

Clinical Features, Antiviral Treatment, and Patient Outcomes: A Systematic Review and Comparative Analysis of the Previous and the 2022 Mpox Outbreaks

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Background. This study aims to comparatively analyze clinical features, treatment, and patient outcomes between the previous and the 2022 mpox (monkeypox) outbreaks.

Methods. Five bibliographic databases were searched for studies reporting clinical features, management, and patient outcomes of mpox. Systematic review and meta-analysis were performed.

Results. In total, 73 studies were included in the systematic review, of which 33 studies were subjected to meta-analysis. Previous outbreaks substantially affected children, whereas the 2022 outbreak primarily affected male adults, of which 94.66% (95% confidence interval [CI], 88.03–98.95) were men who have sex with men. Furthermore, 72.47% (95% CI, 51.04–89.71) reported high-risk sexual activity and the overall human immunodeficiency virus (HIV) prevalence was 37.65% (95% CI, 30.09–45.50). Skin lesions remain the typical symptom; however, their anatomic distribution differed. Systemic manifestations were common, but rectal pain was unique to the 2022 outbreak. The estimated overall fatality during past outbreaks in Africa was 4.61% (95% CI, 2.39%–7.35%), whereas 6.34% (95% CI, 3.35%–10.10%) of patients from the 2022 outbreak required hospitalization. Antiviral treatment, in particular tecovirimat, has been prescribed for a subset of patients, but the efficacy remains inconclusive.

Conclusions. These findings are important for better understanding the disease and guiding adequate response to mpox outbreaks.

Keywords. mpox; outcomes; sexual activity; symptoms; treatment.

As a member of the *Orthopoxvirus* genus, mpox (monkeypox) virus (MPXV) infection can cause smallpox-like illness, with classical symptoms such as skin lesions [1]. Since the first identification in human in 1970, mpox outbreaks have occurred periodically in Africa and it has become endemic in West and Central Africa [2]. In general, MPXV is confined to tropical regions within African countries. It was accidentally carried to the United States in imported small mammals, which infected nearby housed pet prairie dogs, and the virus was then transmitted to human hosts [3]. This eventually resulted in 47 infection cases in 2003 [4]. Since then, sporadic cases have been

occasionally reported in America, Europe, and Asia, but all these cases can be traced back to African origins [5]. Unexpectedly, the world is currently facing widespread mpox outbreaks across many nonendemic countries, starting in May 2022 [6]. This is the first time that sustained person-to-person transmission of MPXV without travel history to any endemic countries in Africa has been recognized. MPXV is thought to not easily spread between people, but spreads through close contact, for example, with skin lesions, body fluids, respiratory droplets, and contaminated materials [7, 8]. However, this assumption fails to explain why cases rose rapidly in the initial phase of the outbreak and now are declining, and more strikingly, the vast majority of cases identified so far have been men who have sex with men (MSM) [9].

To adequately respond and contain the 2022 outbreak, timely deployment of both nonpharmacological and pharmacological interventions is essential. Smallpox vaccination is postulated to provide cross-immunity against MPXV, and a third-generation vaccine, named Jynneos, has been approved for preventing smallpox and mpox [10]. But the efficacy of this vaccine in people remains inconclusive due to the lack of smallpox cases [11]. In recent decades, smallpox vaccinations have only been implemented in small-scale populations, such

Received 12 October 2022; editorial decision 31 January 2023; accepted 6 February 2023; published online 3 February 2023

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The Journal of Infectious Diseases® 2023;228:391–401

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as US military recruits and specific scientific researchers, and thus the majority of the global population are expected to be susceptible to MPXV infection. Antiviral drugs, including tecovirimat and brincidofovir, have been approved by the Food and Drug Administration (FDA) for treating smallpox and the related poxviruses, but efficacy against MPXV infection was only demonstrated in experimental models [12]. Despite empirical use in some infected cases, their clinical efficacies in treating mpox remain unknown.

Given the lack of knowledge on the disease, this study first aims first to systematically review the existing clinical data by retrieving studies published over the past 5 decades. Second, we comparatively analyzed the clinical features, treatment strategies, and patient outcomes between the previous and the 2022 outbreaks.

METHODS

We conducted a systematic search through 5 databases, that is Medline, Embase, Web of Science, Cochrane Central, and Google Scholar. Databases were searched with restrictions to only English language and studies from inception until 10 January 2023, using search terms relating to epidemiological and clinical features of monkeypox/mpox. Studies with original data were included in terms of the following criteria: studies containing mpox cases that were confirmed by laboratory diagnostics, and studies containing mpox cases with a clinical diagnostic definition. Studies with mpox cases but failed to report any information about clinical symptoms, treatments, or outcomes were excluded. The full search strategies and selection criteria are provided in the [Supplementary Material 1 and 2](#). Three reviewers (P. L., J. L., and I. A.) worked independently to determine whether a study met inclusion criteria. A fourth reviewer (Q. P.) functioned as an arbiter when there was discrepancy in determining whether to include or exclude a study. This study was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [13].

Evaluation of Study Quality and Data Extraction

Eligible studies were further divided into 2 sections: mpox outbreaks/cases before 2022, and mpox outbreak/cases (outside of Africa) since May 2022. Two reviewers (P. L. and J. L.) extracted the following information: first author, publication year, outbreak identification year, country, age, sex, clinical symptom, skin lesion distribution, clinical management, outcome, number of deaths, and total number of cases. A third reviewer (I. A.) checked and corrected the extracted information. Studies describing human immunodeficiency virus (HIV) infections, high-risk sexual activities (condomless sex/multiple sexual partners), clinical symptoms, skin lesions distributions, and clinical outcomes (hospitalization and death) were

processed for meta-analysis. The quality of these studies were assessed according to the Joanna Briggs Institute checklist [14]. Studies were classified as high quality (score 7–9 points), moderate quality (4–6 points), and low quality (1–3 points). We here only included studies with moderate to high quality for meta-analysis ([Supplementary Table 1](#)).

