51). All samples were positive on RT-PCR (maximum viral copies for the 2 cases: lesions: $2.7x10^8$ and $4.4x10^8$, throat: $1.3x10^6$ and $2.1x10^7$).

Peiró-Mestres and others collected lesion, saliva, rectal, and nasopharyngeal swabs, and semen, urine, faeces samples from 12 cases in Spain in May and June 2022 (31). Samples were collected on varying days since symptom onset, from one to 16 days, and all cases were tested more than once. All cases had positive lesion samples on RT-PCR, both at the time of diagnosis and on samples taken between 4 and 16 days after symptom onset (Ct values: 16.2 to 27.8), all cases had positive saliva samples (Ct values: 20.3 to 37.9), 11 of 12 cases (92%) had positive rectal swabs (Ct values: 17.6 to 38.4), 10 of 12 cases (83%) had positive nasopharyngeal swabs (Ct values: 25.4 to 40.0), 7 of 9 cases (78%) had positive semen samples (Ct values: 20.9 to 40.0), 9 of 12 cases (75%) had positive urine samples (Ct values: 26.7 to 40.0), and 8 of 12 cases (67%) had positive faeces samples (Ct values: 17.8 to 31.4).

Pfafflin and others collected blister and anal swabs from 6 cases in Germany in May and June 2022 (45). All 6 blister swabs were positive on RT-PCR, as were all 3 of the anal swabs (Ct values not reported).

Raccagni and others collected cutaneous, rectal, oropharyngeal or genital swabs, and seminal fluid, urine, and plasma or serum samples from 36 cases in Italy in 2022 (32). All cases had positive cutaneous swabs on RT-PCR (Ct values not reported), 22 cases (61%) had positive seminal fluid samples (median Ct value: 34, IQR: 29 to 36.5), 8 cases (22%) had positive urine samples (Ct values not reported), and 24 cases (67%) had positive serum or plasma samples (median Ct value: 34, IQR: 33 to 36).

Seang and others collected skin, oropharynx, and anal swabs from 2 cases in France in June 2022 (34). In one case, skin and oropharynx swabs were positive on RT-PCR, and in the other case, oropharynx and anal swabs were positive. Additionally, the dog owned by the 2 cases had positive skin, anus and oral swabs (Ct values not reported).

Tarin-Vicente and others collected skin lesion, throat and anal swabs from up to 180 cases at hospitals in Spain in May and June 2022 (42). In total, 178 of 180 cases (99%) had positive skin lesion swabs on RT-PCR (mean Ct value: 23, standard deviation [SD]: 4), 82 of 117 cases (70%) had positive throat swabs (mean Ct value: 32, SD: 6), and 43 of 55 cases (78%) had positive anal swabs (mean Ct value: 27, SD: 7). Men reporting anal-receptive sex had a higher positive rate in throat swabs than men not reporting anal-receptive sex: 49 of 60 cases (82%) compared with 24 of 42 cases (57%).

Thornhill and others reported the positivity of skin or anogenital lesion and nose or throat swabs, and blood, urine, and semen samples in 528 cases from 16 different countries between April and June 2022 (36). Different swabs and samples were obtained for different cases in different countries, so only the number of positive results were reported. The cases reported here may be included in the results of other studies. Positive results on RT-PCR were obtained from skin or anogenital lesion swabs in 97% of cases, from nasopharyngeal swabs in 26% of cases, from urine samples in 3% of cases, and from blood samples in 7% of cases. Additionally, semen samples were positive in 29 of 32 cases (91%) (Ct values no reported).

Veintimilla and others collected lesion, oropharyngeal, and anal swabs (oropharyngeal and anal swabs dependent on type of sexual intercourse and symptoms), and plasma samples from 37 cases in May and June 2022 in Spain (53). Samples were collected one to 15 days after symptom onset. All but 10 of the 140 samples from the 37 cases were positive on RT-PCR (Ct values: skin lesions: 14 to 33, plasma: 28 to 40, oropharyngeal swabs: 19 to 37, anal swabs: 14 to 37): one lesion, 4 oropharyngeal and 2 anal swabs were negative, and 3 plasma samples were negative. Swabs of skin lesions had the lowest Ct values, and plasma samples had the lowest Ct values.

