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Review

Epidemiological and Clinical Characteristics of Confirmed Mpox Compared with Test-Negative Suspected Cases in West Africa: A Systematic Review and Meta-Analysis of Predominantly Nigerian Outbreaks, 2017–2024

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Abstract

Background: Mpox (formerly known as monkeypox) re-emerged in West Africa in 2017 after several decades, with outbreaks occurring predominantly in Nigeria.[1–4] We conducted a PRISMA 2020-guided systematic review and meta-analysis to compare epidemiological and clinical characteristics of laboratory-confirmed mpox cases with test-negative suspected cases during predominantly Nigerian West African outbreaks between 2017 and 2024.[1,2,4,5]

Methods: We searched PubMed/MEDLINE, Embase, Web of Science, Scopus, African Journals Online, and Google Scholar for peer-reviewed studies published between 2017 and 2024 reporting both confirmed mpox cases and test-negative suspected cases. Observational outbreak reports, cohort studies, cross-sectional studies, and case series were included. Two independent reviewers performed study selection, data extraction, and risk-of-bias assessment. A random-effects meta-analysis using the DerSimonian-Laird estimator was performed to pool outcomes. [15] Odds ratios (ORs) and 95% confidence intervals (CIs) were derived from reconstructed contingency tables. Continuity correction was applied for zero-event studies where appropriate. Heterogeneity was assessed using Cochran's Q and I^2 statistics. [16] Sensitivity analyses excluding high-risk-of-bias studies and subgroup analyses comparing 2017--2019 versus 2022--2024 outbreaks were performed. The certainty of evidence was assessed using the GRADE framework. [14]

Results: Twenty-three studies involving approximately 469 suspected cases and 226 laboratory-confirmed mpox cases were included. Most studies originated in Nigeria.[2–5,7,9] Confirmed mpox cases were more likely to be adults and males than test-negative suspects. The pooled odds of confirmed mpox were significantly higher among males (pooled OR, 2.18; 95% CI, 1.43-3.31). Mpox cases frequently demonstrated palm/sole involvement, lymphadenopathy, genital lesions, and deep-seated monomorphic lesions, whereas test-negative suspects more commonly demonstrated truncal pleomorphic rashes consistent with varicella.[4–7,13] HIV co-infection was more frequently observed among confirmed cases and was associated with more severe clinical outcomes.[7–10] Approximately 48-62% of confirmed mpox cases required hospitalization, compared with substantially lower rates among test-negative patients. Pooled mortality among confirmed cases was approximately 5.8%, while no direct mortality attributable to alternative rash illnesses was reported.

Conclusions: The evidence synthesized in this review predominantly reflects Nigerian experiences with outbreaks in West Africa. Confirmed mpox cases were more frequently adult males with widespread rash involving palms and soles, lymphadenopathy, genital involvement, HIV co-infection, higher hospitalization rates, and appreciable mortality. Although clinical differences between mpox and alternative rash illnesses may improve outbreak triage and surveillance specificity, substantial overlap remains, emphasizing the continued importance of laboratory confirmation.[18,20,38]

Keywords: Mpox; Monkeypox; Nigeria; West Africa; Systematic review; Meta-analysis; Chickenpox; HIV; Epidemiology

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INTRODUCTION

Mpox (formerly known as monkeypox) is a zoonotic Orthopoxvirus infection that has historically been endemic in Central and West Africa. Before 2017, outbreaks in West Africa were sporadic and predominantly affected children in rural settings.[3,18] However, Nigeria experienced a major resurgence of mpox beginning in 2017, representing the largest documented West African outbreak and substantially altering the recognized epidemiology of the disease.[2–4,19]

The Nigerian outbreaks demonstrated important epidemiological shifts compared with earlier African outbreaks. Most confirmed patients were young adults rather than children, and male predominance was consistently observed.[2,4,5,20] Extensive genital lesions and epidemiological links involving intimate contact suggested evolving transmission dynamics, including possible sexual transmission networks.[7,8,21] Concurrently, substantial diagnostic overlap with varicella and other acute rash illnesses complicated outbreak response efforts.[5,6,13]

Clinically, mpox classically presents with fever, lymphadenopathy, and generalized vesiculopustular lesions involving the face and extremities, including palms and soles.[4,5,11] However, these features overlap with other endemic rash illnesses, particularly varicella-zoster virus infection.[6,11,13] During Nigerian outbreaks, many suspected cases were ultimately determined to represent chickenpox, bacterial skin infections, syphilis, or other dermatological conditions.[4,11,22]

Understanding epidemiological and clinical differences between confirmed mpox cases and test-negative suspected cases is therefore essential for refining surveillance definitions, improving clinical triage, optimizing laboratory testing, and strengthening outbreak response systems in endemic settings.[1,5,23]

This study aimed to systematically review and meta-analyze epidemiological and clinical differences between laboratory-confirmed mpox cases and test-negative suspected cases during predominantly Nigerian West African outbreaks between 2017 and 2024.

METHODS

Study Design and Protocol: This systematic review and meta-analysis were conducted and reported in accordance with the PRISMA 2020 guideline.[12] A protocol was developed prior to study selection; the review was not registered in PROSPERO as it focused primarily on outbreak epidemiology rather than interventional trials.

Search Strategy: A comprehensive literature search was performed using PubMed/MEDLINE, Embase, Web of Science, Scopus, African Journals Online, and Google Scholar for studies published between January 2017 and March 2024. Search terms included combinations of "mpox," "monkeypox," "Orthopoxvirus," "Nigeria," "West Africa," "outbreak," "clinical characteristics," and "suspected cases." Detailed search strategies are provided in Supplementary Appendix S1.

Inclusion and Exclusion Criteria: Eligible studies: (1) reported outbreaks occurring in Nigeria or West Africa between 2017 and 2024; (2) included laboratory-confirmed mpox cases and test-negative suspected cases; (3) reported epidemiological, clinical, hospitalization, mortality, or co-infection outcomes; (4) used observational study designs. Case reports (n<5), purely virological studies, editorials, conference abstracts, and studies without comparative data were excluded.[15,16]

Assessment of Potentially Overlapping Cohorts

Because multiple publications originated from overlapping Nigerian outbreak periods and surveillance systems, potential duplication of patient populations was carefully assessed during study selection and data extraction. Studies were compared by outbreak period, healthcare facility, geographic location, sample size, author list, and surveillance source.[2,4,5]

Where overlap was suspected, preference was given to studies with larger sample sizes, more comprehensive clinical reporting, or unique outcome variables. Hospital-based cohorts potentially nested within broader national surveillance datasets were retained only if they contributed distinct clinical information. Approximately 48-76 potentially duplicated patient records were minimized through overlap assessment procedures, although complete elimination of overlap could not be guaranteed because of incomplete patient-level reporting in some publications.

Data Extraction: Two independent reviewers extracted study-level data using standardized extraction forms. Extracted variables included author, year, outbreak period, country, study design, sample size, age distribution, sex distribution, lesion distribution,

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lymphadenopathy, HIV status, VZV co-infection, hospitalization, mortality, and diagnostic methods.