Statistical Analysis

We estimated the pooled prevalence rate by operating the “Meta” package in R version 3.5.3 statistical software. Briefly, Freeman-Tukey double arcsine transformation was used for analysis. Wilson score method was used to calculate the 95% confidence interval (95% CI), and Cochran Q statistics and I^2 statistics were used to judge heterogeneity. I^2 with 25%–50%, 50%–75%, and >75% values were considered as mild, moderate, and severe heterogeneity. Funnel plot and Egger test were used to assess the potential publication bias.

RESULTS

Systematic searching of literature databases identified a total of 2789 studies. Of these, 73 studies met the inclusion criteria for analyzing epidemiological and/or clinical features of mpox ([Figure 1](#)). By pooling documented cases from these 73 studies, we found distinct patterns of sex distribution between the previous and the 2022 outbreaks. A total of 1465 cases from 31 studies of the outbreaks during 1970–2021 included information on sex. The percentage of men was only slightly higher than that of women (55.7% vs 44.3%). In contrast, the vast majority of patients in the included studies from the 2022 outbreak were men (99.0%). Next, the age distribution was comparatively analyzed; 1117 cases during 1970–2021 were divided into 5 age groups, with the highest percentage of cases belonged to the 0–9 years age group (38.9%), followed by 10–19 (27.8%), 20–29 (17.2%), 30–39 (10.1%), and older than 40 years of age (6.0%) ([Supplementary Table 2](#)). In contrast, the majority of patients in the 2022 outbreak were 30–39 years of age (46.7%), followed by 40–49 (23.2%), 20–29 (21.7%), 50–59 (6.5%), older than 60 (1.1%), and younger than 20 years (0.8%). We then further analyzed the prevalence of MSM, high-risk sexual activity, as well as HIV infection status in patients of the 2022 outbreak. By pooling data related to sexual activity, 94.66% (95% CI, 88.03%–98.95%; $I^2 = 98\%$) of patients are estimated to have MSM activity ([Figure 2](#)), and 72.47% (95% CI, 51.04%–89.71%; $I^2 = 98\%$) have high-risk sexual activities (condomless sex or multiple sexual partners) ([Figure 3A](#)). Based on data from 3226 patients describing HIV infection status, 37.65% (95% CI, 30.09%–45.50%; $I^2 = 93\%$) were HIV positive ([Figure 3B](#)).

We next estimated the incidence rate of common symptoms of MPXV infection. During the outbreaks before 2022, apart from skin lesions, the most prevalent symptom was fever

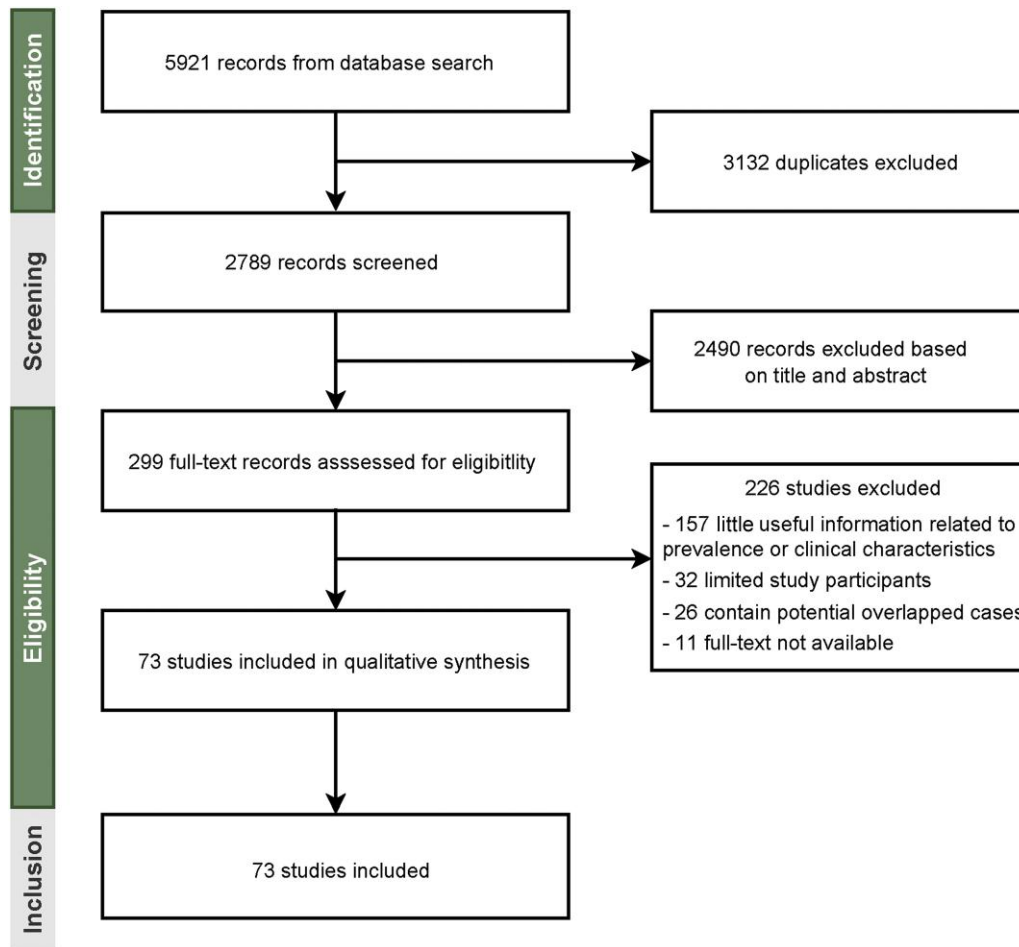


Figure 1. Study selection.

