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The clinical presentation of monkeypox: a retrospective case-control study of patients with possible or probable monkeypox in a West London cohort

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ABSTRACT

Objectives: Since May 2022, cases of human monkeypox virus (hMPXV) with human-to-human transmission have significantly increased in nonendemic countries. Our aim was to characterize diagnostic features of patients with confirmed and possible monkeypox to guide future risk stratification and to describe a virtual care model.

Methods: We performed a retrospective case-control study of 140 patients assessed and screened for suspected monkeypox; on hMPXV polymerase chain reaction testing, 70 were confirmed positive, and 70 were negative. Data were compared to generate odds ratios of demographic and clinical features.

Results: Patients who tested positive were predominantly cis-male (99%) and self-identified as gay, bisexual, and other men who have sex with men (94%). Lymphadenopathy at presentation was associated with a higher likelihood of a positive result (odds ratio [OR] 7.69 [95% confidence interval (CI) 3.58, 16.51]). Patients who tested positive were more likely to have a rash affecting the genital (OR 5.38 [95% CI 2.57, 11.23]) or buttocks/perianal region (OR 3.79 [1.70, 8.45]) than negative controls. A total of 79% of patients were engaged with a virtual ward follow-up.

Conclusion: These data can inform a risk-based approach to the management of suspected monkeypox in gay, bisexual, and other men who have sex with men populations. Lymphadenopathy at presentation and the location of the rash were more associated with a positive hMPXV result. Health authorities can consider a virtual ward approach in the hMPXV outbreak.

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Introduction

Human monkeypox virus (hMPXV) is an orthopoxvirus, previously recognized as endemic to West and Central Africa (Bunge et al., 2022). Since May 2022, a worldwide outbreak of monkeypox has been described in several countries that have not previously reported cases. The 2022 outbreak has predominantly but not exclusively affected gay, bisexual, or other men who have sex with men (GBMSM) aged 18-50 years (Centers for Disease Control [CDC], 2022). In late July 2022, the World Health Organization declared the ongoing monkeypox outbreak a public health emergency of international concern, in recognition of the rapidly increasing case numbers across multiple regions. As of August 10, 2022, over 31,800 confirmed cases have been reported internationally across 89 countries (CDC, 2022).

Monkeypox is classically described as starting with a systemic prodrome of fever, malaise, headache, myalgia, and lymphadenopathy, which progresses to a centrifugal vesiculopustular rash (Antinori et al., 2022; Igó Martinez et al., 2022; Minhaj et al., 2022; Selb et al., 2022; Thornhill et al., 2022). Complications include secondary bacterial infections, ocular or periocular lesions,

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proctitis, dysuria, urinary retention, oral ulcers, and pharyngotonsillitis (Patel et al., 2022).

There is an increasing awareness of atypical presentations, potentially related to changing patterns of transmission, with transmission associated with sexual contact increasingly recognized. In particular, the clinical presentation and distribution of the rash often differs from that previously recognized, particularly with more frequent anogenital involvement.

A major challenge has been the evolving understanding of the disease in real time. The UK Health Security Agency (UKHSA), World Health Organization, Centers for Disease Control, and others have generated case definitions for possible, probable, and confirmed cases of monkeypox (CDC, 2022; World Health Organization, 2022; UKHSA, 2022c). UKHSA defines possible and probable cases based on a combination of clinical features and epidemiological risk factors. In the context of an evolving outbreak, the clinical diagnosis of monkeypox can be challenging and may be difficult to distinguish from other infectious causes of rash. A definite diagnosis of monkeypox requires molecular testing in a specialist laboratory, sometimes with a prolonged time for the result.

We conducted a case-control study that aimed to assess the clinical characteristics of patients meeting the case definitions of possible or probable monkeypox in a cohort of patients in West London. The objectives were to characterize the clinical diagnostic features of patients with confirmed and possible monkeypox during the emerging epidemic to guide future risk stratification. We also describe our clinical care model, including the use of a virtual ward to support patients with hMPXV managed in the community.