Environmental sampling

Atkinson and others collected swab and vacuum samples from the residences of a case and their sibling in the UK in 2019 (49). The case experienced fever and a persistent widespread pustular rash, but their sibling did not experience any symptoms of mpox (it is unclear if the sibling was tested for mpox). Samples were collected 3 days after the case was admitted to hospital. Of 42 samples collected, 37 (88%) were positive on RT-PCR, including all 21 samples from the case's single-room residence (Ct values: 22.6 to 32.3), 5 of 6 samples from the case's sibling's residence (same floor and apartment complex as the case, CT values: 30.5 to 25.3), 5 of 8 samples from the bathroom facilities (Ct values: 29.9 to 33.5), and 6 of 7 samples from the landing area between the residences (Ct values: 28.1 to 38.1). Viral isolation was successful from all 4 samples tested from the case's residence, in 2 of 3 samples from the case's sibling's residence, and in none of 3 samples from other areas.

Atkinson and others also collected swab, vacuum and wearable samples from the office of a case in the UK in May 2022 (3). The case worked in the office for one day following the onset of a mild, influenza-like illness (2 days before the onset of skin lesions), and coronavirus (COVID-19) control measures were in place, including wearing a medical mask and practicing regular hand hygiene. Samples were taken 4 days after the case was in the office. In total, 3 of 34 surface samples were positive on RT-PCR (from the case's telephone [Ct value: 37.7], keyboard [Ct value: 36.9], and desk [Ct value: 34.3]). Viral isolation was attempted from the positive desk sample, but no live virus was detected after 10 days of monitoring.

Gould and others collected surface, air and wearable samples from 5 hospital rooms of cases in the UK in May and June 2022 (6). In total, 56 of 60 surface samples (93%) from the cases' bedrooms and bathrooms were positive on RT-PCR, including from the floor, light switch, TV

remote control, air vent, and toilet flush handle (Ct values: 24.7 to 37.4). No positive samples were detected from the wearable air sampler, though 5 of the 8 air samples collected in a large volume air sampler in one room were positive (Ct values: 32.7 to 36.5), with the sample obtained during a bedding change having the lowest Ct value. However, the other 3 rooms had negative air samples. Four virus isolate samples, all with Ct values below 30 (light switch, 2 samples from the floor after personal protective equipment (PPE) doffing, and an air sample obtained during a bed linen change), were tested for live virus, and 2 samples were positive for DNA replication, indicating live virus in the samples. This study was used as a source of evidence for environmental sampling in the third UKHSA technical briefing on mpox (37), which stated that initial findings showed widespread shedding of live virus on multiple surfaces within the isolation rooms of cases in hospital, and that some air samples from patient rooms were positive during bed linen changing, with one sample containing live virus.

Morgan and others collected surface samples from a residence of a single case in the US in 2021 (50). The samples were collected 15 days after the case was admitted to hospital from the bedroom, bathroom, living room, kitchen and closet. In total, 27 of 31 samples (87%) were positive on RT-PCR (mean Ct value: 25.8, range: 16.1 to 36.7), with no difference (p=0.94) between porous (90% of samples, mean Ct value: 22.0) and non-porous surfaces (90% of samples, mean Ct value: 27.7), though porous material had higher detected levels of viral DNA (Ct values of 22.0 vs 27.7, p<0.01). Additionally, 7 of 31 samples (23%) contained live virus (Ct values: 14.2 to 16.0), and porous materials (6 of 10 samples, 60%) were more likely to be positive for live virus than non-porous materials (one of 21 samples, 5%).

Norz and others collected surface samples from the hospital rooms of 2 hospital cases in Germany in May 2022 (51). All surfaces touched by the cases' hands were positive on RT-PCR (viral copies per cm^2 up to 240,000, highest in the bathroom [tap control lever]), and there was a mix of positive and negative samples for other surfaces. Virus isolation to detect live virus was attempted for 40 of the 50 samples collected, with evidence of live virus in 3 samples (all from one case, and all samples had more than 10^3 viral copies per cm^2 per sample).

