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Systematic Review

Mpox Clinical and Epidemiological Patterns in the Central African Republic: A Systematic Review and Meta-analysis

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Highlight

- **High disease burden in car:** Based on the study findings, the Central African Republic presents a high pooled severity rate of 60.9% and a case fatality rate (CFR) of 10.7% among confirmed cases which is significantly higher than that observed at the global level.
- **Significant regional disparities:** The Health Region 6 had the highest severity rate (77.3%), while the eastern regions presented a higher mortality burden (CFR: 10.8%) than western regions (0.0%).
- **Vaccination gap:** The response to the outbreak and the prevention strategy were weakened by the low Mpox vaccination uptake of 20.0%.
- **Clinical presentation:** Symptoms like fever (91.1%), rash (85.5%), and lymphadenopathy (57.0%) were the most commonly reported, and this clinical feature was consistent with the more virulent Clade I virus known to circulate in the region.
- **Contextualizes risk with conflict and zoonotic exposure:** the Central African Republic socio-political context with disrupted healthcare services due to armed conflict might have favor the high mortality observed. In addition, the exposure due to hunting habits and forest-based livelihood increase the risk of high transmission of the disease.

Abstract

This study included 40 years evidences (1984-2024) describing the Mpox epidemiology, vaccination and clinical pattern in the Central African Republic (CAR), informing targeted control strategies for this re-emerging threat. This systematic review and meta-analysis followed the PRISMA guidelines. The searches was conducted on PubMed, Scopus, ScienceDirect, Web of science, Embase, Cochrane Library, and AJOL. The random effect model was used to pooled estimates with R version 4.5.2. A *p*-value <0.05 was considered statistically significant. We included a total of seven studies conducted from 1984 to 2023. Our analysis revealed a pooled severity rate of 60.92% (95% confidence interval (CI): 47.54-72.83), peaking at 77.27% (95%CI: 55.64-90.21) in Health Region 6. Before the global Mpox outbreak in 2022, the case fatality rate (CFR) for confirmed cases was 10.71% (95% CI: 4.52-23.28). Eastern Health Regions had a higher CFR of 10.81% (95% CI: 4.03-25.93), while Western Regions reported 0.00% (95% CI: 0.00-100.00). For suspected cases, the CFR was 12.13% (95% CI: 5.59-24.34), slightly declining to 9.09% (95% CI: 0.23-41.28) post-2022. This geographic disparity remained, with Eastern Regions at 10.17% (95% CI: 4.64-20.84) and Western Regions at 5.26% (95%

CI: 0.74-29.39). Vaccination uptake in CAR was 20.00% (95% CI: 10.33-35.17). The clinical profile included fever (91.1% (95%CI: 42.9-99.3)), rash (85.5% (95%CI: 75.7-91.8)), and lymphadenopathy (57.0% (95%CI: 34.3-77.1)). The CAR is one of the most affected countries in Africa by Mpox. This was characterized by high severity, elevated mortality, and suboptimal vaccine coverage, particularly in eastern regions. In order to prevent future outbreak in the country, these findings point the necessity to improve vaccination distribution, give priority to high (risk populations, and improve the surveillance systems with genomic sequencing capacity. In context-specific interventions, including community education on prevention measures and healthcare worker training will help reducing the mpox-related morbidity and mortality.

Keywords: Mpox; severity rate; case fatality rate; vaccination; clinical manifestation; public health emergency

1. Introduction

The monkeypox disease (Mpox) is an infectious viral disease caused by the monkeypox virus (MPXV) [1]. In 2022, the World Health Organization (WHO) declared Mpox a Public Health Emergency of International Concern for the second time, highlighting that the disease continue to represent a threat to global health security [2]. As of May 2025, 142,151 confirmed Mpox cases with 328 deaths reported in 133 countries globally, resulting in a CFR of 0.09% [3].

By June 2025, the MPXV clade Ib was responsible of community transmission of Mpox in several African countries [4]. A human-to-human transmission of the was observed in countries like Burundi, the Democratic Republic of the Congo, Ethiopia, Kenya, Malawi, Rwanda, South Sudan, Tanzania, Uganda, and Zambia, The Democratic Republic of the Congo (DRC) which the country reporting the highest number of confirmed Mpox cases in Africa in 2025 [5]. Since its initial discovery in the DRC, MPXV has spread to neighboring non-endemic African nations [6]. Such countries include the Central African Republic (CAR) and the Republic of the Congo, where studies have shown that there were ongoing community transmission [7,8].

In order to prevent avoidable deaths both in hospital and in the community, the CAR health authorities' response to this public health threat should be based on strong surveillance and healthcare systems ready to identify, diagnose, and promptly manage all notified cases [9]. This is a major issue, as the under-resourced health systems like CAR could be rapidly overwhelmed by the burden, the complexity and the severity of the Mpox outbreak. In addition, marginalized and hard-to-reach populations, such as refugees, internally displaced persons, nomadic population and migrants, may experience limited access to healthcare and become more vulnerable to the disease [10]. The Central African Republic's (CAR) situation regarding this outbreak is particularly sensitive due to its socioeconomic and political condition. The nation is one of the least developed in the world, and its socio-economic status was significantly impacted by decades of political instability, armed conflict, and mass displacement [11]. This has resulted in a high rate of poverty, food insecurity, with a significant proportion of the population living in difficult conditions, often with limited access to basic necessities like clean water and sanitation facilities [12]. Because communities often rely on traditional healers and informal healthcare providers that can delay diagnosis and appropriate management of infectious diseases like Mpox, can worsen the disease transmission and hinder effective public health responses [13,14]. In this case, prevention remains one of the key strategies to control the spread of the disease within hotspots and across the country.

By implementing immunization activities among populations most at risk of contracting Mpox, health authorities could effectively respond to the outbreak [15,16]. This most at risk population includes individuals living in close proximity to wildlife reservoirs, particularly in forested, rural, and remote areas that experience a severe shortage of qualified health personnel, medical supplies, and diagnostic capabilities [8].