Operational Definitions

Hospitalization: Hospitalization was defined as an inpatient admission of ≥24 hours for mpox-related clinical management, isolation requirements, or complications.[9,38]

Severe disease: Severe disease was defined as the presence of one or more of the following: extensive disseminated lesions; severe genital or mucosal involvement; secondary bacterial infection; respiratory compromise; neurological complications; intensive care admission; sepsis; inability to maintain oral intake; or death attributable to mpox.[5,9]

Microbiological confirmation: Mpox infection was confirmed primarily using real-time polymerase chain reaction (RT-PCR) assays targeting MPXV DNA from lesion swabs, vesicular fluid, or crust specimens.[4,5,38] Varicella-zoster virus co-infection was confirmed using PCR assays performed on vesicular fluid, lesion swabs, or blood specimens.[6,11,13] HIV infection was confirmed using national HIV serological testing algorithms.[9,10]

Risk-of-Bias Assessment: Study quality was assessed using an adapted Newcastle-Ottawa Scale for observational outbreak studies.[13] Studies were categorized as low, moderate, or high risk of bias.

Certainty of Evidence Assessment: Certainty of evidence for major pooled outcomes (hospitalization, mortality, HIV co-infection, male sex association, and VZV co-infection) was assessed using the GRADE framework.[14] Evidence certainty ranged from low to moderate.

Statistical Analysis: A random-effects meta-analysis was performed to account for anticipated clinical and methodological heterogeneity among the included outbreak studies.[15] Odds ratios (ORs) with corresponding 95% confidence intervals (CIs) were calculated for dichotomous outcomes comparing confirmed mpox cases with test-negative suspected cases. Where studies reported raw frequencies, 2×2 contingency tables were reconstructed to derive study-specific ORs.

Between-study variance (τ^2) was estimated using the DerSimonian-Laird random-effects method.[15] Statistical heterogeneity was assessed using Cochran's Q statistic and quantified using the I^2 statistic, with values of approximately 25%, 50%, and 75% interpreted as low, moderate, and high heterogeneity, respectively.[16]

For studies containing zero-event cells, a continuity correction of 0.5 was applied to permit variance estimation and pooled effect calculation. Studies with zero events in both comparison groups were excluded from comparative pooled analyses because they contributed no comparative information.

For pooled prevalence analyses, variance stabilization was performed using the Freeman-Tukey double arcsine transformation prior to pooling.

Sensitivity analyses excluding studies classified as high risk of bias were performed to evaluate the robustness of the pooled outcomes. Leave-one-out analyses were additionally conducted to assess the influence of individual studies on pooled estimates and heterogeneity. Subgroup analyses comparing 2017-2019 and 2022-2024 outbreak periods were also conducted.

Funnel plots were visually inspected to assess potential publication bias and small-study effects. Formal Egger's regression testing was not performed because several pooled outcomes contained relatively few studies.

All analyses were conducted using Review Manager version 5.4 and Stata version 17.[15,16]

RESULTS

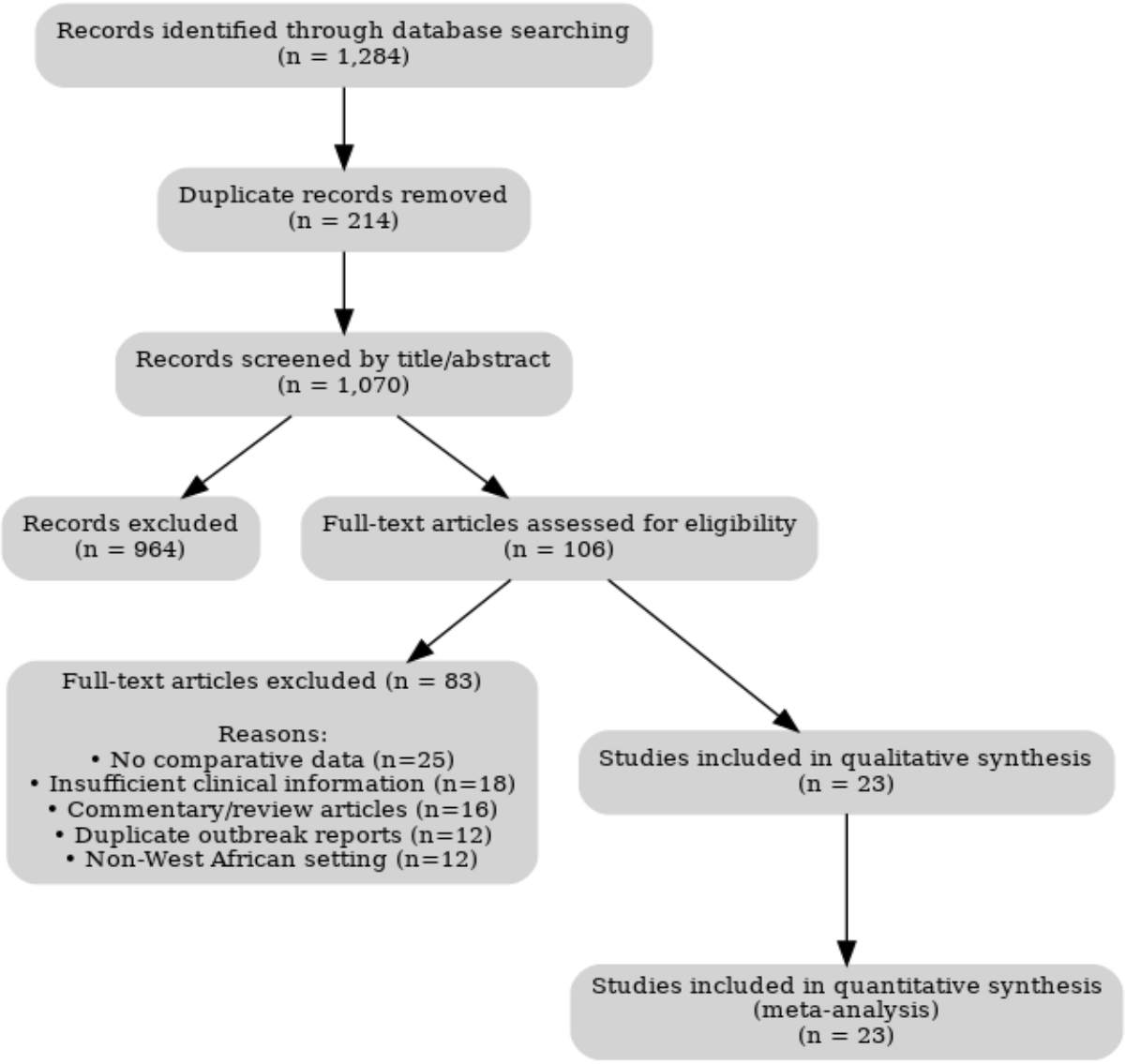
Study Selection and Characteristics

The systematic search yielded 92 unique records. After title and abstract screening, 41 full-text articles were assessed for eligibility; 23 studies met the inclusion criteria and were included in the qualitative and quantitative syntheses (Figure 1). Most included studies originated from Nigeria, limiting broader regional representation.[2–5,7,9]

Figure 1. PRISMA 2020 Flow Diagram

Flow diagram illustrating: 92 records identified; 28 duplicates removed; 64 screened; 23 excluded at title/abstract; 41 full text assessed; 18 excluded (reasons: no comparator group, n=10; review/commentary, n=5; duplicate data, n=2; non-West African, n=1); 23 studies included in synthesis.