Wolfe and others collected wastewater solid and liquid samples at 9 wastewater plants in the US in June and July 2022 (8). mpox DNA was consistently detected in samples from 8 of the 9 plants, and in all 15 liquid samples.

Summary

For individual sampling, there was evidence from across 16 studies conducted in at least 16 countries in 2022 that mpox DNA was present on RT-PCR in lesion, anorectal, and nasopharyngeal swabs, and in serum, plasma, blood, saliva, faeces, urine, and semen and seminal fluid samples taken from mpox cases. Live virus was isolated from semen in one study, and from a skin lesion in another study, although the remaining studies did not report testing for live virus (detection of viral DNA does not necessarily indicate infectious virus). While many studies had few cases (9 studies had fewer than 10 cases), 3 studies each had more than 100 cases, although there may be overlap of cases between these studies.

For environmental sampling, there was evidence from 6 studies conducted in 3 countries (3 studies reported on the UK) in 2019 and 2022 of the presence of mpox DNA on RT-PCR in a high proportion of surface and air samples taken from the residences or hospital rooms of mpox cases. Many of these samples contained live virus, although some studies only tested samples with low Ct values. The 2 studies that collected wearable air samples did not report any positive samples on RT-PCR. One further study suggested that wastewater sampling consistently tested positive for mpox DNA.

GRADE assessment: very low certainty of evidence.

Inequalities

There was little evidence available to explore inequalities through variations across populations and subgroups, for example cultural variations or differences between ethnic, social or vulnerable groups. As such, it was not possible to examine inequalities in this report.

Limitations

The source of evidence in this review included peer-reviewed and preprint articles. We did not conduct an extensive search of other sources (such as websites of public health organisations). As with all reviews, the evidence identified may be subject to publication bias, whereby null or negative results are less likely to have been published by the authors, though descriptive studies may be less susceptible to publication bias than other study types. Seven of the 40 studies identified and summarised in this report were preprints and should be treated with caution as they have not been peer reviewed or subject to publishing standards, and may be subject to change. In addition, this rapid review is limited by the fact that we were reviewing evidence from an emerging and ongoing outbreak that has only lasted for 4 months. These studies may have been conducted at pace, with the aim to provide evidence in a timely manner, which may have impacted on the quality of the studies, both in term of design (especially limited statistical analyses) and reporting (insufficient detail). This is especially noticeable in studies that are still collecting data.

Evidence gaps

While many studies reported on the incubation period of mpox, no studies reported directly on the infectious period.

Additionally, while many studies suggested different samples taken from people with mpox could be positive for mpox DNA on RT-PCR, there was little evidence for whether those samples contained live virus capable of infecting others.

Conclusion

For transmission of mpox in the 2022 outbreak, the evidence suggested that, up to August 2022, transmission was mostly from sexual contact, with the vast majority of cases being gay, bisexual, or other men who have sex with men, most commonly between 30 and 50 years of age, reporting multiple sexual partners (5 or more within the last 3 months), previous or current sexually transmitted infections (including HIV), and use of HIV pre-exposure prophylaxis. There was some evidence of transmission from non-sexual contact, but no evidence of transmission through the air, although the transmission route remains unknown for some cases.

Eight studies reported the incubation period of mpox cases, with estimates of the median or mean incubation period ranging from 6 to 10 days in 2022, shorter than the 12 days estimated in the 2003 outbreak.

For individual sampling, there was evidence that mpox DNA was present in lesions, anorectal, and nasopharyngeal swabs, and in serum, plasma, blood, saliva, faeces, urine, and semen and seminal fluid samples taken from mpox cases. Live virus was isolated from semen in one study, and from a skin lesion in another study, but other studies did not test for live virus, and detection of mpox DNA does not necessarily indicate infectious virus. For environmental sampling, there was evidence of mpox DNA in a high proportion of surface and air samples taken from the residences or hospital rooms of mpox cases. Additionally, there was evidence that many of these samples contained live virus. One further study suggested that wastewater sampling consistently tested positive for mpox DNA.