Most earlier evidences on Mpox in CAR were conducted with small sample sizes, thereby limiting the generalizability of their findings across the country [8,17–19]. Understanding the evolution of this disease and its regional distribution in this setting is essential for designing and implementing effective Mpox prevention and control strategies tailored to the realities of the CAR. Therefore, this study aimed to provide insight into the epidemiological and clinical profile of the multiple Mpox outbreaks reported in CAR.

2. Methods

2.1. Study design

The study was reported based on the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines [20]. The protocol for this study was not prospectively registered online.

2.2. Operational definition

In primary studies included, a suspected monkeypox case was defined as an individual presenting with a vesicular or pustular rash characterized by deep-seated, firm pustules, and at least one of the following symptoms: fever preceding the eruption, lymphadenopathy (inguinal, axillary, or cervical), or pustules or crusts on the palms of the hands or soles of the feet. A case was defined as laboratory-confirmed Mpox if at least one specimen yielded a positive result in the *Orthopoxvirus*-specific assay, Mpox-specific real-time polymerase chained reaction, or Mpox in culture [21,22]. Cases were classified as severe or grave (requiring hospitalization) if one or more of the following were present: extensive lesions (>100), hemorrhagic or pustular lesions, mucosal involvement (oral, genital, conjunctival), or systemic complications. Systemic complications included high fever (>39°C), altered general state (bedridden), sepsis, encephalitis, secondary bacterial infections, hypotension, septic shock, severe dehydration, and keratitis potentially leading to corneal scarring and blindness [5,21,23]. Vaccination uptake refers to individuals who declared having received an Mpox vaccine or presented an Mpox vaccination card [15,24].

2.3. Article searching strategy

We conducted literature searches on PubMed, Scopus, ScienceDirect, Web of Science, Embase, Cochrane Library, and AJOL to identify published research. Screening process involved the title and abstract of each study. A synthesis of keywords and Medical Subject Headings (MeSH) was used, in combination with Boolean logic operators to narrow the search for each database used (Supplementary File 1, Supplementary Table 1). To ensure completeness, a supplementary manual searching was conducted to identify additional relevant publications not found in electronic databases such as Google scholar (first 1000 entries assessed and no filter applied). Additionally, the reference lists of included studies were reviewed to identify further relevant articles. Last literature search was concluded on February, 2025.

2.4. Eligibility criteria

Inclusion criteria: This systematic review and meta-analysis included all published reports, including preprints were also eligible regardless of study type or design, which documented Mpox in CAR. Only articles published in English or French were included, and no temporal restrictions were applied to the publication date.

Exclusion criteria: Studies whose research focus diverged from our objectives or overlap with other existing results were excluded. In addition, letters to editor, commentary or reports not specifying the sample size were not included.

2.5. Data extraction

A structured Microsoft Office Excel 2016 form was used to collect data from all included articles. The data extraction checklist included the first author's name, study year, region, study design, setting, number of suspected, confirmed, severe, and death cases, the number of individuals who received the Mpox vaccine, sample size, and the number of events of each clinical manifestation. Two authors independently assessed each article for quality and relevance. Discrepancies between reviewers were resolved through discussion with a third reviewer to achieve consensus.

2.6. Data quality assessment

The quality of included studies was assessed using the Joanna Briggs Institute quality assessment tool for cross-sectional studies generated following outbreak surveillance and investigations activities [25]. For cross-sectional studies, assessment criteria encompassed studies clear definition of inclusion criteria, comprehensive descriptions of study subjects and settings, validity and reliability of exposure measurements, use of objective, standardized criteria for outcome assessment, identification potential confounding factors, implementation of appropriate strategies to address them, and the appropriateness of statistical methods. A binary score of 0 (no or unclear) or 1 (yes) was given after evaluation of each criterion. The overall risk of bias was categorized as low (>50%), moderate (>25-50%), or high (≤25%).

2.7. Outcome measurement

The primary outcomes of this systematic review and meta-analysis were Mpox severity and CFR. The secondary outcomes included the vaccination uptake and the clinical manifestations among suspected and confirmed cases. Mpox severity rate was determined by calculating the proportion of participants exhibiting severe or grave clinical manifestations of Mpox out of the total number of confirmed cases. CFR was calculated by dividing the number of deaths observed within the population of suspected or confirmed cases. The Mpox vaccination uptake rate/coverage was obtained by dividing the total number of people who received the vaccine by the number of eligible participants. The frequency of each clinical manifestation was computed by dividing the number of events of each reported symptom or observed sign by the number of suspected or confirmed cases.

2.8. Statistical analysis and synthesis

The I^2 statistic was used to assess heterogeneity of pooled estimates between studies. It was categorized as low (<25%), moderate (25−75%), or high (>75%). Subgroup analyses were conducted for temporal trends (study period), geographical disparities (study location), and disease burden. The disease burden cutoff was set based on the median of suspected or confirmed cases reported across included studies. Because of the evolving case definitions/diagnostics, conflict disruptions, clinical and epidemiologic diversity, the random effect was preferred over the fixed-effect model for primary outcomes. Timeframes for this analysis were defined based on the global outbreak that led to a heightened global response [26]. Generalized Linear Mixed Models (GLMM), coupled with the Probit-Logit Transformation (PLOGIT: a method for stabilizing variance when pooling binomial proportions) were employed [27]. This approach is ideal for meta-analyses of binary or proportion data because it directly models binomial outcomes and inherently handles studies with 0% or 100% events without needing continuity corrections. A *p*-value of <0.05 was considered significant. All analyses were performed using the 'meta' package in R Software version 4.5.2 [28].

2.9. Publication bias and sensitivity test

A visual analysis using funnel plot was carried out to assess publication bias. Absence of publication bias was assumed based on observed symmetry of the inverted funnel shape. To further investigate potential bias, Egger's regression and Begg's rank correlation tests were performed. Sensitivity analysis was conducted by iteratively excluding one study at a time to assess the robustness of the pooled estimate.

3. Results

From an initial search yielding 604 records (595 online databases, 9 from other sources), we removed 26 duplicates and screened the remaining 578 by title/abstract and full text. Seven studies met our inclusion criteria and were analyzed [8,17–19,29–32] (Fig. 1).