(81.34%; 95% CI, 60.36%–96.21%; $I^2 = 94\%$), followed by dysphagia (70.08%; 95% CI, 19.55%–100%; $I^2 = 99\%$), chills (67.91%; 95% CI, 47.05%–85.77%; $I^2 = 98\%$), fatigue (67.32%; 95% CI, 42.57%–88.07%; $I^2 = 89\%$), lymphadenopathy (64.43%; 95% CI, 52.90%–75.23%; $I^2 = 94\%$), headache (61.91%; 95% CI, 36.64%–84.38%; $I^2 = 98\%$), sore throat (54.11%; 95% CI, 26.74%–80.30%; $I^2 = 91\%$), cough (48.55%; 95% CI, 34.67%–62.54%; $I^2 = 74\%$), sweat (43.31%; 95% CI, 13.46%–75.77%; $I^2 = 90\%$), myalgia (43.01%; 95% CI, 17.47%–70.58%; $I^2 = 99\%$), conjunctivitis (20.17%; 95% CI, 7.12%–37.17%; $I^2 = 88\%$), vomiting (12.77%; 95% CI, 5.16%–22.66%; $I^2 = 93\%$), and diarrhea (5.45%; 95% CI, 1.25%–11.52%; $I^2 = 23\%$) (Figure 4A and Supplementary Figures 1–13). For the included patients from nonendemic countries in the 2022 outbreak, apart from skin lesions, the most frequent symptom was fever (59.35%; 95% CI, 53.74%–64.84%; $I^2 = 89\%$), followed by lymphadenopathy (56.26%; 95% CI, 50.44%–61.99%; $I^2 = 89\%$), fatigue (46.18%; 95% CI, 36.20%–56.31%; $I^2 = 92\%$), chills (42.35%; 95% CI, 9.75%–79.16%;

$I^2 = 99\%$), myalgia (38.31%; 95% CI, 31.05%–45.83%; $I^2 = 91\%$), headache (33.21%; 95% CI, 27.24%–39.45%; $I^2 = 92\%$), sore throat (23.31%; 95% CI, 20.01%–26.77%; $I^2 = 63\%$), rectal pain (16.82%; 95% CI, 11.23%–23.25%; $I^2 = 93\%$), and cough (10.17%; 95% CI, 1.68%–23.50%; $I^2 = 71\%$) (Figure 4B and Supplementary Figures 14–22).

Although skin lesions was the most common presentation, the anatomical distribution of lesions varied considerably among individuals. We thus estimated the body distributions of skin lesions in patients of past outbreaks before 2022 by extracting data from 5 studies. We estimated that 98.2% of infected patients showed facial lesions (95% CI, 95.87%–99.71%; $I^2 = 15\%$), followed by 93.8% with trunk lesions (95% CI, 83.68%–99.59%; $I^2 = 88\%$), 91.02% with limb lesions (95% CI, 74.47%–99.76%; $I^2 = 86\%$), 53.58% with genital lesions (95% CI, 27.23%–78.92%; $I^2 = 97\%$), and 37.47% with oral lesions (95% CI, 22.43%–53.79%; $I^2 = 96\%$) (Figure 5A and Supplementary Figures 23–27). In contrast, patients from the 2022 outbreak showed distinct patterns of skin lesion

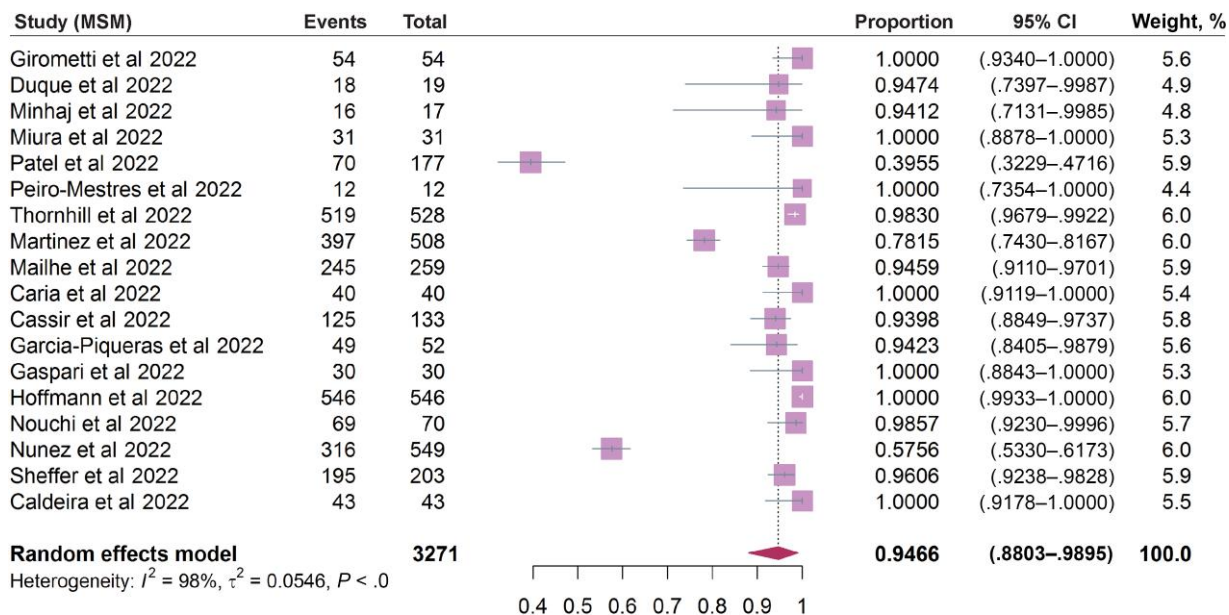


Figure 2. The incidence rate of MSM in 18 studies included in the analysis. Abbreviations: CI, confidence interval; MSM, men who have sex with men. Complete reference information for the following references Duque et al (2022), Minhaj et al (2022), Miura et al (2022), Patel et al (2022), Peiro-Mestres et al (2022), Martinez et al (2022), Mailhe et al (2022), Caria et al (2022), Cassir et al (2022), Garcia-Piqueras et al (2022), Gaspari et al (2022), Hoffmann et al (2022), Nouchi et al (2022), Nunez et al (2022), Sheffer et al (2022), Caldeira et al (2022) cited in Figure 2 are listed in the Supplementary Material.

distribution. Genital lesions were most common (50.83%; 95% CI, 40.12%–61.50%; $I^2 = 96\%$), followed by perianal lesions (35.44%; 95% CI, 28.04%–43.19%; $I^2 = 94\%$), limb lesions (30.82%; 95% CI, 14.24%–50.37%; $I^2 = 96\%$), facial lesions (27.67%; 95% CI, 22.78%–32.82%; $I^2 = 78\%$), trunk lesions (26.74%; 95% CI, 18.16%–36.24%; $I^2 = 93\%$), and oral lesions (9.86%; 95% CI, 2.13%–21.59%; $I^2 = 86\%$) (Figure 5B and Supplementary Figures 28–33).