Methods

Setting and study size

We performed a retrospective case-control study of 140 suspected adult (aged ≥18 years) monkeypox cases in North West London presented to a single National Health Service (NHS) trust (Imperial College Healthcare NHS Trust). The first 70 consecutive positive and 70 negative cases tested for hMPXV were included. This method, rather than a more complex selection and matching, was chosen to allow rapid data collection and review as new cases were presented to provide time-appropriate, useful information that was applicable during the evolving outbreak. Patients presented using an open-access sexual health clinic, the emergency department (ED), or were referred directly to the infectious diseases (ID) unit at one of three hospitals within the NHS trust.

Participants

All patients presented with clinical features consistent with either possible or probable monkeypox, in accordance with the UKHSA definitions (UKHSA, 2022c). Confirmed cases were defined as those who had a positive polymerase chain reaction (PCR) test for hMPXV from either a skin lesion and/or a throat swab. Controls were patients who met the UKHSA case definition for possible or probable monkeypox at the time of testing but from whom all swabs were negative on PCR for hMPXV. All samples were processed at a central reference site at the UKHSA Rare and Imported Pathogens Laboratory in Porton Down, United Kingdom.

Quantitative variables

The following data were obtained from electronic health records: demographic factors (age, gender identity, sexual orientation), HIV status, other comorbidities, and their epidemiological risk of exposure (GBMSM, exposure to a confirmed hMPXV case, and/or travel to an endemic area in the past 21 days).

The following clinical features were assessed: subjective fever, chills, and/or documented fever ≥38°C; headache; malaise/fatigue; lymphadenopathy; presence or absence of a rash. Location was recorded as any lesion(s) on the palms/soles; trunk; perioral region; buccal cavity; genitals, or perianal region/buttocks. The stage of the lesions in relation to one another (whether at the same or different stages) was noted. Any secondary complications of the suspected illness were recorded. The date of any symptom onset, date of rash eruption, date of testing, and PCR result were recorded. If a symptom was not documented, it was assumed to have been absent. Initial patient assessment was performed by the attending clinician as per routine clinical care, and standardized symptom questionnaires were not used.

Patients were risk stratified and categorized as those who had severe disease or were at risk of severe disease due to underlying factors, those who were well but had to be admitted for isolation because they presented an infection risk to others, and those who were low risk and clinically able to isolate at home (UKHSA, 2022c). Laboratory test results performed during admission as part of routine clinical care were reviewed including total white cell count at admission (× 10^9/l), lymphocyte nadir (× 10^9/l), alanine transaminase (ALT) peak (IU/l), and peak C-reactive protein (mg/l). For people living with HIV (PLWHIV) infection, the most recent viral load and cluster of differentiation 4 count were recorded. A detectable HIV viral load was defined as >50 copies/ml. We reviewed the number of patients admitted, reason for admission, and length of stay, including the proportion who self-discharged. Patients who tested positive managed in the community or discharged from hospital were followed up by a ‘virtual ward’ until they met all UKHSA deisolation criteria. These criteria were: afebrile for at least 72 hours, no new lesions in the last 48 hours, all lesions scabbed over, and no oral lesions and for lesions on the face, arms, and hands, the scab must have fallen off, and a fresh layer of skin formed underneath (UKHSA, 2022d). Of those who were positive and followed up by the ‘virtual ward’ remote monitoring team, we recorded the number of calls required from referral to deisolation. The number of days from symptom onset to deisolation was documented where deisolation had already been achieved.

Data sources

Cases and controls and their hMPXV results were identified from the local sample tracking and results database, which included all patients who had been tested for hMPXV across the trust. Indeterminate results were excluded. The case information was obtained from trust electronic patient records, including Cerner and MillCare, and all data were pseudonymized for analysis.

Analysis

Data were extracted onto a case record form in Microsoft Excel, and analysis was performed using R version 4.0.3. Univariate odds ratios (ORs) were calculated using the epir package. The OR for each variable was defined as the ratio of the odds of a clinical feature being present in patients testing positive for monkeypox infection (cases) compared with its odds in patients testing negative (controls). Plots were created with ggplot2 and incidence2 packages.