3.1. Studies selection

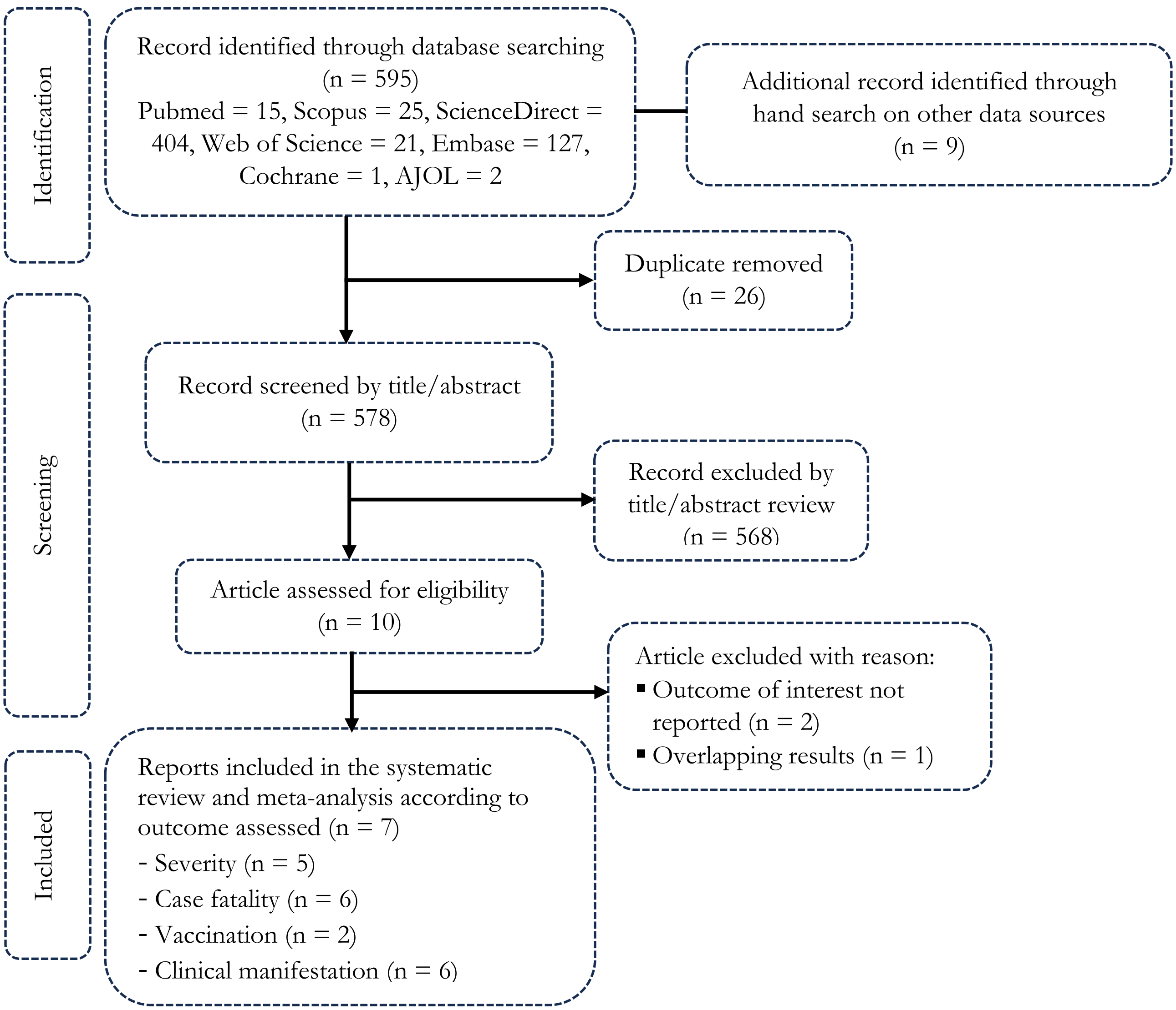

Fig. 1 PRISMA diagram flow from study identification to inclusion in the meta-analysis

3.2. Characteristic of reports included

A comprehensive analysis included 7 studies. Those reports findings dated back from 1984 to 2023 and involved population from community and hospital settings. The studies were conducted nationally or in various regions from CAR including the Region 2, 4 and 6. All studies used surveillance and investigation methodology for data collection and a non-probabilistic sampling technique (Table 1).

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Table 1 Characteristic of included studies

Author	Study Year[1]	Region	Setting	Study population	Sampling	Risk of bias	Outcome of interest	Summary of findings
Durski *et al.* [32]	2017	Multicentric	Community	General population	Non-probabilistic	Moderate	Case fatality rate	Since 2016, cases have been confirmed in Central African Republic (19 cases), Democratic Republic of the Congo (>1,000 reported per year), Liberia (two), Nigeria (>80), Republic of the Congo (88), and Sierra Leone (one). The reemergence of monkeypox is a global health security concern.
Berthet *et al.* [18]	2010	NR	Community	General population	Non-probabilistic	Low	Severity and case fatality rates	In June 2010, two teenage boys in the Central African Republic developed pustular skin lesions after eating a wild rodent, later confirmed as monkeypox virus (identical to the DRC strain from a 2001 outbreak). Both recovered after isolation and treatment, highlighting monkeypox's zoonotic risk in forested regions.
Kalthan *et al.* [29]	2016	Region 4	Community	General population	Non-probabilistic	Low	Severity, case fatality, and vaccine uptake rates	A study identified 26 monkeypox cases, with the highest attack rates in children (<10 years) and young adults (21–30 years). The overall attack rate was 5 per 1,000 inhabitants, severe disease occurred predominantly (87.5% of cases) in unvaccinated younger individuals.
Kalthan *et al.* [19]	2015	Region 6	Community	General population	Non-probabilistic	Low	Severity and case fatality rates	A 2015–2016 monkeypox outbreak in Bangassou, Central African Republic, affected 12 patients (mostly adults aged 31–40 and children under 10), with a 25% fatality rate (67% in children). The disease, marked by fever, rash, and lymphadenopathy (54.5%), had an attack rate of 0.2/1,000 inhabitants, highlighting the need for isolation, community education, and animal reservoir surveillance to curb transmission.
Nakoune *et al.* [17]	2016	Region 6	Community	General population and healthcare workers	Non-probabilistic	Moderate	Severity and case fatality rates	A 2015/2016 familial monkeypox outbreak in Central African Republic infected 10 individuals through household, healthcare, and transport-related transmission. The Zaire genotype strain caused characteristic fever and skin lesions, with two fatal pediatric cases highlighting the disease's severity in children.
Besombes *et al.* [31]	2018	Region 1	Community	General population and healthcare workers	Non-probabilistic	Moderate	Severity, case fatality, and vaccine uptake rates	In September 2018, a monkeypox outbreak involving an Aka Pygmy family in Central African Republic began when a 25-year-old woman developed symptoms after butchering wild animals, leading to three waves of intrafamilial transmission that ultimately infected five family members. While PCR confirmed six cases