The presentation and progression of mpox disease range from mild to severe, and even death. Thus, pharmacological interventions have been empirically explored in patient management. We identified 17 studies describing treatment of infected cases (Table 1 [4, 15–30]). Antibiotics were prescribed to 19 hospitalized patients aiming at preventing secondary infection of bacteria. Antiviral drugs (acyclovir, valacyclovir, tecovirimat, and brincidofovir) were administered to 63 patients. Combination use of tecovirimat with intravenous vaccinia immune globulin was given to a severe case. Because of the severe pain and accompanied sleeping trouble due to skin lesions, 3 cases received either acetaminophen, analgesic, or morphine to relieve these symptoms. Other symptomatic therapeutics, such as paracetamol, diphenhydramine, and steroids, were administered in several cases, for relieving fever and treating inflammation (Table 1).

Finally, we estimated the fatality rate based on 831 cases in 10 included studies, mainly from Central African Republic, Nigeria, and Republic of the Congo. The estimated overall

fatality rate was 4.61% (95% CI, 2.39%–7.35%; $I^2 = 53\%$) in these African patients (Figure 6A). No death was reported from the included studies of the 2022 outbreak. By including 2275 mpox patients from 9 studies, we estimated a hospitalization rate of 6.34% (95% CI, 3.35%–10.10%; $I^2 = 91\%$), and the major reason for hospitalization was for relieving pain of the lesions (Figure 6B).

DISCUSSION

Through systematic review and comparative analysis, this study identified several distinct epidemiological and clinical features of MPXV infection between the previous and the 2022 outbreaks. We found children younger than 9 years of age constitute the highest proportion of cases during 1970–2021, whereas the included cases from the 2022 outbreak were predominantly adults. It has been reported that young children but not adults are more prone to develop severe symptoms and account for the majority of lethal cases [31]. This disparity in age distribution may partially explain the favorable clinical outcomes of patients in the 2022 outbreak. The 2 distinct clades of MPXV are thought to be an important factor in disease severity. Infection caused by clade I MPXV can cause up to 10% fatality, whereas less than 1% of fatal cases have been reported for the clade II MPXV. Viral genome sequenced isolates from patient in the 2022 outbreak indicated that the circulating strains belong to the clade II virus [32].