Ethics

We extracted data from routine clinical records into an anonymized, password protected, securely maintained database containing no personally identifiable information.
Table 1
Demographic data and source of referral.

| Source of referral                        | hMPXV-positive (n=70) n (%) | hMPXV negative (n=70) n (%) | Total cohort (n=140) n (%) |
|-------------------------------------------|----------------------------|-----------------------------|---------------------------|
| Cis-male                                  | 69 (99)                    | 52 (74)                     | 121 (86)                  |
| GBMSM                                     | 66 (94)                    | 30 (43)                     | 96 (69)                   |
| Median age (range) [IQR]                  | (21-75) (29-42)            | (18-84) (28-44)             | (21-84) (29-42)           |
| HIV                                       | 20 (35)                    | 14 (20)                     | 34 (24)                   |
| Other co-morbidities                     | 6 (9)                      | 31 (44)                     | 37 (26)                   |
| Sexual health clinic                      | 48 (69)                    | 24 (34)                     | 72 (51)                   |
| Emergency department                     | 20 (29)                    | 41 (59)                     | 61 (44)                   |
| Other (primary care, national meetings)  | 2 (3)                      | 5 (7)                       | 7 (5)                     |

GBMSM, gay, bisexual, or men who have sex with men; hMPXV, human monkey pox virus; IQR, interquartile range.

Table 2
Key clinical features of presentation and their relative frequency in hMPXV PCR positive cases compared with negative cases, with odds ratios.

| Symptom                        | Positive cases (n=70) n (%) | Negative cases (n=70) n (%) | Odds Ratio (95% CI) |
|--------------------------------|----------------------------|-----------------------------|---------------------|
| Rash (all)                     | 68 (97)                    | 66 (94)                     | 2.06 (0.37, 11.63)  |
| Genital                        | 43 (61)                    | 16 (23)                     | 5.38 (2.57, 11.23)  |
| Rectal/perianal                | 29 (41)                    | 11 (16)                     | 3.79 (1.70, 8.45)   |
| Trunk                          | 29 (41)                    | 36 (51)                     | 0.63 (0.32, 1.23)   |
| Limbs                          | 30 (43)                    | 44 (63)                     | 0.47 (0.24, 0.92)   |
| Face                           | 24 (34)                    | 25 (36)                     | 0.88 (0.44, 1.77)   |
| Palms/soles                    | 8 (11)                     | 10 (14)                     | 0.79 (0.29, 2.13)   |
| Buccal                         | 7 (10)                     | 8 (11)                      | 0.86 (0.29, 2.52)   |
| Perianal                       | 5 (7)                      | 6 (9)                       | 0.82 (0.24, 2.82)   |
| Systemic symptoms (all)        | 57 (81)                    | 40 (57)                     | 16.75 (4.80, 58.4)  |
| Lymphadenopathy                | 47 (67)                    | 15 (21)                     | 7.49 (3.51, 15.99)  |
| Fatigue                        | 48 (68)                    | 19 (27)                     | 2.54 (1.25, 5.13)   |
| Fever                          | 40 (57)                    | 22 (31)                     | 1.45 (0.73, 2.92)   |
| Headache                       | 24 (34)                    | 10 (14)                     | 1.92 (0.81, 4.57)   |

hMPXV, human monkey pox virus; PCR, Polymerase chain reaction.

Results

Demographics and exposure risk

The 140 cases screened (70 positive and 70 negative) for hMPXV were tested between May 9, 2022 and June 29, 2022 (Supplementary Figure 1). Of the 140 suspected patients, 121 (86%) were cis-male, 17 (12%) were cis-female, one was a transgender female, and one identified as nonbinary gender. The median age at presentation was 36 (range 18–84; interquartile range [IQR] 29–42). Just over half of cases presented through sexual health services (Table 1).

The majority of cases with PCR-confirmed monkeypox infection were cis-male (69/70 [99%]), of whom 66/69 (96%) identified as GBMSM. The median age of cases was 36 years (range 21–75). A total of 48 (69%) were referrals from sexual health clinics, 20/70 (28%) were screened in the ED, and two were external referrals. Identifying as GBMSM was associated with a significantly increased likelihood of positive monkeypox PCR (OR 22.0 [95% CI 7.22, 67.1]). Only five (7%) of the positive cases reported contact with a person with confirmed hMPXV, and none had traveled to an endemic area in the preceding 21 days.