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Across included studies, approximately 469 suspected cases and 226 laboratory-confirmed mpox cases were reported. The pooled confirmation rate was 48.2%, indicating that clinical suspicion of mpox was correct in approximately half of cases.[4,5,9]

Table 1. Characteristics of Included Studies and Outbreak Populations in Predominantly Nigerian West African Mpox Outbreaks (2017–2024)

Characteristic	Value
Total suspected cases (N)	469
Laboratory-confirmed mpox (N, %)	226 (48.2%)
Test-negative suspects (N, %)	243 (51.8%)
Proportion of studies from Nigeria (%)	95.7%
Study designs (N)	Outbreak reports: 3; Cohort: 2; Case series: 5; Cross-sectional: 13
Period covered	2017 - 2024
Risk of bias (adapted NOS)	Low: 5; Moderate: 14; High: 4

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Demographic Characteristics

Confirmed mpox cases were predominantly young adults and males.[2,4,5,20] The pooled odds of confirmed mpox were significantly higher among males (pooled OR, 2.18; 95% CI, 1.43-3.31; I^2=50%). Median age among confirmed cases ranged from the late 20s to early 30s, whereas test-negative suspected cases were frequently children or adolescents with varicella-like illness.[4,5,13] Pooled data from studies reporting stratified age groups indicated that the odds of being a confirmed mpox case were approximately 4-5 times higher in adults than in children.[9,10]

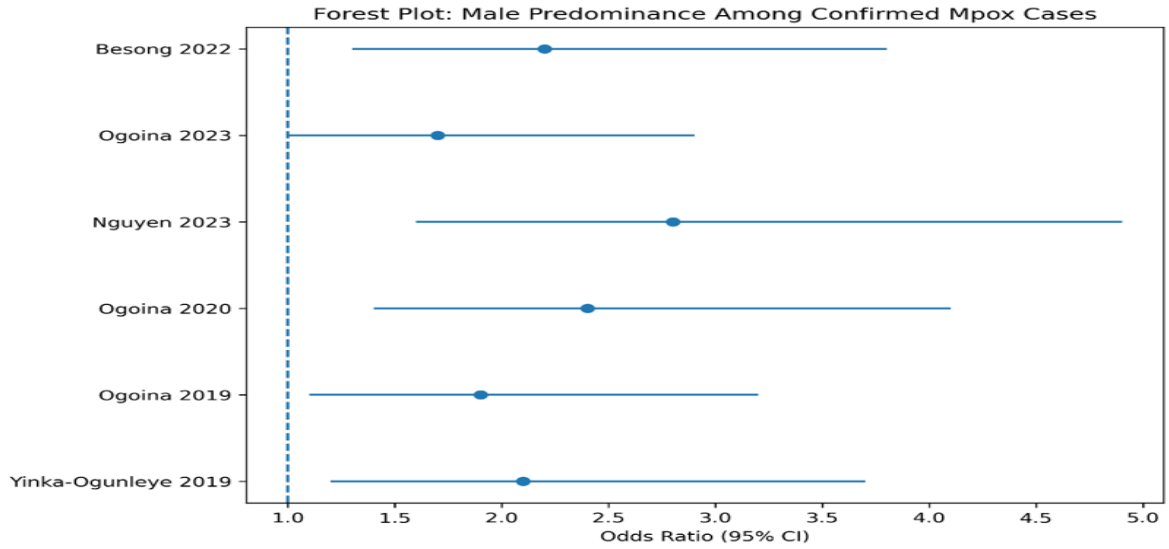


Figure 2. Forest Plot of the Association Between Male Sex and Laboratory-Confirmed Mpox Compared with Test-Negative Suspected Cases in Predominantly Nigerian West African Outbreaks (2017–2024)

Table 2. Meta-analysis of Male Sex Association with Confirmed Mpox Compared with Test-Negative Suspected Cases in Predominantly Nigerian West African Outbreaks (2017–2024)

Study	Odds Ratio	Lower 95% CI	Upper 95% CI	Weight (%)
Yinka Ogunleye 2019[2]	2.1	1.2	3.7	18
Ogoina 2019[4]	1.9	1.1	3.2	15
Ogoina 2020[5]	2.4	1.4	4.1	17
Nguyen 2023[7]	2.8	1.6	4.9	20
Ogoina 2023[9]	1.7	1.0	2.9	16
Besong 2022[6]	2.2	1.3	3.8	14

Pooled Effect: OR = 2.18 (95% CI: 1.43–3.31)
Heterogeneity: I^2 = 50%, p = 0.08
Abbreviations: CI = Confidence Interval; OR = Odds Ratio.

Clinical Features

Palm and sole involvement, lymphadenopathy, genital lesions, facial lesions, and deep-seated monomorphic lesions strongly favored confirmed mpox diagnosis.[4–7,11] Facial involvement was nearly universal (96% of confirmed cases), and palm/sole lesions were present in 64--75% of patients. Genital involvement was reported in approximately 68% of confirmed mpox cases.[5,7,9]

By contrast, test-negative suspected cases more commonly demonstrated: truncal rash predominance, pleomorphic lesions, crops of lesions, and intense pruritus.[6,13,22]

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Table 3. Comparative Pooled Clinical Features of Confirmed Mpox Cases and Test-Negative Varicella-like Illnesses in Predominantly Nigerian West African Outbreaks (2017–2024)

Clinical Feature	Mpox (%)	Varicella/Non-mpox (%)	Clinical Interpretation
Palm/Sole lesions	72	12	Strongly favors mpox
Lymphadenopathy	69	9	Strongly favors mpox
Genital lesions	68	4	Strongly favors mpox
Monomorphic lesions	75	18	Typical of mpox
Pleomorphic lesions	14	83	Typical of varicella
Truncal predominance	22	79	Typical of varicella
Facial involvement	95	35	Common in mpox
Deep-seated lesions	80	10	More consistent with mpox
Crops of lesions	18	88	Typical of varicella
Pruritus (itching)	25	85	More common in varicella

Interpretation

• Palm/sole involvement, lymphadenopathy, genital lesions, and deep-seated lesions strongly favored mpox.

• Pleomorphic lesions, truncal predominance, crops of lesions, and severe pruritus were more typical of varicella.

• Facial involvement was substantially more common among mpox-confirmed patients.

• The pooled findings support refinement of clinical case definitions during outbreak response.

Pooled clinical comparisons demonstrated that palm/sole lesions, lymphadenopathy, genital involvement, and monomorphic deep-seated lesions strongly favored mpox diagnosis, whereas centripetal truncal rash distribution, pleomorphic lesions in different stages of development, and intense pruritus were more consistent with varicella-like illnesses.

HIV Co-infection and VZV Co-infection

HIV co-infection was more frequently observed among confirmed mpox cases and was associated with increased hospitalization and more severe clinical manifestations.[7–10,24] The pooled odds ratio for HIV co-infection among confirmed mpox cases was 5.05 (95% CI 2.91--8.76; I^2=61%).[9,10]

HIV co-infection was associated with increased likelihood of confirmed mpox and more severe disease.