								(including three children), serologic evidence suggested prior Orthopoxvirus exposure may have limited secondary spread, highlighting the role of zoonotic exposure and the waning protection from historic smallpox vaccination campaigns.
Besombes *et al.* [8]	2022	Region 2	Community	General population	Non-probabilistic	Low	Severity and case fatality rates	A November 2021 monkeypox outbreak in Central African Republic originated from a hunter's contact with a primate, sparking four transmission waves across two families with a 59.5% secondary attack rate (14 confirmed cases). The clade I virus caused severe complications (63.2% of cases) including bronchopneumonia and skin sequelae, with 4% mortality, demonstrating both the high transmissibility and clinical severity of endemic strains that risk international spread

[1] Date of study completion; NR: Not reported; PCR: Polymerase Chain Reaction

3.3. Disease severity among confirmed Mpox cases

The overall pooled Mpox severity rate among confirmed cases was 60.92% (95% confidence interval (CI): 47.54-72.83; I^2 = 9.7% and p = 0.351) (Fig. 2).

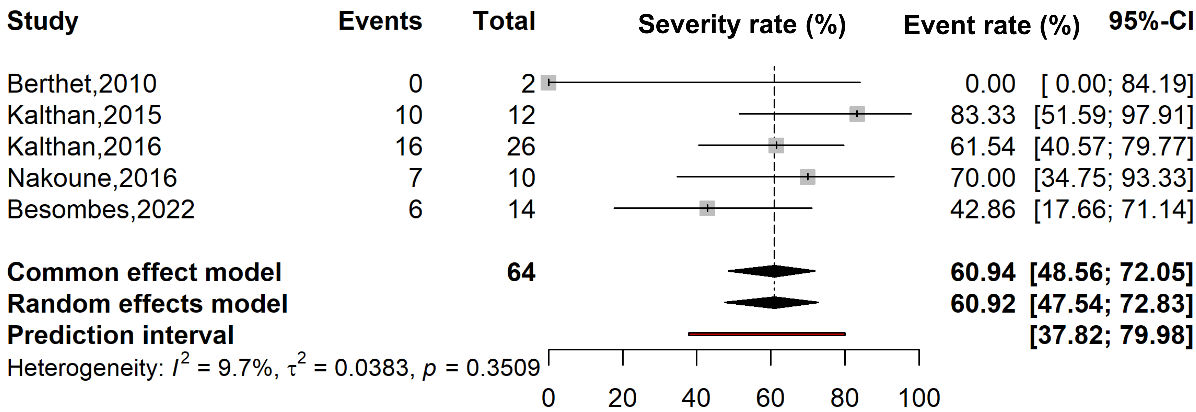

Fig. 2 Pooled severity rate of Mpox cases in CAR

The subgroup analysis according to the study period revealed a non-significant decrease in Mpox severity rate from 66.00% (95% CI: 51.95-77.70; n = 4 reports) before 2022 [17–19,29] to 42.86 (95% CI: 17.66-71.14; n = 1 reports) [8]. The highest severity rate was observed in Region 6 (77.27%; 95% CI: 55.64-90.21; n = 2 reports) [17,29], however there was no significant difference between severity rate across regions (p = 0.245) (Table 2 and Supplementary File 2, Supplementary Figs. 1-3).

Table 2 Subgroup meta-analysis of confirmed Mpox severity rate pooled estimates in CAR

Subgroup	Confirmed cases	Event rate[1] (%)	95% CI limits [1]		Number of studies	Heterogeneity statistic[1]	
			Lower	Upper		I^2(%)	p-value
Period [2]							
< 2022	50	66.00	51.95	77.70	4	0	0.630
2022+	14	42.86	17.66	71.14	1	-	-
Region							
Region 2	14	42.86	17.66	71.14	1	-	-
Region 4	26	61.54	40.57	79.77	1	-	-
Region 6	22	77.27	55.64	90.21	2	0	0.463
Not specified	2	0.00	0.00	84.19	1	-	-
Participant							
General population	54	58.52	40.09	74.84	4	26.6	0.252
General population and HCW	10	70	34.75	93.33	1	-	-

[1]Random effects model; CI: Confidence interval; [2]Period before and after the 2022 global outbreak; HCW: Healthcare worker

3.4. Mortality among confirmed Mpox cases

The pooled CFR among confirmed Mpox cases was 10.71% (95% CI: 4.52-23.28; I^2 = 0.0% and p = 0.894) (Fig. 3).