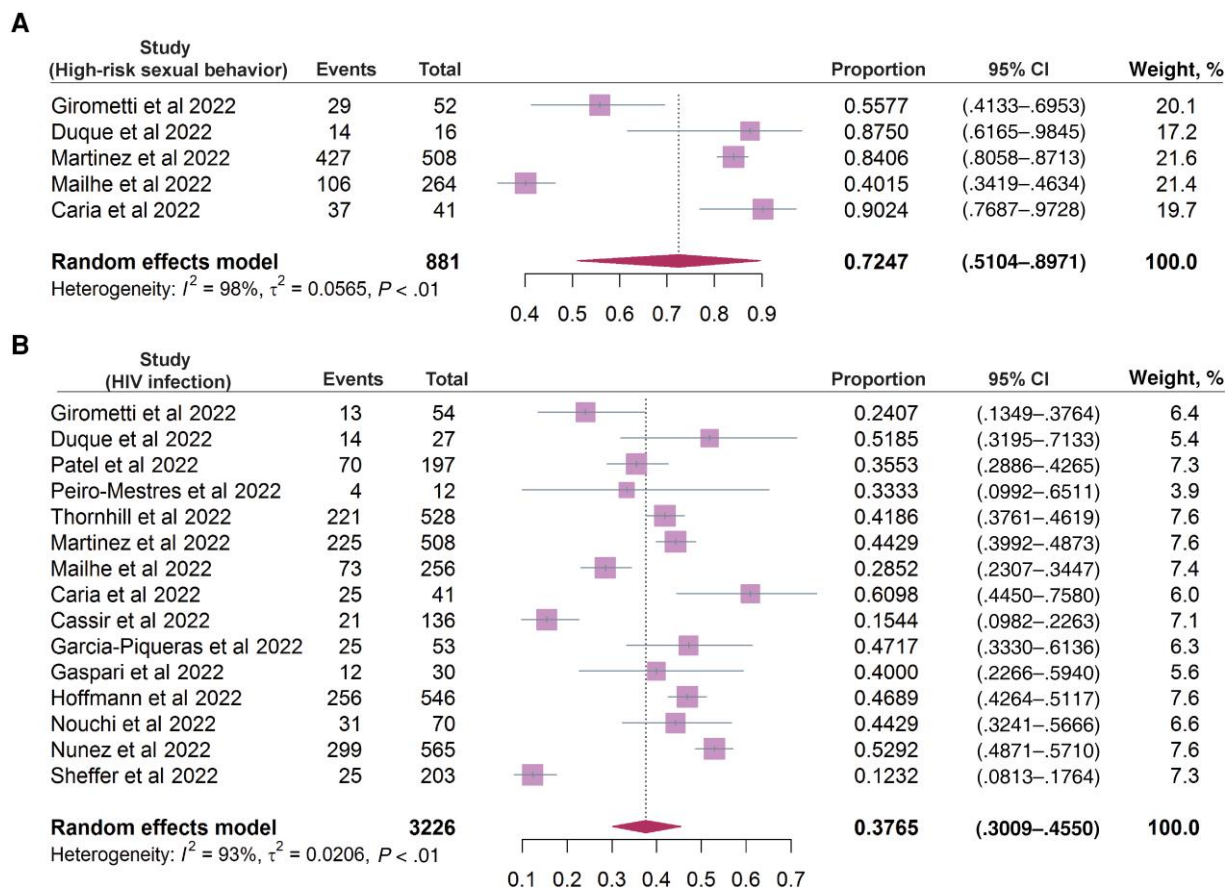


Figure 3. The incidence rate of (A) high-risk sexual activities (condomless/multipartner sexual activity; 5 studies included) and (B) human immunodeficiency virus (HIV) positivity rate (15 studies included) in patients of the 2022 mpox outbreak.

Complete reference information for the following references Duque et al (2022), Patel et al (2022), Peiro-Mestres et al (2022), Martinez et al (2022), Mailhe et al (2022), Caria et al (2022), Cassir et al (2022), Garcia-Piqueras et al (2022), Gaspari et al (2022), Hoffmann et al (2022), Nouchi et al (2022), Nunez et al (2022), and Sheffer et al (2022) cited in Figure 3 are listed in the Supplementary Material.

All MPXV strains from the 2022 outbreak sequenced so far tightly cluster together, suggesting a single origin [33]. In addition, the distinct availabilities of health care service for patients from the previous outbreaks (mainly low-income countries/regions) and from the 2022 outbreaks (mainly European and American countries) also likely contributed to the different clinical outcomes.

Nevertheless, we should not underestimate the clinical burden of the 2022 outbreak. As the virus is spreading, it has reached vulnerable populations such as young children, elderly people, and immunocompromised patients [34, 35]. Previous evidence has indicated that pregnant women are highly vulnerable to both mpox and smallpox, causing maternal mortality and morbidity [36]. Furthermore, mpox can be transmitted to an unborn fetus via the placenta, leading to congenital infection and abortion [37]. Guidelines for clinical management of pregnant women with suspected MPXV exposure have recently been proposed [36]. Although deaths have not been reported in the 2022 outbreak in our included studies, 106 confirmed

deaths have been recorded in public database, of which 92 cases were from nonendemic regions, whereas 14 were in locations that have historically reported mpox [38]. Thus, health care providers and public health professionals should be aware that severe morbidity and mortality associated with mpox have been observed in several countries, including Spain, the United States, Peru, and Brazil during the 2022 outbreak, particularly among highly immunocompromised patients [39]. Although for some cases it remains unclear whether mpox was a causal or contributing factor, several infected patients have died of complications associated with encephalitis [34, 40], which requires specific attention.

A striking feature of the 2022 outbreak is that a large number of cases identified in nonendemic countries were MSM [30]. We estimated that approximately 94% of patients have MSM activity, and 72% of patients have high-risk sexual behaviors, including condomless sex and multiple sexual partners, in the 2022 outbreak. Recently, sexual transmission has been proposed as a novel route of MPXV infection. Changing sexual

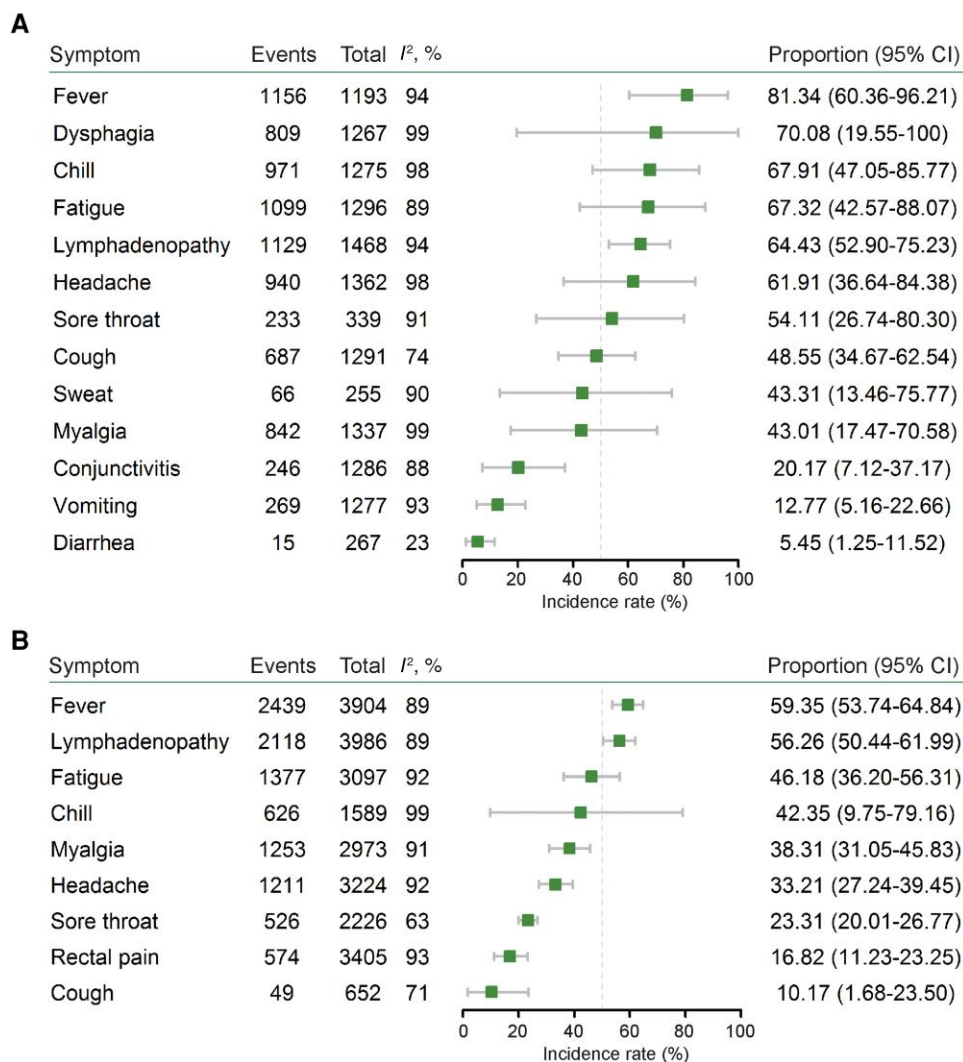


Figure 4. Comparison of clinical symptoms of patients between (A) the previous (9 studies included) and (B) the 2022 (16 studies included) mpxv outbreaks.