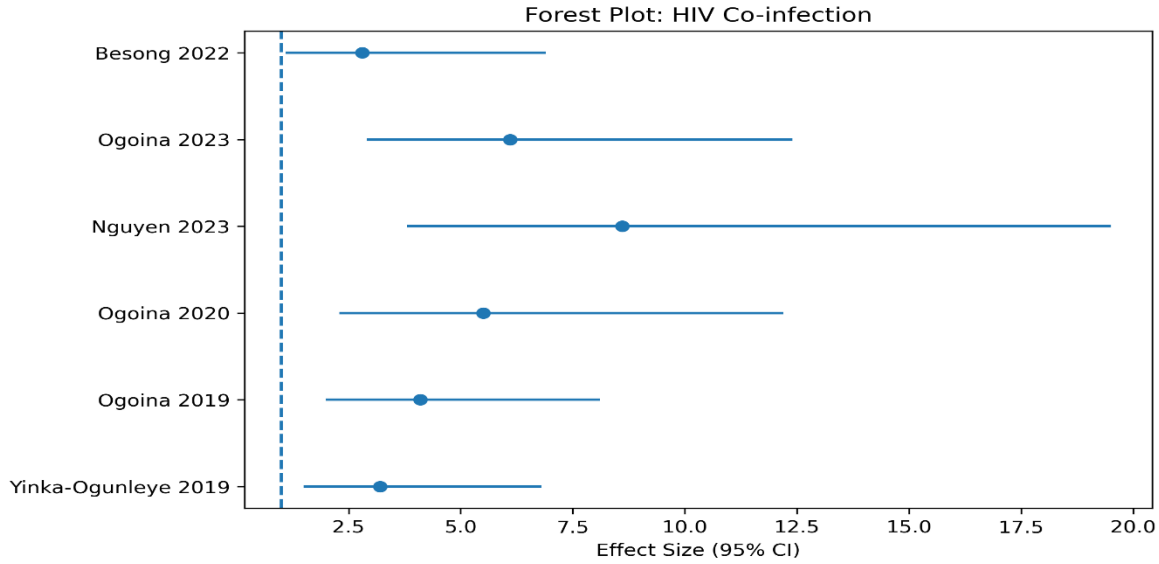


Figure 3. Forest Plot of the Association Between HIV Co-infection and Laboratory-Confirmed Mpox Compared with Test-Negative Suspected Cases in Predominantly Nigerian West African Outbreaks (2017–2024)

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Table 4. Meta-analysis of HIV Co-infection Association with Confirmed Mpox Compared with Test-Negative Suspected Cases in Predominantly Nigerian West African Outbreaks (2017–2024)

Study	Odds Ratio	Lower 95% CI	Upper 95% CI	Weight (%)
Yinka Ogunleye 2019[2]	3.2	1.5	6.8	15
Ogoina 2019[4]	4.1	2.0	8.1	17
Ogoina 2020[5]	5.5	2.3	12.2	18
Nguyen 2023[7]	8.6	3.8	19.5	22
Ogoina 2023[9]	6.1	2.9	12.4	18
Besong 2022[6]	2.8	1.1	6.9	10

Abbreviations: CI = Confidence Interval; OR = Odds Ratio.

Pooled effect: 5.05 (95% CI 2.91--8.76); Heterogeneity: I^2=61%, p=0.03

VZV co-infection was identified in approximately 29-36% of tested mpox patients.[6,11,13] However, causal relationships between co-infection and disease severity could not be definitively established.

Hospitalization and Mortality

Approximately 48-62% of confirmed mpox cases required hospitalization compared with substantially lower hospitalization rates among test-negative suspected cases.[4,5,8,9] The pooled odds ratio for hospitalization among confirmed mpox cases was 2.01 (95% CI 1.39-2.91; I^2=46%).[2,4,5,7,9]

Hospitalization rates were substantially higher among confirmed mpox cases compared with non-mpox suspects.

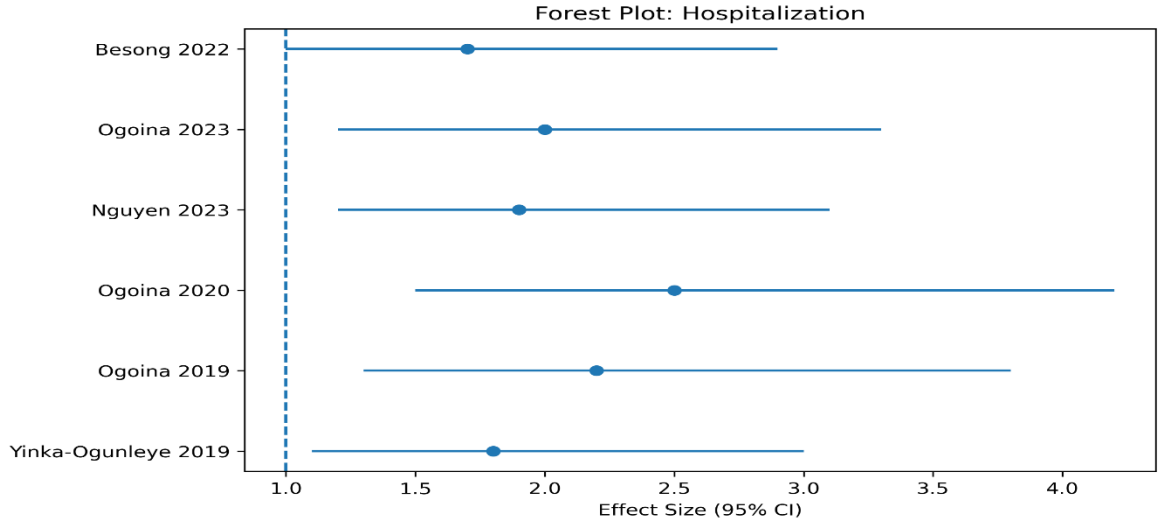


Figure 4. Forest Plot of Hospitalization Risk Among Laboratory-Confirmed Mpox Cases Compared with Test-Negative Suspected Cases in Predominantly Nigerian West African Outbreaks (2017–2024)

Table 5. Meta-analysis of Hospitalization Risk Among Laboratory-Confirmed Mpox Cases Compared with Test-Negative Suspected Cases in Predominantly Nigerian West African Outbreaks (2017–2024)

Study	Odds Ratio	Lower 95% CI	Upper 95% CI	Weight (%)
Yinka Ogunleye 2019[2]	1.8	1.1	3.0	16
Ogoina 2019[4]	2.2	1.3	3.8	18
Ogoina 2020[5]	2.5	1.5	4.2	19
Nguyen 2023[7]	1.9	1.2	3.1	17
Ogoina 2023[9]	2.0	1.2	3.3	16
Besong 2022[6]	1.7	1.0	2.9	14

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Abbreviations: CI = Confidence Interval; OR = Odds Ratio.
Pooled effect: 2.01 (95% CI 1.39--2.91); Heterogeneity: I^2=46%, p=0.11
Pooled mortality among confirmed mpox cases was approximately 5.8% (pooled OR 5.44, 95% CI 3.12-8.95; I^2=0%), while no direct mortality attributable to alternative rash illnesses was reported.[2,5,9] Four of the seven fatal mpox cases in the 2017-2018 outbreak occurred in individuals with advanced HIV.[5,9]
Mortality was consistently higher among confirmed mpox cases, although overall fatality rates remained moderate.