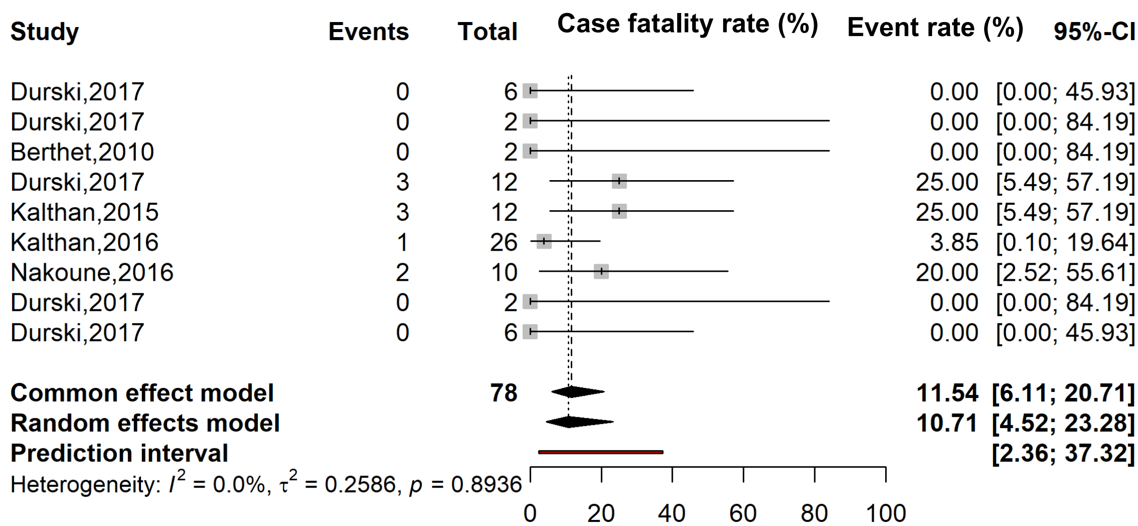

Fig. 3 Pooled case fatality rate among confirmed Mpox cases in CAR

All included studies were conducted in before the global outbreak. The geographical trend highlighted higher mortality was recorded in Eastern Health Regions (10.81%; 95% CI: 4.03-25.93) [17,19,29,32] and the lowest in Western Health Regions with no reported death (0.00%; 95% CI: 0.00-100.00) [32], however this should be interpreted with caution due the small sample size for studies conducted in Westen Health Regions (n = 8 participants) (Table 3 and Supplementary File 3, Supplementary Figs. 1-3).

Table 3 Subgroup meta-analysis of confirmed Mpox case fatality rate pooled estimates in CAR

Subgroup	Confirmed cases	Event rate[1] (%)	95% CI limits [1]		Number of studies	Heterogeneity statistic[1]	
			Lower	Upper		I^2(%)	p-value
Region							
Region 1	2	0.00	0.00	84.19	1	-	-
Region 2	6	0.00	0.00	45.93	1	-	-
Region 4	26	3.85	0.10	19.64	1	-	-
Region 6	28	17.86	7.63	36.38	3	0.0	0.962
Multicentric	12	25.00	5.49	57.19	1	-	-
Not specified	4	0.00	0.00	100.00	2	0.0	1.000
Region group							

Western	8	0.00	0.00	100.00	2	0.0	1.000
Eastern	54	10.81	4.03	25.93	4	5	0.368
Multicentric	12	25.00	5.49	57.19	1	-	-
Not specified	4	0.00	0.00	100.00	2	-	-
Participant							
General population	68	8.56	2.51	25.34	8	0.0	0.894
General population and HCW	10	20.00	2.52	55.61	1	-	-

[1]Random effects model; CI: Confidence Interval; Western = Health Regions 1 and 2; Eastern = Health Regions 4 and 6; HCW: Healthcare worker

3.5. Mortality among suspected Mpox cases

The pooled CFR among suspected Mpox cases was 12.13% (95% CI: 5.59-24.34; I^2 = 0.0% and p = 0.897) (Fig. 4).

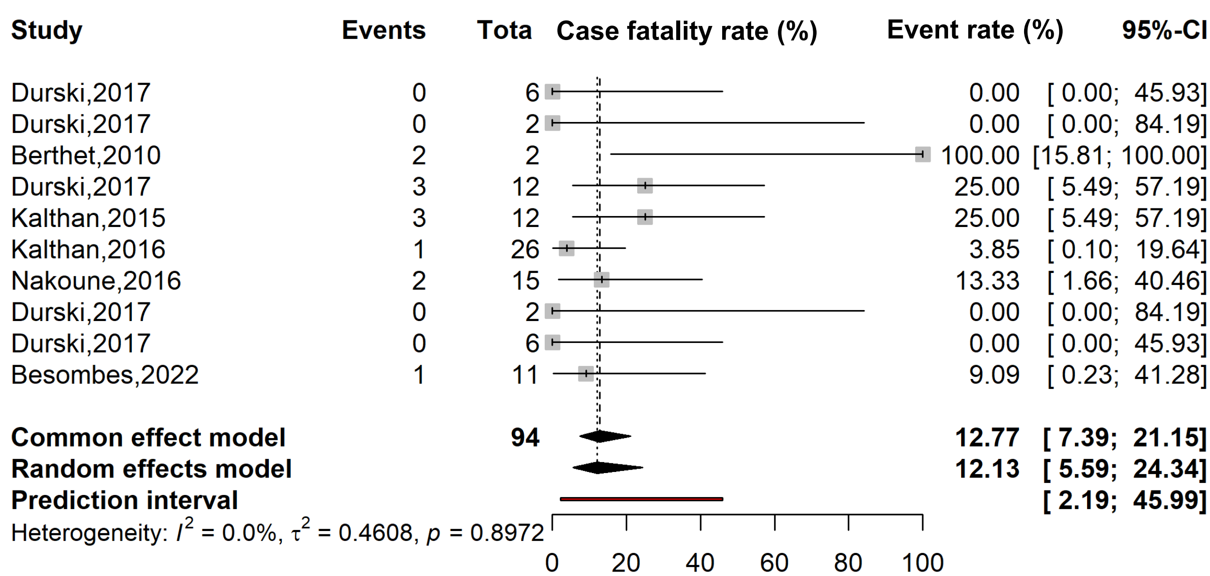

Fig. 4 Pooled case fatality rate among suspected Mpox cases in CAR

The subgroup analysis shows a modest decline in CFR among suspected Mpox cases from the pre-2022 period (12.19%, 95% CI: 4.65-28.34) [17–19,29,32] to the post-2022 period (9.09%, 95% CI: 0.23-41.28) [31]. Geographic disparities existed, with Eastern Health Regions maintaining higher CFR (9.95%, 95% CI: 3.39-22.71) compared to Western Health Regions (5.26%, 95% CI: 0.74-29.39). The general population CFR (10.00%, 95% CI: 3.56-29.30) [8,18,19,29,32] aligns with overall trends, with no significant heterogeneity detected (I^2 = 0.0-1.6%) across subgroups (Table 4 and Supplementary File 4, Supplementary Figs. 1-4).