behaviors in MSM has been shown to reduce mpxv cases, which in turn supports sex-related transmission of this disease [41]. Cases during 1970–2021 mainly presented with lesions on the face, but the majority of cases in the 2022 outbreak have not shown this commonly reported symptom. Instead, the lesions presented in patients from the 2022 outbreak are more common in genital and perianal areas. Given the major lesions are present in genital-perianal areas, direct physical contact with lesions during sexual contact is likely the route of MPXV transmission. Notably, a substantial proportion of MPXV-infected cases in the 2022 outbreak are people with HIV and receiving antiretroviral therapy. Whether compromised immune systems have played any role in viral evolution and transmission is interesting to investigate [30]. With the wide spread of the outbreak, the affected populations will inevitably diversify.

MPXV infection has characteristic lesions and is spread through close contact, as the virus primarily infects skin and injures skin mucosa [42]. Interestingly, we estimated approximately 48% and 10% incidence rate of cough in infected patients from previous and the 2022 mpxv outbreaks, respectively. This may indicate that MPXV also infects the human airway respiratory tract, but whether this is sufficient to support the hypothesis of possible transmission through direct contact with respiratory secretions remains to be investigated [43]. We also identified a proportion of gastrointestinal symptoms including vomiting and diarrhea, and thus it is interesting to investigate whether the intestine is susceptible to MPXV infection. If this is the case, vomiting and diarrhea could discharge virus particles to the environment, providing new routes of transmission such as fecal-oral transmission. In line with recent reports that some patients were hospitalized because of

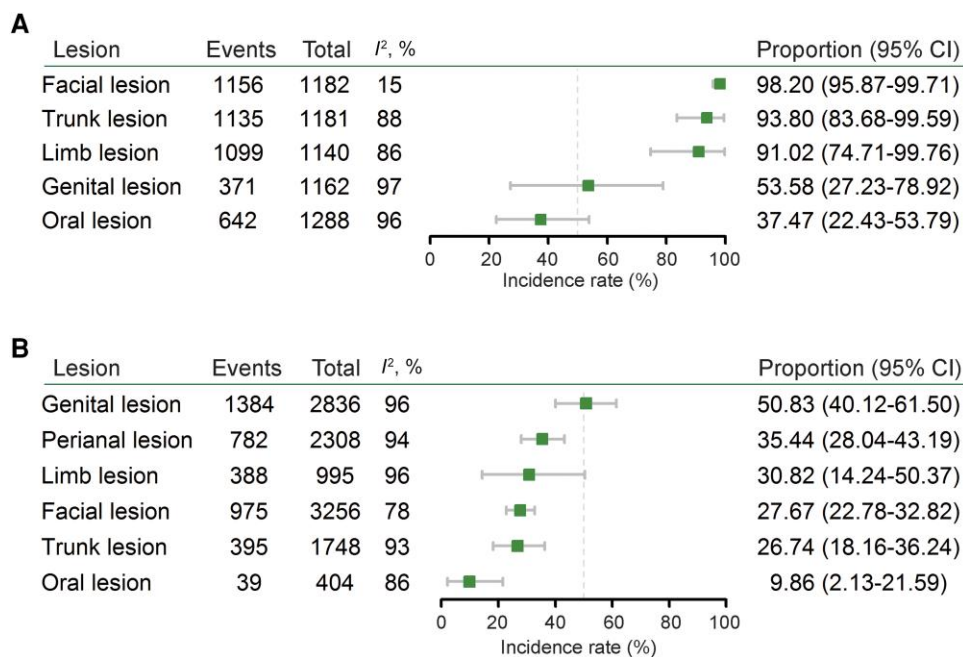


Figure 5. Distribution of skin lesions in patients of the previous and the 2022 outbreaks. *A*, The distribution of skin lesions in patients from the previous outbreaks (5 studies included). *B*, The distribution of skin lesions in patients from the 2022 outbreaks (14 studies included).

severe rectal pain, we estimated that approximately 17% of patients had rectal pain and proctitis in the 2022 outbreak. This suggests that MPXV may directly infect the rectum and cause severe inflammation, requiring further investigations and the development of specific treatment strategies.

An important lesson learned from the coronavirus disease 2019 (COVID-19) pandemic is that specific populations, such as health care workers and household members of infected cases, are at high risk of infection [44]. Ring vaccination is recommended to protect these at-risk/vulnerable populations. A third-generation smallpox vaccine has been authorized for use against mpox. Recent evidence indicates reduced risk for mpox in people after receiving 1 or 2 doses of this vaccine [45]. Two types of antiviral drugs, tecovirimat and brincidofovir (an oral lipid conjugate derivative of cidofovir), have been approved by the FDA for treating smallpox virus infection [46]. Tecovirimat inhibits the production of infectious orthopoxvirus by disrupting a major envelope wrapping protein, VP37 [47]. Brincidofovir and cidofovir are viral DNA polymerase inhibitors to suppress viral replication [48]. These antivirals have shown promise for treating MPXV infection based on experimental data (Supplementary Table 3). In cell culture models infected with MPXV isolates obtained from several patients of the 2022 outbreak, the 50% inhibitory concentrations of tecovirimat, cidofovir, and brincidofovir were within the range of therapeutic concentrations observed in patient plasma, suggesting that the currently circulating MPXV strains are likely

sensitive to these antiviral drugs [49]. However, so far, only a small proportion of patients with MPXV infection have been treated with these antiviral drugs. Thus, the clinical efficacy remains far from conclusive (Table 1), and well-designed clinical trials are urgently required to confirm the efficacy for treating MPXV infection. Given the complementary mechanism of actions, we postulate that a combination of these 2 types of antiviral drugs may result in synergistic effects, and deserves to be further investigated.