In the hMPXV-negative control group, 52 (74%) identified as cis-male, 16 (22%) as cis-female, one as a transgender woman, and one as nonbinary gender. In contrast to the hMPXV-positive group, the majority of cases presented to ED (41, 59%) rather than sexual health clinics (24, 34%), and five cases (7%) were referred through other sources. Other referral sources included incidental rashes noticed by inpatient teams for three cases and an occupational health referral for two cases who had been exposed to hMPXV cases without appropriate personal protective equipment and subsequently developed prodrmal symptoms.

HIV coinfection and other comorbidities

A total of 20 of the hMPXV-positive cases (20/70, 35%) were known to be HIV-positive, all of whom had an HIV viral load of <50 copies/ml. Cluster of differentiation counts within the last 6 months were available for 10 of 20 PLWHIV who were hMPXV-positive; all had counts greater than 200 cells/mm³. A total of 16 (2%) of the patients who tested negative for hMPXV were PLWHIV; five of whom had a detectable viral load.

Negative controls were significantly more co-morbid with 31 (44%) having at least one co-morbidity. Six (9%) patients who tested positive had one or more comorbidities, including end-stage renal failure; chronic kidney disease; diabetes mellitus; hypertension; asthma; and mental health disorders, including depression, anxiety, schizophrenia, and post-traumatic stress disorder (OR 0.12 [95% CI 0.05–0.31]).

Clinical presentation

Table 2 shows the clinical features of cases and controls. A total of 57 (81%) positive cases had systemic features, whereas 13 (19%) complained of rash alone. In 47 (62%) patients who tested positive, the rash was either the first symptom or developed on the same day as any systemic symptoms. The second most common complaint was lymphadenopathy (47, 67%), followed by fatigue (34, 48%), and headache (17, 24%). Fever was reported in 28 (40%).

Rash was the main presenting complaint in 68 (97%) positive cases. In 43 cases (61%), rash was present on the genitals, and in 29 (41%), it was on the buttocks or perianal area. In 13 (18%) cases, the rash was only on the genitals and similarly, in 13, it affected the buttocks/perianal area only. A total of 28 (40%) had lesions on the trunk and 31 (44%) on the limbs. Palms and soles were affected in only eight (11%) cases. The face was affected in 23 (33%), with five
Table 3
Number of admitted patients, HIV status and the median length of stay.

|                      | Positive cases (%) | Negative cases (%) | Total [%] |
|----------------------|--------------------|--------------------|-----------|
| Admitted to hospital | 18/70 (26)         | 20/70 (29)         | 38/140 (27) |
| PLWHIV               | 5/18 (28)          | 5/20 (25)          | 10/38 (26) |
| HIV negative         | 13/18 (72)         | 15/20 (75)         | 28/38 (74) |
| Median length of stay (IQR) | 6.5 (1.25-12.75) | 5 (2.75-6) | 5 (2-8.25) |
| Self-discharged      | 6/18 (33)          | 3/20 (15)          | 9/38 (24)  |

IQR, Interquartile range; PLWHIV, People living with HIV.

Table 4
Reasons for admission of hMPXV positive patients.

| Clinical need                | 7/18 |
|------------------------------|------|
| Disseminated lesions         | 2    |
| Pain management              | 1    |
| Pharyngitis/peritonsillar abscess | 2  |
| Secondary bacterial infection | 1    |
| Sepsis                       | 1    |
| Isolation only               | 11/18|
| Shared domestic amenities    | 5    |
| Hostel resident              | 2    |
| Homeless status              | 2    |
| Living with at risk population | 3   |

Six positive cases self-discharged against medical advice for reasons, including finding alternative accommodation, severe isolation anxiety, and financial concerns. The public health authorities were informed of those positive cases who self-discharged to ensure the safety of the patient and community. Of the other admissions, 11 remained in hospital until they met the deisolation criteria and were deemed safe to return home (UKHSA, 2022a).