Table 4 Subgroup meta-analysis of suspected Mpox case fatality rate pooled estimates in CAR

Subgroup	Suspected cases	Event rate[1] (%)	95% CI limits [1]		Number of studies	Heterogeneity statistic[1]	
			Lower	Upper		I^2(%)	*p*-value
Period [2]							
< 2022	83	12.19	4.65	28.34	9	0.0	0.877
2022+	11	9.09	0.23	41.28	1	-	-
Region							
Region 1	2	0.0	0.18	33.87	1	-	-
Region 2	17	5.88	0.82	32.03	2	0.0	0.999
Region 4	26	3.85	0.10	19.64	1	-	-
Region 6	33	15.15	6.45	31.62	3	0.0	0.746
Multicentric	12	25.00	5.49	57.19	1	-	-
National	14	7.14	0.18	33.87	1	-	-
Not specified	4	0.00	0.00	99.99	2	0.0	0.999
Region group							
Western	19	5.26	0.74	29.39	3	0.0	1.000
Eastern	59	9.95	3.99	22.71	4	1.6	0.384
Multicentric/National	12	25.00	5.49	57.19	1	-	-
Not specified	4	0.00	0.00	99.99	2	0.0	0.999
Participant							
General population	125	11.00	3.56	29.30	14	0.0	0.848
General population and HCW	15	13.33	1.66	40.46	1	-	-

[1]Random effects model; CI: Confidence interval; [2]Period before and after the 2022 global outbreak; Western = Health Regions 1 and 2; Eastern = Health Regions 4 and 6; HCW: Healthcare worker

3.6. Mpox vaccine uptake

The pooled vaccination uptake estimate was 20.00% (95% CI: 10.33-35.17) in CAR, this meant that eight individuals out of ten reported no active immunization against Mpox (Fig. 5)

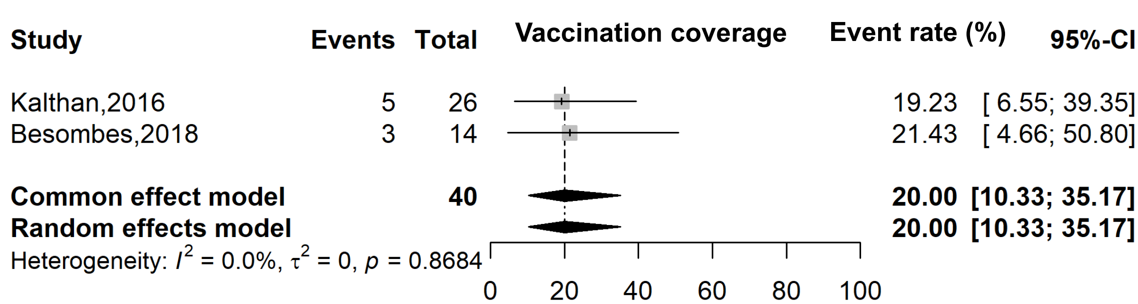

Fig. 5 Pooled Mpox vaccination uptake rate in CAR

3.7. Mpox clinical pattern

The most reported clinical manifestations associated with confirmed Mpox disease included fever and rash with pooled frequencies of 91.05 and 85.53% of cases respectively. Other commonly presented manifestations included chills or sweat (90.00%) and light sensitivity (88.89%), reported in one study each [8,17–19,29,31] (Table 5 and Fig. 6).

Table 5 Clinical patterns of confirmed Mpox cases in CAR

Rank	Clinical manifestation	Confirmed cases examined (n)	Frequency (%)	95% CI Limits		k	Heterogeneity statistic		Model
				Lower	Upper		I^2 (%)	*p*-value	
1	Fever	70	91.05	42.88	99.28	5	74.1	0.004	Random
2	Chills or sweat	10	90.00	55.50	99.75	1	-	-	-
3	Light sensitivity	9	88.89	51.75	99.72	1	-	-	-
4	Rash	76	85.53	75.72	91.80	6	15.8	0.312	Fixed
5	Oral lesions	20	59.16	8.56	95.73	2	86.5	0.007	Random
6	Pruritus or itchy lesion	46	58.57	31.53	81.27	3	59.1	0.087	Random
7	Genital lesions	19	57.43	8.76	94.99	2	85.4	0.009	Random
8	Lymphadenopathy	58	57.00	34.27	77.12	4	57.2	0.072	Random
9	Fatigue or asthenia	20	55.00	33.62	74.68	2	0.0	0.999	Fixed
10	Palm lesions	20	50.00	3.03	96.97	2	88.5	0.003	Random
11	Sole lesions	19	48.36	3.12	96.46	2	87.8	0.004	Random
12	Lesions	12	41.67	15.17	72.33	1	-	-	-
13	Headache	45	39.22	7.56	83.58	3	78.5	0.010	Random
14	Sore throat or dysphagia	35	37.87	11.67	73.76	2	83.5	0.014	Random
15	Myalgia	45	37.78	24.94	52.59	3	0.0	0.5770	Fixed
16	Cough	36	34.18	5.91	81.10	2	89.7	0.002	Random
17	Conjunctivitis	20	31.14	6.38	75.00	2	77.4	0.035	Random
18	Hemorrhagic skin lesions	9	22.22	2.81	60.01	1	-	-	-
19	Bedridden status	10	20.00	2.52	55.61	1	-	-	-
20	Vomiting or nausea	10	20.00	2.52	55.61	1	-	-	-
21	Diarrhea	9	11.11	0.28	48.25	1	-	-	-
22	Dyspnea	10	10.00	0.25	44.50	1	-	-	-
23	Facial oedema	10	10.00	0.25	44.50	1	-	-	-
24	Hypothermia	10	10.00	0.25	44.50	1	-	-	-

k = Number of studies; CI: Confidence interval;