Of note, there are several limitations to this study. Firstly, the overall number of qualified studies was small. In particular, studies related to treatment were very limited and mainly descriptive of segmented cases. This will likely cause bias and prevent us from drawing firm conclusions. Secondly, there was a relatively large heterogeneity in studies reporting different symptoms, which may be attributed to the huge diversity in sample size among different studies. Some analyses with heterogeneity exceeding 95% may pose interpretive challenges to the results [50]. Because of the limited number of eligible studies, we included all studies having over 10 cases for meta-analysis. We assessed publication bias by funnel plot and Egger's test, which indicated the presence of potential bias in the included studies (Supplementary Figure 34). Finally, we only included studies in English language, and thus may have missed some (small) studies published in local journals in other languages. However, we think this will not affect the overall analysis and the main conclusions of our study.

Table 1. Treatment and Patient Outcomes During the Previous and the 2022 Mpox Outbreaks

Study	Admission Year, Country	No. of Patients	Therapy	Outcome	Remark
Cases 1982–2021					
Jansheghers et al 1984 [15]	1982, Congo	1	Penicillin and bronchial dilatation; then penicillin was withdrawn, chloramphenicol and corticosteroids were given	Died	Developed into pneumonia despite penicillin therapy
Eltvedt et al 2020 [16]	2016, Congo	1	Started on IV amoxicillin-clavulanic acid, retinol tablets, paracetamol, diluted plumpynut, and IV maintenance fluids; changed to IV ceftriaxone and morphine	Died	Severe skin and oral manifestations
Berthet et al 2011 [17]	2010, CAR	1	Cloxacillin for treating a possible staphylococcal skin infection	Discharged	...
McCollum et al 2015 [18]	2012, Congo	1	Treated with erythromycin, acetaminophen, promethazine, and vitamin C for 7 d; then transferred to another hospital and treated with gentamicin, cloxacillin, narcotic analgesics, and a warm bath of permanganate	...	The first 7 d treatment did not relieve any symptoms
Froeschl et al 2015 [19]	2012, CAR	1	Cloxacillin, ibuprofen, and paracetamol
Anderson et al 2003 [20]	2003, United States	1	Intravenous diphenhydramine, lorazepam, and morphine	Discharged	...
Reed et al 2004 [4]	2003, United States	11	9 received antibiotics (ciprofloxacin or doxycycline); 1 received acyclovir; 2 received valacyclovir
Adler et al 2022 [21]	2018–2021, United Kingdom	7	3 patients were treated with brincidofovir (orally received 200 mg once/wk); 1 patient was orally treated with tecovirimat (600 mg twice daily for 2 wk)	Discharged	Patients treated with brincidofovir showed elevated liver enzymes resulting in cessation of therapy; patient with tecovirimat treatment had a shorter duration of viral shedding and illness than other 6 patients, no obvious adverse effects
Cases since 2022					
Hammerschlag et al 2022 [22]	2022, Australia	1	Treated with intramuscular ceftriaxone and oral doxycycline	Discharged	...
Noe et al 2022 [23]	2022, Germany	2	Topical zinc oxide suspension
Lucar et al 2022 [24]	2022, United States	2	Both patients received oral tecovirimat with 600 mg twice daily	Relieved pain within 48 h, and no new skin lesions formed	1 patient reported mild, transient fatigue after tecovirimat treatment
Desai et al 2022 [25]	2022, United States	25	All patients received oral treatment with tecovirimat (1 treated for 21 d, the remainder treated 14 d)	Complete resolution of lesions in 10 patients on day 7 of therapy; 23 had resolution of lesions and pain by day 21	Reported adverse events on day 7 of therapy: fatigue in 7 patients, headache in 5, nausea in 4, itching in 2 and diarrhea in 2 patients
Matias et al 2022 [26]	2022, United States	3	All 3 patients received oral tecovirimat at a dose of 600 mg twice daily	1 patient presented no new skin lesions formed by 4 d treatment, and all 3 patients reported near-complete resolution of rash/skin lesions	Patient 1 had mild nonfocal headache after first dose; patient 2 reported 1–2 loose bowel movements a few hours after each dose
Thornhill et al 2022 [27]	2022, Multiple countries	528	5% of the 528 patients received mpox-specific treatment, include intravenous/topical cidofovir (12 patients), tecovirimat (8 patients), vaccinia immune globulin (1 patient), and other treatment (2 patients)	...	The effect of treatment was not commented
Rai et al 2022 [28]	2022, United States	1	This patient was given tecovirimat 600 mg twice daily, artificial tears were given every 4 h, and erythromycin ointment 4 times daily	Conjunctival and caruncular lesions and eye irritation resolved after 4 d treatment; no new lesions developed; discharged on day 6 of treatment without adverse effects	...

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Table 1. Continued

Study	Admission Year, Country	No. of Patients	Therapy	Outcome	Remark
Thet et al 2022 [29]	2022, United States	1	First 2 wk 600 mg 2 times/d of oral tecovirimat; at week 3 600 mg 2 times/d of IV tecovirimat; then single dose of 414 000 U (6000 U/kg) of VIGIV and 2 wk of IV tecovirimat	1 wk after VIGIV administration, the patient significantly improved, and no new lesions developed	This patient had medical history of polysubstance abuse and AIDS
Girometti et al 2022 [30]	2022, United Kingdom	5	Antibiotic treatment (2 received IV ceftriaxone and oral doxycycline; 1 IV ceftriaxone and oral metronidazole, 1 oral doxycycline and antiviral tecovirimat) and analgesia	4 discharged, 1 remained admitted at the time of reporting	...