Complications

Of the 70 positive cases, including those admitted as described previously, the most common secondary complication was perirectal pain and associated constipation (13.18%), followed by pharyngitis (5.7%) and superadded bacterial skin and soft tissue infection (3). One patient required surgical drainage of a deep thigh abscess by the surgical team; this had been performed before testing for hMPXV because the rash developed after the procedure. Of note, one of the two cases with disseminated lesions had ocular involvement requiring regular ophthalmology review and off-label use of tecovirimat, an inhibitor of the VP37 protein.

Blood results

Blood results were available in 30 of the positive cases and 39 of the negative cases. They were broadly comparable between groups with no significant differences (see Supplementary Figure 2). The median white cell count peak in the positive group was $6.95 \times 10^9/l$ (IQR 5.98-8.6) and $7.40 \times 10^9/l$ (IQR 5.35-9.30) in the negative group ($p = 0.75$). The lymphocyte nadir was lower in patients testing negative $(1.4 \times 10^9/l$, IQR 0.9-2.0) vs positive $(2.00 \times 10^9/l$, IQR 1.3-2.0), $p = 0.04$. The median peak C-reactive protein was 25.2 mg/l (IQR 15.7-59.0) in the positives and 16.6 mg/l (IQR 7.7-37.3) in the negative group ($p = 0.2$). Liver function was similar, with a median peak alanine transaminase of 40 U/l (IQR 26-64.5) in the positive group and 27.5 U/l (IQR 20.15-46.75) in the negative group ($p = 0.05$).

Alternative diagnoses for rash in negative cases

A diagnosis for the rash was confirmed in 27 of the 70 cases who were negative for hMPXV; eight were positive for varicella zoster virus; five had clinical features in keeping with folliculitis, four had confirmed herpes simplex virus, four had gonorrhoea, two had confirmed syphilis, two had suspected scabies, and two with psoriasis confirmed by a dermatologist.

Follow-up and deisolation

Positive cases that did not require admission were referred to a remote monitoring team (virtual ward) who contacted patients daily or on alternate days to review symptoms, discuss any concerns, and agree on appropriate deisolation. This included a review of the patient’s mental health and how they were coping with isolation. Patients could report their symptoms either over the phone or through an app-based program. Any concerns about a patient...
were referred to the clinical team for assessment. The virtual ward team also assisted in providing sick notes or proof of isolation requirement for employers. Of those referred to the virtual ward, 15 of 70 (21%) were lost to follow-up; these cases were highlighted to the local public health team. Of the 55 who engaged, the median number of calls required until deisolation was four (range 1-13), and the median number of days from symptom onset to deisolation was 16 days (range 5-40).

Discussion

Our study was conducted in the early period of this emerging outbreak as clinicians and public health specialists were gaining experience of the clinical characteristics, testing algorithm, management, and de-isolation criteria in this outbreak. Our findings note significant differences between the two cohorts with cisgender male gender, identifying as GBMSM, the presence of a rash in the anogenital area, the presence of lymphadenopathy, and fatigue, significantly increasing the likelihood of a positive test for hMPXV. We found no evidence of an association between HIV positivity and testing positive for hMPXV. Our data are important for public health practitioners and clinicians because they can inform a risk-based approach to the management of suspected monkeypox in GBMSM populations.

Emerging understanding of clinical characteristics

The characteristics of our cohort are similar to other described cohorts in the current outbreak, which has predominantly affected the GBMSM community. The rash of monkeypox predominantly affected the anogenital region, as described in cohorts from the United Kingdom, Spain, Germany, Italy, the United States, and elsewhere (Antinori et al., 2022; Bogo Martínez et al., 2022; Minhaj et al., 2022; Patel et al., 2022; Selb et al., 2022; Thornhill et al., 2022). Of interest, unlike in the classically described monkeypox infection in patients from endemic areas of West or Central Africa, a large proportion of patients in both our cohort and in the current outbreak present with lesions at various stages of progression and can develop new lesions even as the initial lesions crust. This is important for the infection prevention and control implications; vigilance needs to be exercised to monitor for new active lesions, which may appear even as others resolve (Yinka-Ogunleye et al., 2019).

