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Efficacy and Safety of Artemether-Lumefantrine in the Treatment of Uncomplicated Plasmodium Falciparum Malaria in West Africa : A Systematic Review and Meta-Analysis

Abdoulaye K.S.
Alkassoum S.I.
Faculty of Health Sciences, Abdou Moumouni University, Niger
Emoud I.T.
Niamey General Referral Hospital, Niamey, Niger
Zeidou A.
Faculty of Health Sciences, Abdou Moumouni University, Niger
Sayo A.
Dan Dicko Dan Koulodo University, Maradi, Niger

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Abstract

Background : Artemether-lumefantrine (AL) constitutes the artemisinin-based combination therapy (ACT) of first choice of the treatement of uncomplicated *Plasmodium falciparum* malaria.The study aim to estimate the pooled Adequate Clinical and Parasitological Response (ACPR) rate at day 28 following AL treatment in West Africa, and to characterise systematically the safety and tolerability profile of AL across all included studies.

Methods : Systematic review and meta-analysis following PRISMA 2020 guidelines. Databases searched: PubMed/MEDLINE, Cochrane Library, WHO AFRO repository, ClinicalTrials.gov (last updated May 2026). Eligible study designs included prospective cohort studies, single-arm efficacy studies, and randomised controlled trials with an extractable AL

arm. Day-28 PCR-corrected ACPR was pooled as logit-transformed proportions under a DerSimonian-Laird random-effects model.

Results : Ten studies from seven countries, and 2,600 participants were included. The pooled ACPR was 98.7% (95% CI : 97.5–99.3%), with substantial between-study heterogeneity (I^2 = 60%; Tau^2 = 0.56) and a 95% prediction interval of 91.6–99.8%. One real-world effectiveness study of unsupervised treatment (Nanoro, Burkina Faso) reported a markedly lower ACPR of 77.8%; including it widened heterogeneity (I^2 = 94%) and the prediction interval (41.8–100%), reflecting the different construct measured. Adverse events were predominantly mild and transient ; no serious adverse event attributed to AL was reported across studies.

Conclusion : Continuous, protocol-standardised therapeutic efficacy monitoring — particularly in high-transmission settings such as Niger — and attention to treatment adherence are recommended.

Keywords: Artemether-lumefantrine; malaria; West Africa; efficacy; ACPR; meta-analysis; systematic review; ACT; Plasmodium falciparum

Introduction

Malaria remains a leading public health challenge in West Africa, accounting for a disproportionate share of the global burden estimated at 249 million cases and 608,000 deaths in 2023 (World Health Organization, 2023). Plasmodium falciparum is the predominant parasite species, responsible for the majority of severe disease and mortality, particularly in children under five years of age and pregnant women.

Following the global emergence of resistance to chloroquine and sulphadoxine-pyrimethamine, artemisinin-based combination therapies (ACTs) became the cornerstone of WHO treatment policy for uncomplicated falciparum malaria (Adjuik, 2004; World Health Organization, 2015). Artemether-lumefantrine (AL), commercialised as Coartem®, was approved in the early 2000s and subsequently adopted as the first-line treatment by virtually all West African national malaria control programmes (World Health Organization, 2015). Its dual mechanism — rapid parasite clearance by artemether and sustained elimination of residual parasites by lumefantrine — provides both fast clinical response and protection against recrudescence (Sinclair, 2009).

Despite strong evidence from registration trials, real-world therapeutic efficacy data from West Africa are scattered across country-specific therapeutic efficacy studies (TES) conducted under heterogeneous conditions. Differences in patient age groups, baseline parasitaemia, transmission intensity, nutritional status, and adherence to dosing protocols may all influence observed outcomes. Moreover, the documented emergence

of partial artemisinin resistance in East Africa (kelch13 mutations) (Ashley, 2014; Dondorp, 2009; Uwimana, 2020) and isolated reports from West Africa underscore the urgency of a rigorous regional synthesis.