No studies reported directly on the infectious period of mpox.

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Disclaimer

UKHSA’s rapid reviews aim to provide the best available evidence to decision makers in a timely and accessible way, based on published peer-reviewed scientific papers, unpublished reports and papers on preprint servers. Please note that the reviews: i) use accelerated

methods and may not be representative of the whole body of evidence publicly available, ii) have undergone an internal, but not independent, peer review, and iii) are only valid as of the date stated on the review.

In the event that this review is shared externally, please note additionally, to the greatest extent possible under any applicable law, that UKHSA accepts no liability for any claim, loss or damage arising out of, or connected with the use of, this review by the recipient and/or any third party including that arising or resulting from any reliance placed on, or any conclusions drawn from, the review.

Table 1: Study characteristics

Author	Country	Study type	Time period	Mpox cases	Transmission	Incubation period	Infectious sampling
Antinori (20)	Italy	Case series	May 2022	4	Yes		Yes
Atkinson (49)	UK	Case report	December 2019	1			Yes
Atkinson (3)	UK	Case report	May 2022	1			Yes
Catala (21)	Spain	Cross-sectional	May to July 2022	185	Yes	Yes	
Charniga (4)	US, The Netherlands	Cross-sectional	May to June 2022	40	Yes	Yes	
Davido (43)	France	Case report	2022	1	Yes		
De Baetselier (5)	Belgium	Cross-sectional	May 2022	4	Yes		Yes
Ferre (52)	France	Case series	June to July 2022	284			Yes
Girometti (22)	UK	Cross-sectional	May 2022	54	Yes		
Gould (6)	UK	Cross-sectional	May to June 2022	NA			Yes
Guzzetta (44)	Italy	Cross-sectional	May to June 2022	255	Yes	Yes	
Heskin (23)	UK	Case series	May 2022	2	Yes		
Huhn (47)	US	Cross-sectional	2003	34		Yes	
Jang (24)	South Korea	Case report	June 2022	1	Yes		Yes
Karan (41)	US	Case report	2022	1	Yes		Yes
Lapa (25)	Italy	Case report	May 2022	1	Yes		Yes
Martinez (26)	Spain	Cross-sectional	May to June 2022	595	Yes		
Minhaj (27)	US	Cross-sectional	May 2022	17	Yes		
Miura (48)	The Netherlands	Cross-sectional	May 2022	18		Yes	
Morgan (50)	US	Case report	July 2022	1			Yes
Noe (28)	Germany	Case series	May 2022	2	Yes		Yes
Norz (51)	Germany	Cross-sectional	June 2022	2			Yes
Orviz (29)	Spain	Cross-sectional	May to June 2022	48	Yes		

Author	Country	Study type	Time period	Mpox cases	Transmission	Incubation period	Infectious sampling
Patel (30)	UK	Case series	May to July 2022	197	Yes		
Peiro-Mestres (31)	Spain	Case series	May to June 2022	12	Yes		Yes
Pfafflin (45)	Germany	Case series	May to June 2022	6	Yes		Yes
Raccagni (32)	Italy	Case series	2022	36	Yes		Yes
Rodriguez (33)	Spain	Cross-sectional	May to June 2022	1,256	Yes	Yes	
Seang (34)	France	Case series	June 2022	2	Yes		Yes
Selb (35)	Germany	Cross-sectional	May to June 2022	521	Yes		
Tarin-Vicente (42)	Spain	Cohort	May to July 2022	181	Yes	Yes	Yes
Thornhill (36)	Global	Case series	April to June 2022	528	Yes	Yes	Yes
Thy (7)	France	Vaccine study	May to July 2022	12	Yes		
UKHSA (37)	UK	Cross-sectional	May to July 2022	1,517	Yes		Yes
Veintimilla (53)	Spain	Cross-sectional	May to June 2022	37			Yes
Vivancos (38)	UK	Case series	May 2022	86	Yes		
Vusirikala (39)	UK	Cross-sectional	May 2022	45	Yes		
Wolfe (8)	US	Cross-sectional	June to July 2022	NA			Yes
WHO (40)	Global	Cross-sectional	January to July 2022	16,016	Yes		
Zucker (9)	Israel	Retrospective cohort	January to June 2022	8089	Yes		

Acronyms: NA = not applicable (environmental, not case, testing), UKHSA = UK Health Security Agency, WHO = World Health Organization

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Annexe A: methods

This rapid review aimed to answer the following 2 research questions:

1. What are the routes of transmission for mpox, and the risks associated with these routes?
2. What are the infectious and incubation periods for mpox?