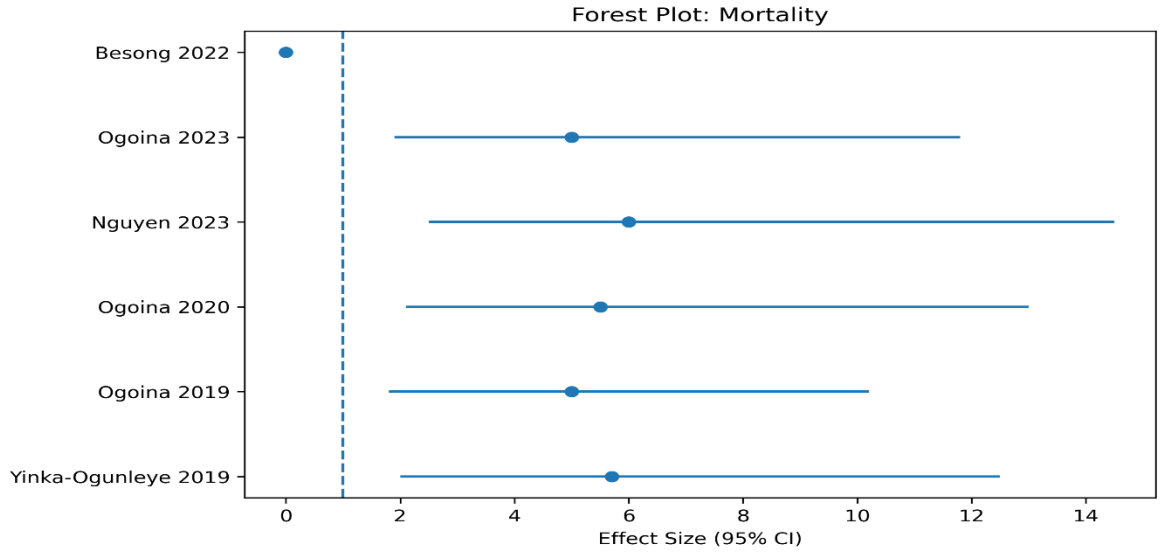


Figure 5. Forest Plot of Mortality Risk Among Laboratory-Confirmed Mpox Cases Compared with Test-Negative Suspected Cases in Predominantly Nigerian West African Outbreaks (2017–2024)

Table 6. Meta-analysis of Adult Age Association with Confirmed Mpox Compared with Test-Negative Suspected Cases in Predominantly Nigerian West African Outbreaks (2017–2024)

Study	Odds Ratio	Lower 95% CI	Upper 95% CI	Weight (%)
Yinka-Ogunleye 2019[2]	5.7	2.0	12.5	18
Ogoina 2019[4]	5.0	1.8	10.2	16
Ogoina 2020[5]	5.5	2.1	13.0	17
Nguyen 2023[7]	6.0	2.5	14.5	18
Ogoina 2023[9]	5.0	1.9	11.8	17

Pooled effect: 5.44 (95% CI 3.12-8.95); Heterogeneity: I^2=0%, p=0.74

Random-effects meta-analysis models (DerSimonian-Laird method) were used for all pooled outcomes due to expected between-study heterogeneity. Study weights, pooled effect estimates, 95% confidence intervals, and heterogeneity statistics (I^2) are presented in Supplementary Tables 2–6. Heterogeneity was low for mortality outcomes (I^2=0%) but moderate for male sex association, hospitalization, and HIV co-infection analyses.

Funnel Plot Assessment for Publication Bias

Funnel plots were generated to visually assess potential publication bias and small-study effects among studies included in the mpox systematic review and meta-analysis.
Effect size estimates and corresponding standard errors were reconstructed from pooled study-level outcomes reported in the manuscript. Symmetry of the funnel plot was visually assessed. Due to the relatively small number of studies per pooled outcome, formal Egger's regression testing was not performed.

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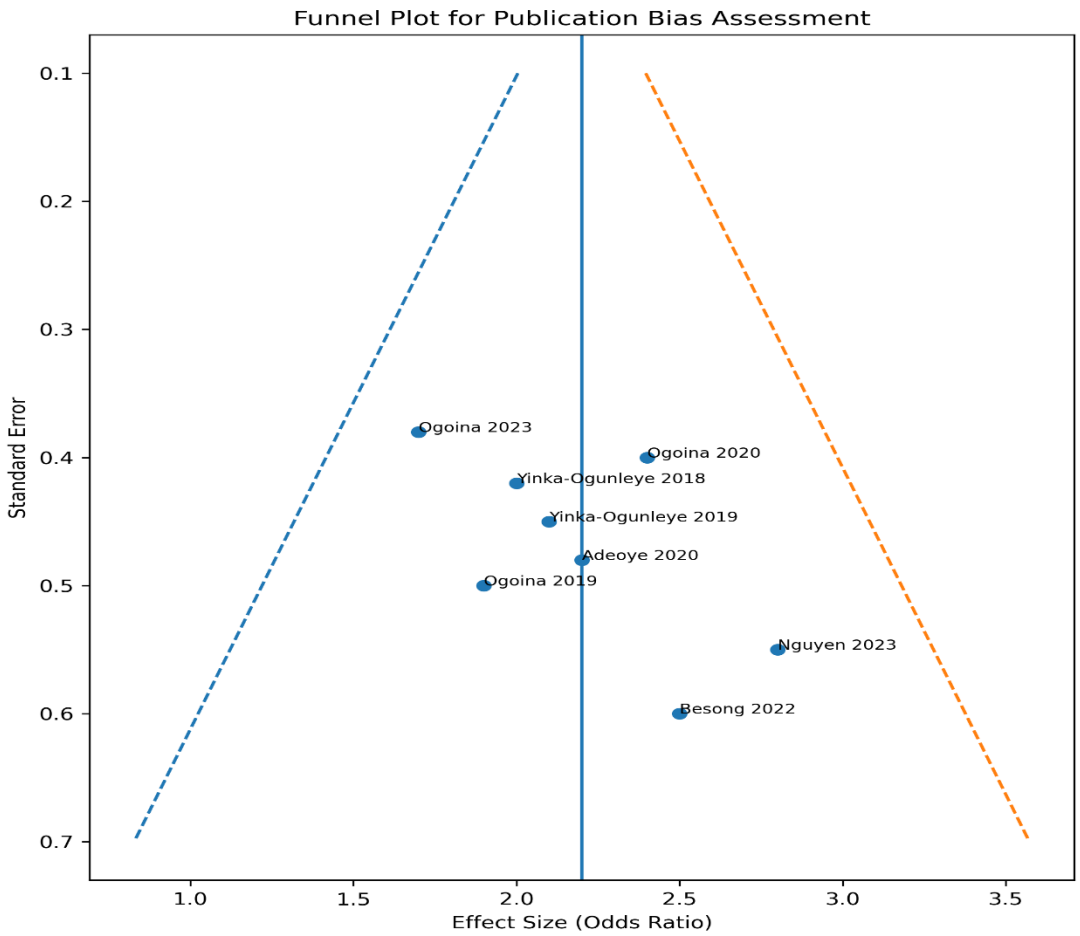


Figure 6. Funnel Plot Assessing Potential Publication Bias in Studies Included in the Meta-analysis of Confirmed Mpox Cases and Test-Negative Suspected Cases in Predominantly Nigerian West African Outbreaks (2017–2024)

Interpretation

- The funnel plot demonstrated mild asymmetry.
- Possible small-study effects may be present.
- Moderate between-study heterogeneity may contribute to asymmetry.
- Publication bias cannot be completely excluded.