Abbreviations: AIDS, acquired immunodeficiency syndrome; CAR, Central African Republic; IV, intravenous; VIGIV, vaccinia immune globulin intravenous.

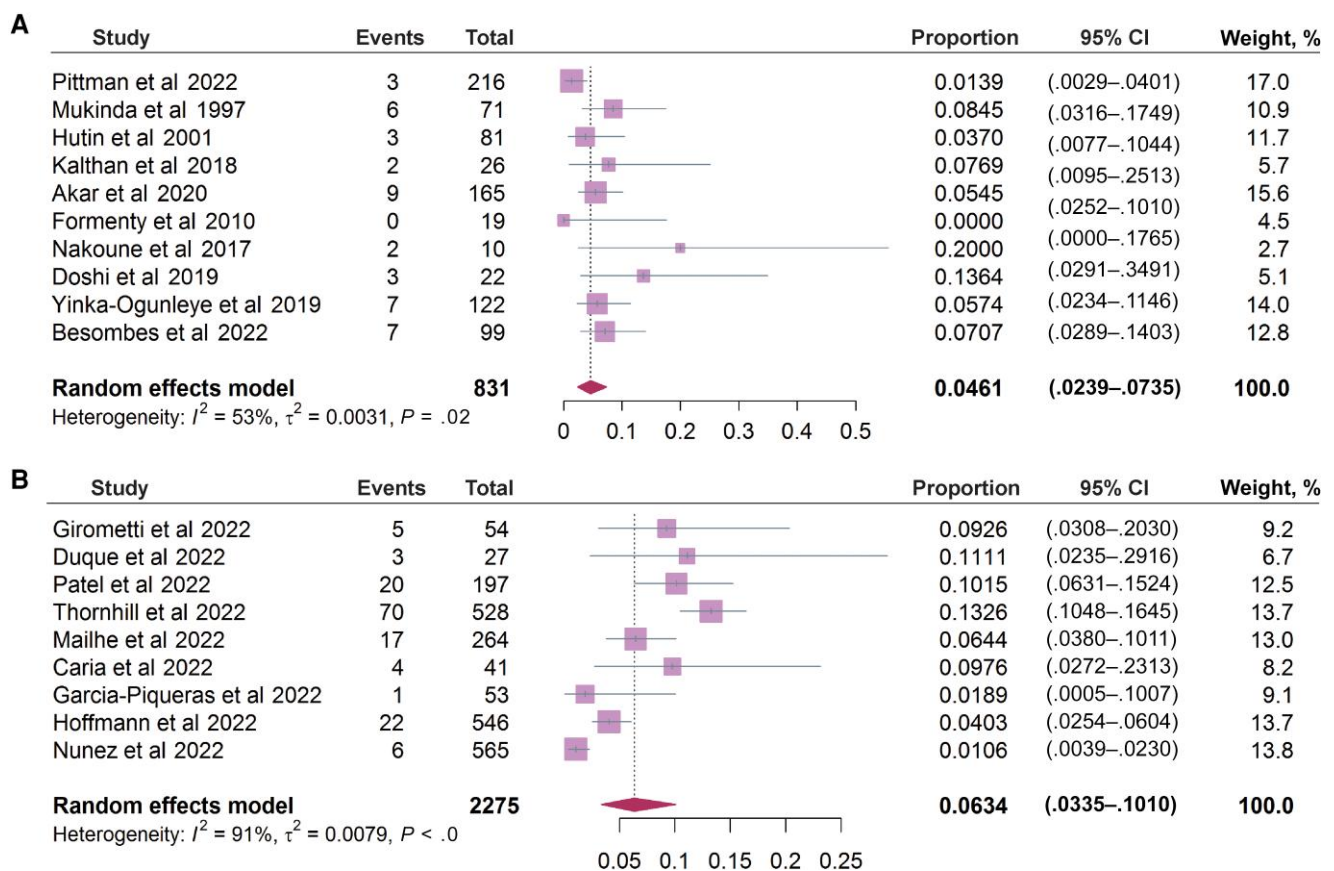


Figure 6. Clinical outcomes in patients during the previous and the 2022 outbreaks. *A*, The fatality rate of patients from major endemic African countries in previous mpxv outbreaks (10 studies included). *B*, The rate of hospitalization in the current outbreak (9 studies included).

Complete reference information for the following references Pittman et al (2022), Mukinda et al (1997), Hutin et al (2001), Kalthan et al (2018), Akar et al (2020), Formenty et al (2010), Nakoune et al (2017), Doshi et al (2019), Yinka-Ogunleye et al (2019), Besombes et al (2022), Duque et al (2022), Patel et al (2022), Mailhe et al (2022), Caria et al (2022), Garcia-Piqueras et al (2022), Hoffmann et al (2022), Nunez et al (2022) cited in Figure 6 are listed in the Supplementary Material.

CONCLUSIONS

In summary, this study revealed distinct epidemiological and clinical features as well as patient outcomes of the mpxv outbreaks during 1970–2021 and 2022. The current use of antiviral treatment is mainly based on experimental evidence and thus well-designed clinical trials are urgently needed to confirm their

efficacy. These findings are important for better understanding the disease and guiding an adequate response to mpxv outbreaks.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online. Consisting of data provided by the

authors to benefit the reader, the posted materials are not copy-edited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Acknowledgments. The authors thank Dr Wichor Bramer and Dr Maarten Engel (biomedical information specialists, Erasmus MC Rotterdam) for assisting with the database search for this study.

Disclaimer. The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Financial support. This work was supported by the Netherlands Organization for Scientific Research (grant number 91719300 Vidi grant to Q. P.); and the Dutch Cancer Society (grant number 10140 young investigator grant to Q. P.). Funding to pay the Open Access publication charges for this article was provided by Netherlands Organization for Scientific Research.

Potential conflicts of interest. All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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