A further research question on what evidence is available for barriers and adherence to mpox isolation guidance uses the same search strategy, but is addressed in a separate report.

Our rapid review approach follows streamlined systematic methodologies (1). In particular, 10% of the screening on title and abstract were screened in duplicate, and full text screening, data extraction and risk of bias assessment were performed by one reviewer and checked by another. The review has been reported according to PRISMA guidelines (54).

Protocol

A protocol was produced a priori and is available on request.

Sources searched

OVID Medline, OVID Embase, Scopus, MedrXiv, Preprints.org, Google, Google Scholar, and an internal mpox digest, which included searches in pubmed, direct websites, Government, and grey literature documents.

Search strategy

Searches were conducted for papers published up to 15 August 2022.

Search terms covered key aspects of the review question. The search strategies for all databases are presented below. Additionally, we checked reference lists of relevant systematic reviews and evidence summaries and consulted with topic experts. All papers that had been identified as preprints were last checked and updated (if necessary) on 26 September 2022.

Search strategy for Ovid Medline

1. Monkeypox/
2. Monkeypox virus/
3. ("monkey pox" or monkeypox or monkeypoxvir* or hMPXV or MPXV or MPX).kf,tw.
4. ((Infect* or symptom* or incubat* or contag* or transmissi*) adj3 (time* or period* or timing or duration)).kf,tw.
5. Infectious Disease Incubation Period/
6. 1 or 2 or 3
7. 4 or 5
8. exp Disease Transmission, Infectious/
9. exp "Chain of Infection"/
10. ((infectio* or disease*) adj2 (transmission or reservoir* or carrier*)).kf,tw.
11. "transmission*".ti.
12. 8 or 9 or 10 or 11
13. exp Public Policy/
14. (guidance or adher* or advice).tw.
15. Guideline Adherence/
16. 13 or 14 or 15
17. 7 or 12 or 16
18. 6 and 17

PrePrint (MedRxiv, Preprints.org, OSF Preprints, Google Scholar)

"monkey pox" or monkeypox or monkeypoxvir* or mpx (manually filtered for relevance)

Prospero

"monkey pox" or monkeypox or monkeypoxvir* or mpx (manually filtered for relevance)

Scopus

(TITLE-ABS-KEY ("monkey pox" OR monkeypox OR monkeypoxvir* OR hmpxv OR mpxv OR mpx) AND TITLE-ABS-KEY (infection OR symptom OR transmission OR guidance OR advice OR adherence OR compliance)) AND (LIMIT-TO (LANGUAGE , "English"))

African Index

(tw:("monkey pox" or monkeypox or monkeypoxvir* or hMPXV or MPXV or MPX))

Other /Grey Lit

"monkey pox" or monkeypox or monkeypoxvir* or mpx (manually filtered for relevance)

Inclusion and exclusion criteria

Article eligibility criteria are summarised in Table A.1.

Table A.1. Inclusion and exclusion criteria

	Included	Excluded
Population	Any	
Settings	Any	
Context	Mpox infections (clade II) and outbreaks	Other diseases
Intervention, exposure	People who have suspected or confirmed mpox	
Outcomes	Transmission and associated risks (including to and from pets and other animals). Infectious or incubation periods.	
Language	English	
Date of publication	Up to 15 August 2022	
Study design	Primary studies that include data for individuals with mpox.	Systematic or narrative reviews. Guidelines (unless they include data on outcome 3 above). Opinion pieces.
Publication type	Published and preprint	

Screening

Title and abstract screening was completed by 2 reviewers: 10% of the eligible studies were screened in duplicate (disagreements were resolved by discussion) and the remainder were screened by one reviewer.