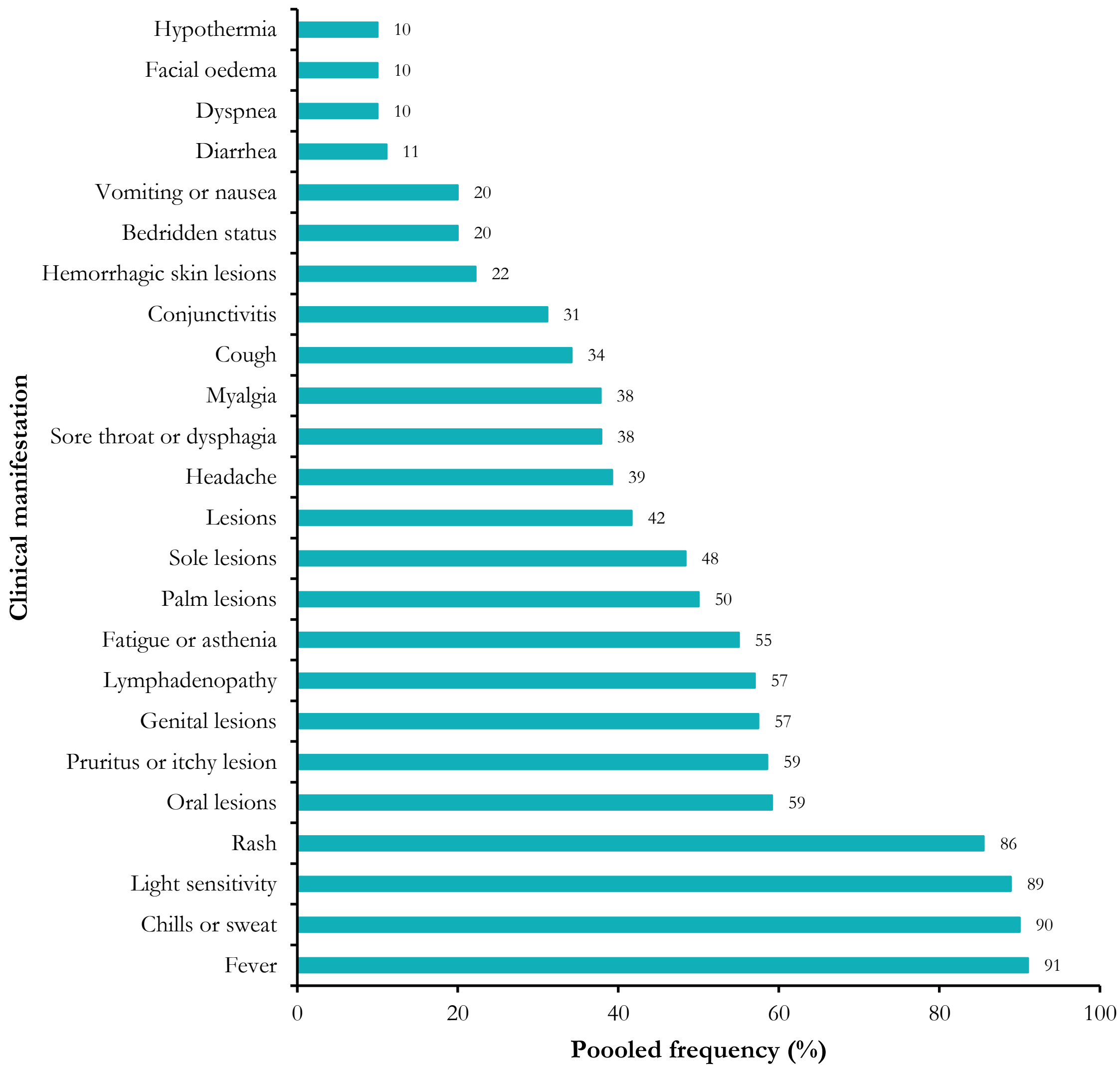

Fig. 6 Clinical profile of confirmed Mpox cases in CAR

3.8. Publication bias and sensitivity test analysis

Publication bias could not be reliably assessed due to limited number of studies for severity rate, morality rate among confirmed cases and vaccination uptake rate. However, the Egger's linear regression and Begg's rank correlation tests confirmed the absence of statistically significant publication bias for the CFR among suspected cases (Supplementary File 2, Supplementary Fig. 4; Supplementary File 3, Supplementary Fig. 4; Supplementary File 4, Supplementary Fig. 5; and Supplementary File 5 Supplementary Fig. 1).

Sensitivity analysis, assessing the impact of individual studies and outliers on the overall results, demonstrated that no study exhibited a significant impact on the overall pooled estimate (Supplementary File 2, Supplementary Fig. 5; Supplementary File 3, Supplementary Fig. 5; and Supplementary File 4, Supplementary Fig. 5).

4. Discussion

This in-depth systematic analysis and meta-analysis involved a comprehensive synthesis of seven studies conducted in CAR between 1984 and 2023. The findings from this study provide evidences on the epidemiological, clinical, and public health patterns of the MPXV in CAR.

The observed CFR was 10.71% among confirmed cases. This was higher than observations reported in recent global outbreaks, where most studies consistently reported CFR below 1% [7, 26, 33]. However, our findings corroborates earlier evidences from the DRC, where reports of surveillance conducted between 2001 and 2013 revealed CFRs ranging from 6% to 10.6%, particularly among children and unvaccinated individuals [34, 35]. Furthermore, similar mortality rates were described in the CAR during earlier outbreaks in the 1980s [36]. The high CFR in CAR could be due to several factors. Such factors include endemic circulation of the more virulent clade I Mpox virus among CAR cases, limited healthcare access, poor health-seeking behavior, and frequent delays in case detection and isolation, especially in rural communities [37,38]. This highlights the need for improved and resilient healthcare systems to reduce this mortality.