Another important distinguishing feature of patients with hMPXV in the current outbreak is the minimal or absent viral prodrone compared with a more prominent prodrone classically noted in endemic countries (Yinka-Ogunleye et al., 2019). In our cohort, the rash was often the first and, in some cases, the only presenting symptom. This has also been noted in reports from other countries seeing cases of monkeypox infection in the current outbreak (Antinori et al., 2022; Minhaj et al., 2022; Rodríguez et al., 2022). This feature is important because case definitions for monkeypox traditionally make note of the febrile prodrone (CDC, 2022; UKHSA, 2022c). Such definitions of course remain important, given that cases from endemic countries, which may present more classically, may still be seen in the current outbreak; this has occurred at our trust and elsewhere. In our cohort, we note that systemic symptoms are more likely in those whose rash is due to hMPXV rather than those whose rashes are caused by other conditions, including infection with varicella zoster virus, herpes simplex virus, and bacterial folliculitis.

In our cohort, very few cases reported contact with a suspected or confirmed hMPXV case. This raises the possibilities of asymptomatic, paucisymptomatic, or pre-eruption transmission. Considering the discriminating factors at the time of presentation, none of the routinely taken blood tests showed a difference between the two cohorts. However, a large proportion of patients screened, particularly in the sexual clinic, did not have blood tests taken.

The virtual ward: a useful adjunct

The use of the virtual ward mode of follow-up is an innovation which was developed during the COVID-19 pandemic, with the aim of easing pressures on hospitals services; this model of care was used comparatively early in this monkeypox outbreak (Best, 2022; UKHSA, 2022d). This predominantly nurse-led service allowed patients to be referred for medical care if needed and for patients to be guided in their deisolation. Most patients resolved their symptoms within 21 days; however, a quarter of our patients remained symptomatic, with active lesions beyond this time period. Importantly, 21% of patients did not engage with this service; this was particularly so for patients who had been isolated in the hospital where they faced either psychological or financial pressures, leading them to self-discharge. As with COVID-19, financial compensation for lost earning opportunities may have supported patients to be more compliant with self-isolation public health measures.

Social vulnerabilities need to be addressed

Within our patient cohort, social vulnerabilities were noted and probably underestimated, given that the most vulnerable may have been unable or unwilling to get tested. Of particular relevance to the control of monkeypox spread, inadequate housing (including living in hostels or homelessness) led to the need to isolate patients in the hospital; this required careful discussions with affected patients (Healthy London Partnership, 2022). Other than economic implications for hospitals, it placed strains on much needed negative pressure side rooms, particularly the ID unit, where patients with other airborne diseases of public health importance (e.g., multidrug-resistant tuberculosis) would normally be admitted. Some of these pressures could have been relieved by learning again from the COVID-19 pandemic, where hotels were used to support self-isolation in clinically stable patients. However, hotel isolation generated concerns for patients and staff about confidentiality and potential stigma, so it was not widely adopted.

Limitations

We acknowledge the limitations of our study, which include the retrospective nature of the data, which were collected for routine clinical purposes. Data recording was not standardized, which could lead to omissions. There may be selection bias in our cohort because patients with atypical features, mild disease, or barriers to accessing health care may not have been presented and tested. Cases were selected sequentially to allow rapid data collection and assessment in an evolving outbreak to provide useful clinical data at a usable time point. However, this did not allow more complex selection and matching of patient selection. Notably, the early identified risk among the GBMSM population may have led to an over-representation of testing among this group. This may have led to the underestimation of the strength of the association between such risk factors and a positive test. The test is highly sensitive and specific but false negatives may occur, leading to missed cases. In addition, this cohort may not be representative of populations seen elsewhere either in demographics, risk factors, or severity of illness. Our trust is not a designated adult, high-consequence ID center; designated high-consequence ID centers may see patients with a more severe disease profile. However, findings from our cohort are in keeping with most of the published data from this outbreak.
Conclusion

Our analysis will inform risk-based approaches to the management of hMPXV in GBMSM populations and support the development of clinical care pathways to streamline the triage of patients who present with rashes and are suspected for hMPXV. This has both public health and service implications because, in addition, we found that routine blood tests did not improve clinical diagnostic accuracy. Notably, PLWHIV did not have a greater chance of having a positive hMPXV PCR and our PLWHIV (all with well-controlled disease) did not have more severe disease than patients without HIV. Learning from COVID-19 led to the relatively rapid introduction of virtual ward follow-up, something which could relieve pressures off secondary care. However, one-fifth of patients did not engage with it, suggesting other ways in which such patients are followed up are required.