Full text screening was completed by one reviewer and checked by a second.

The PRISMA diagram showing the flow of citations is provided in Figure A.1.

Data extraction and risk of bias assessment

Data from included studies were extracted straight into summaries in the report and Table 1, with both the summaries and table checked by a second reviewer.

Studies were planned to be assessed in duplicate using the quality criteria checklist (QCC) for primary research (2). However, as the studies included in this review were almost all descriptive rather than analytical, risk of bias assessments were not performed.

Variations across populations and subgroups, for example cultural variations or differences between ethnic, social or vulnerable groups were considered, where evidence was available.

GRADE assessment

GRADE assessments were conducted for each of the following mpox outcomes, see Table A.2:

- transmission
- incubation period
- infectious sampling

All outcomes included only observational studies and started with low certainty of evidence.

For all outcomes, the risks of bias, indirectness and publication bias were judged as not serious, as for all outcomes most evidence directly reported descriptions of the 2022 mpox outbreak.

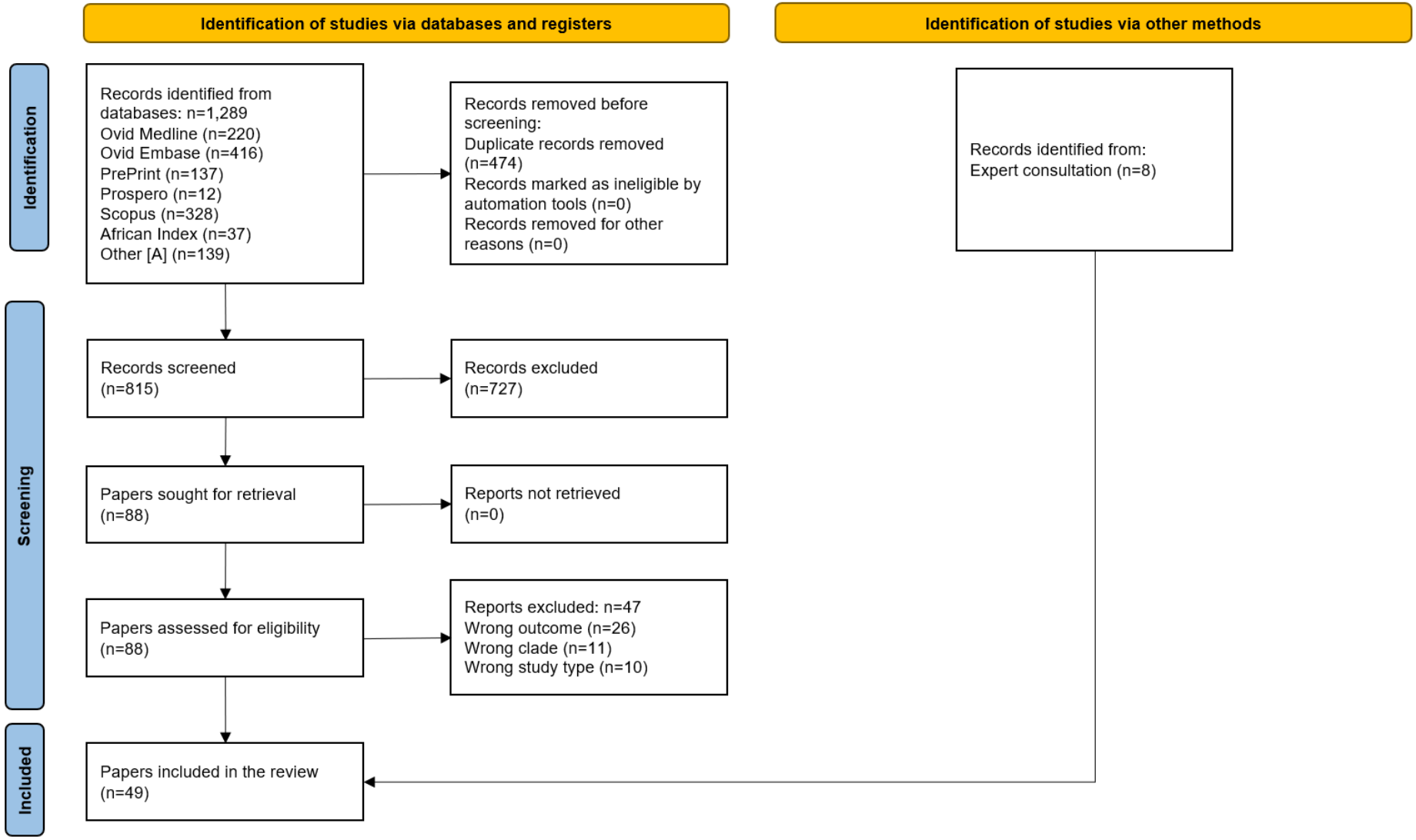
For transmission, the majority of the evidence was consistent, reporting similar demographics and modes of transmission, as well as precise. The transmission outcome was therefore rated as low certainty.