Our analysis showed a higher CFRs among confirmed Mpox cases in the Eastern Health Regions (10.81%) than the Western Regions (0.0%). The Eastern areas include regions most affected by the prolonged conflict following the 2013 arm conflict, such as Haute-Kotto, Vakaga, Mbomou, and Ouham [39]. These regions have experienced repeated armed violence, mass displacement, and targeted attacks on health facilities. This have severely compromised access to healthcare services. Médecins Sans Frontières and other humanitarian agencies have reported recurrent looting, destruction of infrastructure, and limited access to essential health services in conflict-affected health districts such as Batangafo, Bambari, and Bangassou [40]. The persistent insecurity continues to hinder timely diagnosis, isolation, and treatment of Mpox cases. These conflict-driven vulnerabilities likely contribute significantly to the elevated mortality. This emphasizes the necessity of for urgent need for resilient healthcare systems that can function effectively in the political unrest and violence context in order to lower Mpox-related fatalities in CAR.

The CAR's extensive border with the African epicenter of Mpox (DRC) significantly increases the MPXV transmission risk, particularly in Health Region 6 where the highest disease severity rate was documented. This border region's dense forest ecosystems and local populations' dependence on hunting, gathering, and agricultural activities increase the human-animal interactions that facilitate zoonotic spillover [41]. The increased MPXV transmission observed in these communities and the risk high severity of the disease in this context are probably explained by the combination of cross-border travel and traditional livelihood in the forest zones.

About 61% of cases with clinical severity in CAR reported symptoms such as fever (91%), rash (86%), photophobia (89%), and fatigue (55%). These presentations are consistent with earlier descriptions of Clade I infections, which are known to be responsible for systemic illness with complications. Such complications include secondary bacterial infections, dehydration, and acute respiratory distress[18,34]. The WHO has previously identified Clade I as causing more severe and widespread disease, with a higher rate of complications and mortality than the Clade II [42].

However, the Mpox outbreaks in 2022–2023, which were primarily caused by Clade IIb, had milder clinical profiles. An multinational cohort study across 16 countries by found that most patients presented with localized anogenital lesions with minimal systemic symptoms, and less than 10% of cases needed hospitalization [26]. Similarly, another study observed that although pain was a common symptom, particularly with perianal lesions, life-threatening complications were rare, and the CFR was negligible [33]. In many countries in Africa, where timely access to quality and affordable healthcare remains limited, this difference in clinical manifestations including complication occurrence reflects both virological differences and contextual health infrastructure disparities.

The underreporting is another major challenge in CAR, which underestimates the actual burden of Mpox reported over the years. Communities living in rural or remote areas often lack access to quality healthcare, including diagnostic testing and qualified healthcare workers [43]. Studies have highlighted that several cases may go undetected for every confirmed Mpox case in endemic areas due to inadequate surveillance [44]. Moreover, symptoms of Mpox can be mistaken with other endemic illness such as varicella, measles, or bacterial skin infections, leading to misclassification and diagnostic delays [45]. Effective epidemic response, contact tracing, and knowledge of virus evolution are all hampered by poor testing and reporting rates.

The review showed a low vaccination uptake in CAR (20%). These results corroborates finding from the neighboring DRC [35]. This might be the results of vaccine hesitancy among the population, supply constraints, and limited healthcare infrastructural. Historically, Orthopoxvirus-derived vaccination provided cross-protection against Mpox, with immunization estimates of about 85% [46]. However, after the worldwide smallpox vaccination program was discontinued in 1980, the number of susceptible individuals in endemic regions increased [47]. Countries with weak immunization infrastructure like CAR, have since lacked access to new Mpox-specific vaccines or regular smallpox-derived protection.

Conversely, developed countries rapidly deployed targeted vaccination campaigns during the 2022 pandemic. For example, the U.S. administered over 1.2 million doses of JYNNEOS (a commercial brand name for a live, non-replicating smallpox and Mpox vaccine) by early 2023, prioritizing healthcare workers and most vulnerable groups like men who have sex with men [48]. Similarly, the UK initiated a pre-exposure prophylaxis campaign using a ring vaccination strategy [49]. These disparities demonstrated more worldwide health inequities in vaccine delivery and research funding for endemic nations such as CAR, where Mpox morbidity and mortality have affected health for decades.

5. Strength and limitations

This systematic review and meta-analysis provide valuable insights into Mpox severity, mortality and the clinical profile of confirmed cases to tailor a context specific Mpox case definition in the CAR. The findings highlight the continued public health importance of Mpox in the region and underscore the need for ongoing surveillance, research on vaccination uptake, and interventions to reduce the burden of this disease. However, this review has several limitations. First, some death cases might have been unreported due to study design, potentially underestimating the true CFR. Confounding by strain differences remains a concern, as the lack of comprehensive genomic data in many studies obscures the clade-specific mortality rates. Surveillance bias, particularly the potential for improved detection of milder cases in more recent studies, may also influence the CFR estimates. Additionally, the small sample sizes in some subgroup analyses result in wide confidence intervals, limiting the precision of the findings. Study in other language than English and French were not searched.

6. Conclusions

In the CAR, Mpox continues to be a serious public health concern due of its high fatality and severity. In addition to reflecting low vaccination rates, restricted access to healthcare, and a lack of investment in surveillance infrastructure for early disease detection, this epidemiological profile is mostly caused by the spread of the more virulent Clade I virus. These deficiencies in the management of Mpox cases should be investigated and confirmed by future national study. Therefore, improved resource allocation, targeted vaccine administration, community education, healthcare worker training are all necessary to address these structural disparities in the global response to Mpox.

Abbreviations

CAR: Central African Republic

CFR: Case Fatality Rate

CI: Confidence Interval

DRC: Democratic Republic of Congo

HCW: Healthcare worker

MeSH: Medical Subject Headings

Mpox: Monkeypox

MPXV: Monkeypox virus

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analysis

WHO: World Health Organization

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Standards of Reporting

This systematic review was conducted and reported in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.

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Supplementary Material:

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