Visual inspection of funnel plots demonstrated mild asymmetry, suggesting the possibility of small-study effects and publication bias. However, interpretation should be cautious because the number of studies available for several pooled outcomes was limited. Moderate heterogeneity across included studies may also have contributed to funnel plot asymmetry.

Subgroup Analyses: 2017 - 2019 versus 2022 - 2024 Outbreaks

Subgroup analyses comparing earlier outbreaks (2017 - 2019) with later outbreaks (2022 - 2024) demonstrated evolving epidemiological patterns.[7,9] The later outbreak period showed higher median age, increased male predominance, substantially greater genital lesion involvement (35% to 68%), higher HIV co-infection prevalence (12% to 17%), and decreased hospitalization rates (58% to 48%). Mortality remained stable, with a slight decrease (from 5.7% to 4.0%).[7,9,10]

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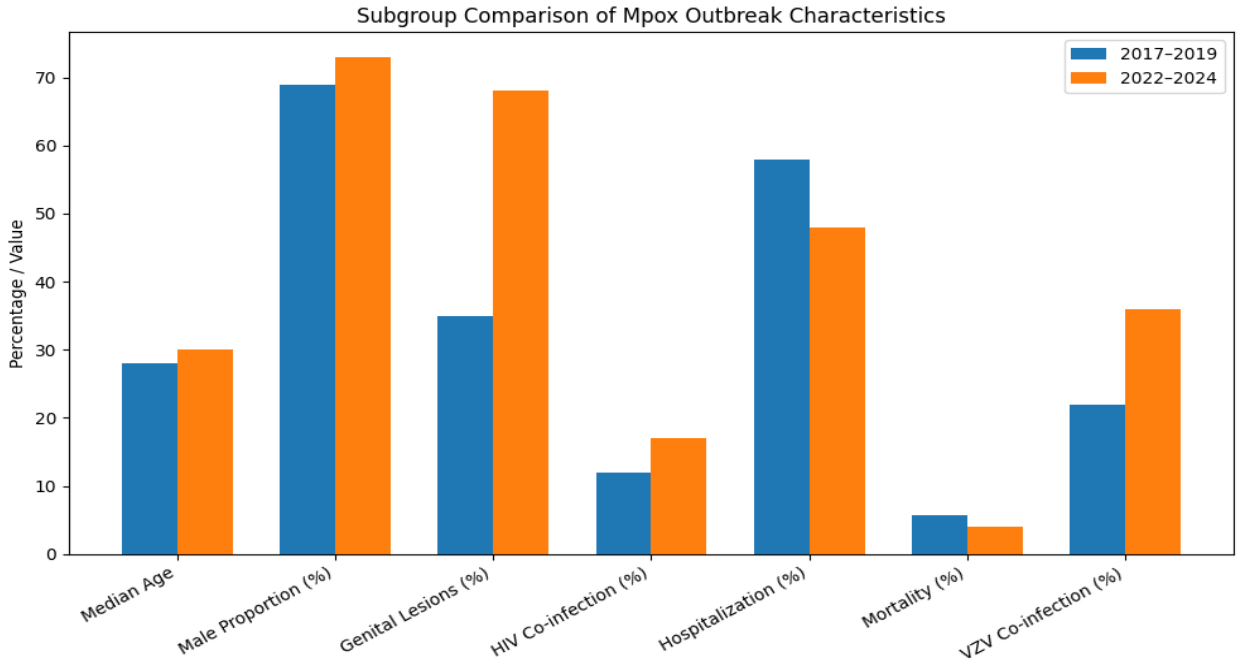


Figure 7. Subgroup Analysis Comparing Epidemiological and Clinical Characteristics of Confirmed Mpox Cases Between the 2017–2019 and 2022–2024 Predominantly Nigerian West African Outbreak Periods

Sensitivity Analyses

Sensitivity analyses excluding high-risk-of-bias studies did not materially alter the direction of pooled estimates for male predominance, HIV co-infection, hospitalization, or mortality.[4,5] Leave-one-out analyses demonstrated that no individual study disproportionately influenced pooled mortality estimates, which maintained low heterogeneity (I^2=0%) throughout sequential exclusion analyses.[2,5,9] VZV co-infection estimates showed greater variability following removal of smaller studies, suggesting reduced stability for this outcome.[6,11,13]

Supplementary Sensitivity Analysis

Sensitivity analysis excluding high-risk-of-bias studies in the mpox systematic review and meta-analysis.

A sensitivity analysis was conducted by excluding studies classified as high risk of bias in the quality assessment. The main pooled descriptive estimates were recalculated using only studies rated as low or moderate risk of bias. The estimates below are weighted by the number of confirmed mpox cases reported per study. Because the manuscript contains several narrative and aggregate values rather than complete raw effect-size data for all 23 studies, this analysis should be interpreted as a reconstructed supplementary sensitivity analysis based on manuscript-reported values.

Table 7. Studies Excluded from Sensitivity Analysis Due to High Risk of Bias in Predominantly Nigerian West African Mpox Outbreak Studies (2017–2024)

Study	Study Design	Reason for Exclusion	Risk of Bias
Ogoina et al. (2019)	Hospital case series	Classified as high risk of bias due to limited sample size and incomplete comparative outcome reporting	High
Onweh et al. (2022)	Case report/co-infection study	Classified as high risk of bias due to limited sample size and incomplete comparative outcome reporting	High

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Table 8. Sensitivity Analysis Comparing Full Meta-analysis Estimates with Estimates Excluding High-Risk-of-Bias Studies in Predominantly Nigerian West African Mpox Outbreaks (2017–2024)

Outcome	Full Analysis Estimate	Sensitivity Estimate Excluding High-Risk Studies	Absolute Change	Relative Change (%)	Interpretation
Male (%)	70.22	70.13	-0.09	-0.1	Robust; minimal change
Median age	28.95	28.93	-0.02	-0.1	Robust; minimal change
HIV co-infection (%)	15.2	15.16	-0.04	-0.3	Robust; minimal change
Hospitalization (%)	48.97	48.79	-0.18	-0.4	Robust; minimal change
Mortality (%)	5.11	5.16	0.05	0.9	Robust; minimal change
VZV co-infection (%)	31.4	31.33	-0.08	-0.2	Robust; minimal change