While there was some heterogeneity in results, the risks of bias from consistency for incubation period and infectious sampling were also judged as not serious. However, there was relatively little evidence for the incubation period and infectious sampling outcomes, and the risk of bias from imprecision was judged as serious. These outcomes were therefore rated as very low certainty.

Table A.2. GRADE assessment: summary of findings

Outcome	Effect	Studies	Certainty in the evidence
Transmission	Evidence from 30 studies suggested that, up to August 2022, transmission of mpox was mostly from sexual contact, with the vast majority of cases being gay, bisexual, or other men who have sex with men, often between 30 and 50 years of age, reporting multiple sexual partners (often 5 or more within the last 3 months), previous or current sexually transmitted infections (including HIV), and use of HIV pre-exposure prophylaxis.	2022 outbreak: 30	⨁⨁◯◯ Low
Incubation period	Evidence from 8 studies suggested a median or mean incubation period ranging from 6 to 10 days in 2022, shorter than the 12 days estimated in the 2003 outbreak.	8	⨁◯◯◯ Very low
Infectious sampling	Evidence from 16 individual sample studies suggested mpox DNA was present in lesion, anorectal, and nasopharyngeal swabs, and in serum, plasma, blood, saliva, faeces, urine, and semen and seminal fluid samples taken from mpox cases, and live virus was isolated from semen in one study, and from a skin lesion in another study, although no other study reported testing for live virus (detection of viral DNA does not necessarily indicate infectious virus). Evidence from 6 environmental sample studies suggested the presence of mpox DNA in a high proportion of surface and air samples taken from the residences and hospital rooms of mpox cases, and that many of these samples contained live virus.	Individual sampling: 16 Environmental sampling: 6	⨁◯◯◯ Very low

Figure A.1. PRISMA diagram



[A] Other = sources included in the internal mpox digest, including pubmed (n=136 of 139 results), direct websites, Government and grey literature documents, excluding OVID Medline and Embase results.

Figure A.1. PRISMA diagram – alt text

A PRISMA diagram showing the flow of studies through this review, ultimately including 49 studies.

From identification of studies via databases and registers, n=1,289 records identified from databases:

- Ovid Medline (n=220)
- Ovid Embase (n=416)
- PrePrint (n=137)
- Prospero (n=12)
- Scopus (n=328)
- African Index (n=37)
- Other [A] (n=139)

From these, records removed before screening:

- duplicate records removed (n=474)
- records marked as ineligible by automation tools (n=0)
- records removed for other reasons (n=0)

n=815 records screened, of which n=727 were excluded, leaving n=88 papers sought for retrieval, all of which were retrieved.

Of the n=88 papers assessed for eligibility, n=47 reports were excluded:

- wrong outcome (n=26)
- wrong clade (n=11)
- wrong study type (n=10)

From identification of studies via other methods, n=8 studies were identified from expert consultation.

n=49 papers included in the review (n=44 from identification of studies via databases and registers, n=8 from expert consultation).

[A] Other = sources included in the internal mpox digest, including pubmed (n=136 of 139 results), direct websites, Government and grey literature documents, excluding OVID Medline and Embase results.

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