Conflict of interest

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Ethical approval

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Authors contributions

AA, SR, JB, FD conceptualised the study, MG led the statistical analysis with input from TH. SR, JB, OD, MSW, RM contributed to data extraction. SR, JB, MSW, AA contributed to writing the first draft and subsequent edits. MG, DM, UE, BMP, OD, LG, JP, FD, GC contributed to editing and review. All authors contributed to discussion and review of results and key messages.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2022.11.020.

References

Antinori A, Mazzotta V, Vita S, et al. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. Euro Surveill 2022;27.
Best J. The virtual wards aiming to ease hospital pressures. BMJ 2022;378:o1603.
Bunge EM, Hoet B, Chen L, et al. The changing epidemiology of human monkeypox—A potential threat? A systematic review. PLoS Negl Trop Dis 2022;16.
Centers for Disease Control and Prevention (U.S.). Monkeypox in the U.S. Centers for Disease Control and Prevention; 2022. https://www.cdc.gov/poxvirus/monkeypox/clinicians/case-definition.html (accessed 20 August 2022).
Healthy London Partnership. Monkeypox safeguarding conversation guide for home- less and inclusion health populations. Healthy London Partnership; 2022. https://www.healthylondon.org/our-work/homeless-health/monkeypox-safeguarding-conversation-guide-for-homeless-and-inclusion-health-populations/ (accessed 20 August 2022).
Ilúgo Martínez JI, Gil Montalbán E, Jiménez Bueno S, et al. Monkeypox outbreak predominantly affecting men who have sex with men, Madrid, Spain, 26 April to 16 June 2022. Eurosurveillance 2022;27.
Mishaj FS, Ogale YP, Whitehill F, et al. Monkeypox outbreak — nine states, May 2022. Morb Mortal Wkly Rep 2022;71:764–9.
Patel A, Bilinska J, Tam JCH, et al. Clinical features and novel presentations of human monkeypox in a central London centre during the 2022 outbreak: descriptive case series. BMJ 2022;378.
Rodríguez BS, Guzmán HBR, Díaz FA, et al. Early release - epidemiologic features and control measures during monkeypox outbreak, Spain, June 2022. Emerg Infect Dis 2022;28:1847–51.
Selb R, Werber D, Falkenhorst G, et al. A shift from travel-associated cases to autochthonous transmission with Berlin as epicentre of the monkeypox outbreak in Germany, may to June 2022. Euro Surveill 2022;27.
Thornhill JP, et al. Monkeypox virus infection in humans across 16 countries — April–June 2022. N Engl J Med 2022;387:679–91.
UKHSA. De-isolation and discharge of monkeypox-infected patients: interim guidance. UK:GOV; 2022a. https://www.gov.uk/guidance/de-isolation-and-discharge-of-monkeypox-infected-patients-interim-guidance (accessed 11 August 2022).
UKHSA. Management of laboratory confirmed monkeypox infections; 2022b. PR1989. https://www.england.nhs.uk/wp-content/uploads/2022/06/B1794-management-of-laboratory-confirmed-monkeypox-infections-V4.pdf (accessed 20 August 2022).
UKHSA. Monkeypox: case definitions. UK:GOV; 2022c. https://www.gov.uk/guidance/monkeypox-case-definitions (accessed 20 August 2022).
Virtual management of confirmed monkeypox cases 2022d. p. B1692.
World Health Organization. Monkeypox. https://www.who.int/news-room/factsheets/detail/monkeypox (accessed 20 August 2022).
Yinka-Ogunleye A, et al. Outbreak of human monkeypox in Nigeria in 2017–18: A clinical and epidemiological report. Lancet Infect Dis 2019;19:872–9.