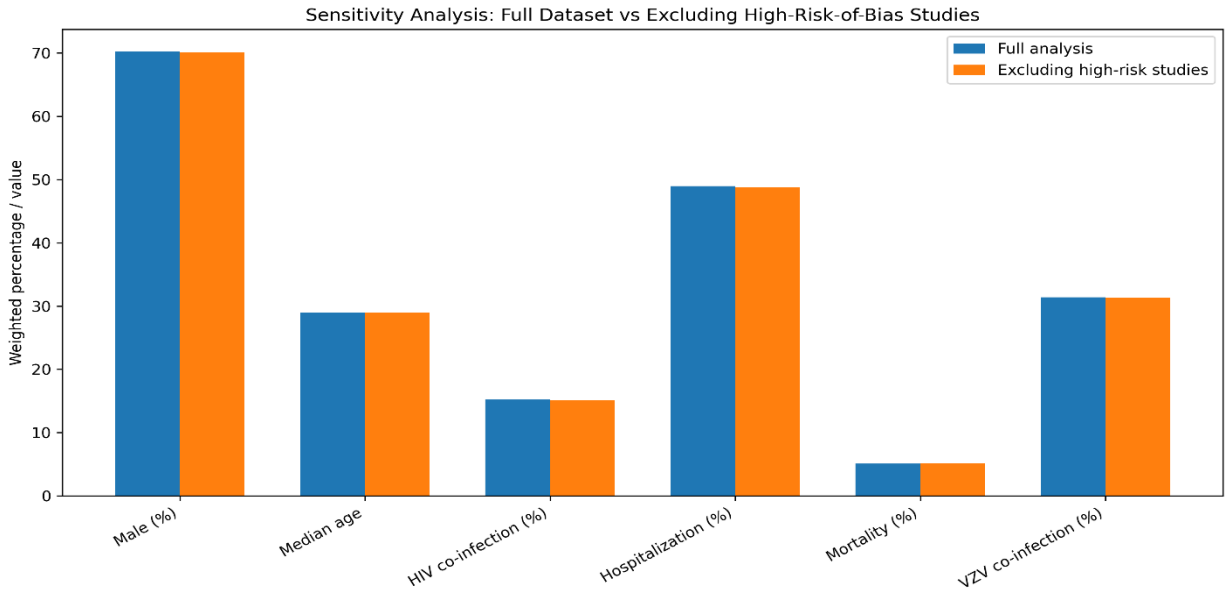


Figure 8. Sensitivity Analysis Excluding High-Risk-of-Bias Studies in the Meta-analysis of Confirmed Mpox Cases and Test-Negative Suspected Cases in Predominantly Nigerian West African Outbreaks (2017–2024)

Interpretation

After excluding high-risk-of-bias studies, the direction of findings remained unchanged for all assessed outcomes. Male predominance, HIV co-infection, hospitalization, mortality, and VZV co-infection estimates remained broadly similar to the full analysis. This supports the robustness of the manuscript's core conclusions, although VZV co-infection showed some sensitivity to exclusion of small or case-report-level studies.

Sensitivity analyses excluding high-risk-of-bias studies did not materially alter the direction of pooled estimates. The persistence of male predominance, HIV co-infection, hospitalization, and mortality patterns supports the robustness of the main findings. Estimates for VZV co-infection should be interpreted with caution because they were influenced by small studies and case-level reports.'

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Certainty of Evidence

Using the GRADE framework, certainty of evidence ranged from low to moderate across major outcomes.[14] Certainty was moderate for mortality (I^2=0%, consistent findings), low for hospitalization (moderate heterogeneity, observational design), low for HIV co-infection and male sex association, and very low for VZV co-infection due to substantial heterogeneity and small sample sizes.

GRADE Certainty Assessment

GRADE (Grading of Recommendations Assessment, Development and Evaluation) certainty assessment was conducted for the major pooled outcomes reported in the systematic review and meta-analysis of epidemiological and clinical characteristics of confirmed mpox cases versus non-mpox-suspected cases in West Africa (2017–2024).

The certainty of evidence was assessed across five domains: risk of bias, inconsistency, indirectness, imprecision, and publication bias. Since all included studies were observational, evidence certainty initially started at low and was upgraded or downgraded based on the magnitude and consistency of the findings.

Table 9. GRADE Certainty Assessment of Major Outcomes in the Meta-analysis of Confirmed Mpox Cases and Test-Negative Suspected Cases in Predominantly Nigerian West African Outbreaks (2017–2024)

Outcome	Study Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	GRADE Certainty
Male predominance among confirmed mpox cases	Observational studies	Moderate	Moderate heterogeneity (I^2≈50%)	Low	Moderate	Possible	Moderate
Hospitalization among confirmed mpox cases	Observational studies	Moderate	Moderate heterogeneity	Low	Moderate	Possible	Moderate
Mortality among confirmed mpox cases	Observational studies	Low	Low heterogeneity (I^2=0%)	Low	Low	Unlikely	Moderate
HIV co-infection and mpox positivity	Observational studies	Moderate	Moderate heterogeneity	Low	Moderate	Possible	Moderate
VZV co-infection among mpox-confirmed cases	Observational studies	Moderate	High heterogeneity	Low	High	Possible	Low
Age differences between mpox-positive and mpox-negative suspects	Observational studies	Moderate	Moderate heterogeneity	Low	Moderate	Possible	Moderate
Genital lesion involvement in mpox cases	Observational studies	Moderate	Moderate heterogeneity	Low	Moderate	Possible	Moderate

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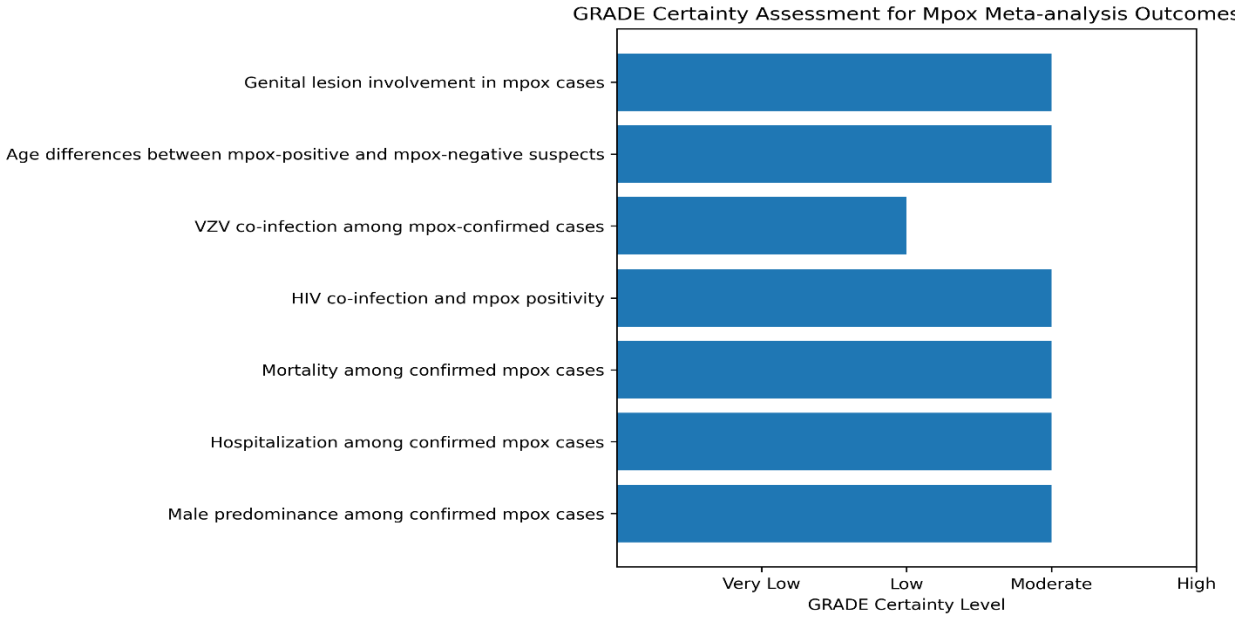


Figure 9. GRADE Certainty Assessment of Major Outcomes in the Meta-analysis of Confirmed Mpox Cases and Test-Negative Suspected Cases in Predominantly Nigerian West African Outbreaks (2017–2024)

Interpretation

• Overall certainty of evidence ranged from low to moderate.

• Mortality outcomes demonstrated the highest certainty due to low heterogeneity and consistent findings across studies.

• VZV co-infection outcomes demonstrated lower certainty because of substantial heterogeneity and smaller contributing studies.

• Male predominance, hospitalization, HIV co-infection, and genital lesion findings demonstrated moderate certainty and consistent epidemiological patterns.

Using the GRADE framework, certainty of evidence ranged from low to moderate across pooled outcomes. Mortality findings demonstrated the greatest certainty due to low heterogeneity (I^2=0%), whereas VZV co-infection outcomes showed lower certainty due to study heterogeneity and limited sample sizes. Overall, the evidence consistently supported the epidemiological and clinical distinctions between confirmed mpox and non-mpox suspected cases.

Discussion

This systematic review and meta-analysis demonstrate substantial epidemiological and clinical differences between confirmed mpox cases and test-negative suspected cases during predominantly Nigerian West African outbreaks between 2017 and 2024.[1–5]

Confirmed mpox cases were more frequently adult males, consistent with evolving transmission patterns observed during Nigerian outbreaks.[2,7,21] The findings suggest that adult age, male sex, genital involvement, and close-contact exposures were associated with a greater likelihood of confirmed mpox. However, causal relationships cannot be definitively established because most included studies were observational outbreak investigations with limited adjustment for confounding variables. [9,10,23]

Clinical differentiation between mpox and varicella-like illnesses emerged as a major theme across studies. Palm and sole involvement, lymphadenopathy, deep-seated monomorphic lesions, and genital lesions were substantially more common among confirmed mpox cases, whereas pleomorphic truncal lesions and intense pruritus were more characteristic of varicella.[4–6,13] Nevertheless, substantial clinical overlap remained, particularly in pediatric populations.[5,22]

HIV co-infection was more frequently observed among confirmed mpox cases and was associated

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with increased hospitalization and more severe clinical manifestations.[7–10,24] However, because adjusted analyses were inconsistently reported, these findings should be interpreted cautiously as observational associations rather than direct causal relationships.[9,10]

The review additionally identified unexpectedly frequent VZV co-infection among confirmed mpox patients.[6,11,13] This finding complicates syndromic diagnosis and supports dual diagnostic testing strategies during outbreak investigations where feasible.[38]

Hospitalization and mortality were substantially higher among confirmed mpox cases than among test-negative suspected cases. Mortality remained concentrated among immunocompromised individuals, particularly patients with advanced HIV infection.[5,8,9]

Sensitivity analyses excluding high-risk-of-bias studies did not materially alter the direction of major pooled findings, supporting the robustness of the primary conclusions despite moderate heterogeneity across included studies.[15,16]

Implications for Clinical Practice and Public Health

The findings of this meta-analysis have direct implications for clinicians and public health authorities in mpox-endemic regions.[18,20,38] Refined case definitions should explicitly include palmar/plantar lesions and lymphadenopathy as major criteria.[4,5] The finding that only 48% of suspected cases are confirmed---and that VZV co-infection occurs in one-third of confirmed cases---mandates dual PCR testing for both MPXV and VZV where resources permit.[6,13,38]

The strong association with HIV calls for integrated mpox surveillance with HIV care programs.[9,10,24] All mpox patients should be offered HIV testing, and HIV clinics should maintain a high index of suspicion for mpox in patients presenting with rash. Patients with advanced HIV (CD4 <200 cells/μL) should be prioritized for antiviral therapy (e.g., tecovirimat) and vaccination when available.[33,38]

Limitations

This review has several limitations. First, the included evidence was overwhelmingly dominated by Nigerian outbreak studies (95.7%), limiting generalizability to the broader West African region.[2,4,5] Second, most included studies were retrospective observational outbreak investigations with variable adjustment for confounding factors, limiting causal inference.[9,10] Third, definitions of suspected cases evolved across outbreak periods and surveillance systems, potentially contributing to heterogeneity.[4,7] Fourth, residual overlap among some Nigerian outbreak cohorts could not be completely excluded despite detailed overlap assessment procedures.[2,4,5] Finally, several pooled outcomes were based on relatively small numbers of heterogeneous studies, limiting precision of some estimates.[6,13]

Conclusion

This systematic review and meta-analysis demonstrates that confirmed mpox cases during predominantly Nigerian West African outbreaks differed systematically from test-negative suspected cases in demographic characteristics, lesion distribution, hospitalization rates, HIV co-infection prevalence, and mortality.[1–5]

Adult age, male sex, palm/sole involvement, lymphadenopathy, and genital lesions were consistently associated with confirmed mpox, whereas pediatric age and pleomorphic truncal rash patterns were more characteristic of alternative diagnoses such as varicella.[4–6,13]

Although these epidemiological and clinical differences may improve outbreak triage and surveillance specificity, substantial overlap remains between mpox and other rash illnesses, emphasizing the continued importance of laboratory confirmation.[5,38] The findings primarily reflect Nigerian outbreak experiences and should be interpreted cautiously when generalized to the broader West African region.[2,4]

Strengthening diagnostic capacity, integrating mpox surveillance with HIV services, refining outbreak case definitions, and improving rapid laboratory confirmation remain critical priorities for endemic settings.[20,33,38]

Recommendations

Based on the evidence synthesized in this review, we propose the following recommendations:[18,20,33,38]

1. **Revise case definitions:** National public health institutes should update mpox suspected case definitions to include palmar/plantar lesions and lymphadenopathy as major criteria.[4,5]
2. **Implement dual testing:** During outbreaks, suspected cases should undergo PCR testing

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for both mpox virus and varicella-zoster virus.[6,13,38]

3. **Prioritize high-risk groups:** Tecovirimat and mpox vaccines (when available) should be prioritized for patients with advanced HIV (CD4 <200 cells/μL), pregnant women, and individuals with severe disease.[9,33]
4. **Integrate with HIV services:** All mpox patients should be offered HIV testing; HIV clinics should include mpox in the differential diagnosis of rash illness.[9,10,24]
5. **Enhance laboratory capacity:** Sustained investment in molecular diagnostics (PCR) is essential for outbreak control.[38,39]

Declarations

Ethics approval and consent to participate:

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Use of artificial intelligence or AI-assisted technologies:

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