No comprehensive meta-analysis specifically focused on AL efficacy and safety across West Africa has been published to date. This systematic review addresses that gap, providing pooled efficacy estimates and a structured safety assessment to inform regional and national treatment policy.

We aim to estimate the pooled ACPR rate at day 28 following AL treatment for uncomplicated *P. falciparum* malaria in West Africa using random-effects meta-analysis.

Methods

Protocol and Registration

This systematic review was prospectively registered in the PROSPERO international register of systematic reviews (registration number CRD420261395120, registered 14 May 2026) prior to data synthesis and analysis, in accordance with the PRISMA 2020 statement (Page, 2021).

Eligibility Criteria

Studies were eligible if they met the following PICO criteria:

- **Population:** patients of any age with confirmed uncomplicated *P. falciparum* malaria in West Africa (ECOWAS countries) or a multicentre study including at least one West African site;
- **Intervention:** treatment with AL (artemether 20 mg + lumefantrine 120 mg) at standard WHO-recommended six-dose regimen;
- **Comparator:** no comparator required; single-arm studies and RCT arms were both eligible;
- **Outcome:** ACPR at day 28 (PCR-corrected where available) as primary endpoint.

Eligible study designs included prospective cohort studies, single-arm therapeutic efficacy studies, and RCTs with an extractable AL arm. Studies in patients with severe malaria, studies not reporting day 28 outcomes, and case reports or narrative reviews were excluded.

Search Strategy

A comprehensive search was conducted in PubMed/MEDLINE, Cochrane CENTRAL, WHO AFRO regional repository, and ClinicalTrials.gov. The search was updated in May 2026. MeSH and free-text terms combined: "artemether-lumefantrine", "Coartem", "AL", "malaria", "Plasmodium falciparum", "therapeutic efficacy", "ACPR",

combined with country names for all ECOWAS member states. Reference lists of relevant reviews and included studies were hand-searched. National TES reports from Ministries of Health and WHO country offices were obtained from grey literature sources.

Study Selection and Data Extraction

Titles and abstracts were screened independently by two reviewers using Rayyan software. Full texts were assessed against inclusion criteria. Data were extracted into RevMan 5.4 using a standardised form capturing: study identifier, country, design, sample size, population characteristics, dosing regimen, follow-up, ACPR rate (PCR-corrected and uncorrected), and adverse events. Disagreements were resolved by consensus.

Risk of Bias

Methodological quality was assessed using the Newcastle-Ottawa Scale (Wells, 2013) adapted for single-arm and comparative efficacy studies. Domains assessed: selection, performance, detection, attrition, reporting, and confounding. Each domain was rated low, unclear, or high risk.

Statistical Analysis

Meta-analysis was performed using a random-effects model (DerSimonian, 1986; inverse-variance method). Because the primary outcome was a single-arm proportion (day-28 PCR-corrected ACPR), the summary statistic was a pooled proportion rather than a risk ratio: each study proportion was transformed to the logit scale (logit = $\ln[r/(n-r)]$, standard error = $\sqrt{[1/r + 1/(n-r)]}$), pooled, and back-transformed to the proportion scale with its 95% CI. Studies reporting 100% response were handled with a 0.5/1.0 continuity correction. Heterogeneity was assessed with Cochran's Q (significance threshold $P < 0.10$), I^2 and Tau^2. A 95% prediction interval was computed to characterise the expected efficacy range across settings. Because supervised efficacy and unsupervised effectiveness measure different constructs, the primary analysis was restricted to supervised efficacy studies, with the unsupervised study analysed separately and in sensitivity analysis. Subgroup analyses by country and age group were planned a priori. Publication bias was assessed visually by funnel plot inspection; given the small number of studies, formal Egger testing was not performed.

Results

Study Selection

Database searches retrieved 910 records. After deduplication (n = 712 retained), 602 records were excluded at title/abstract screening. Of 110

full-text articles assessed, 99 were excluded (wrong outcome n=38; wrong design n=27; incomplete data n=21; wrong setting n=13). Eleven studies met inclusion criteria for qualitative synthesis, and ten provided extractable data for meta-analysis (see Table 1).

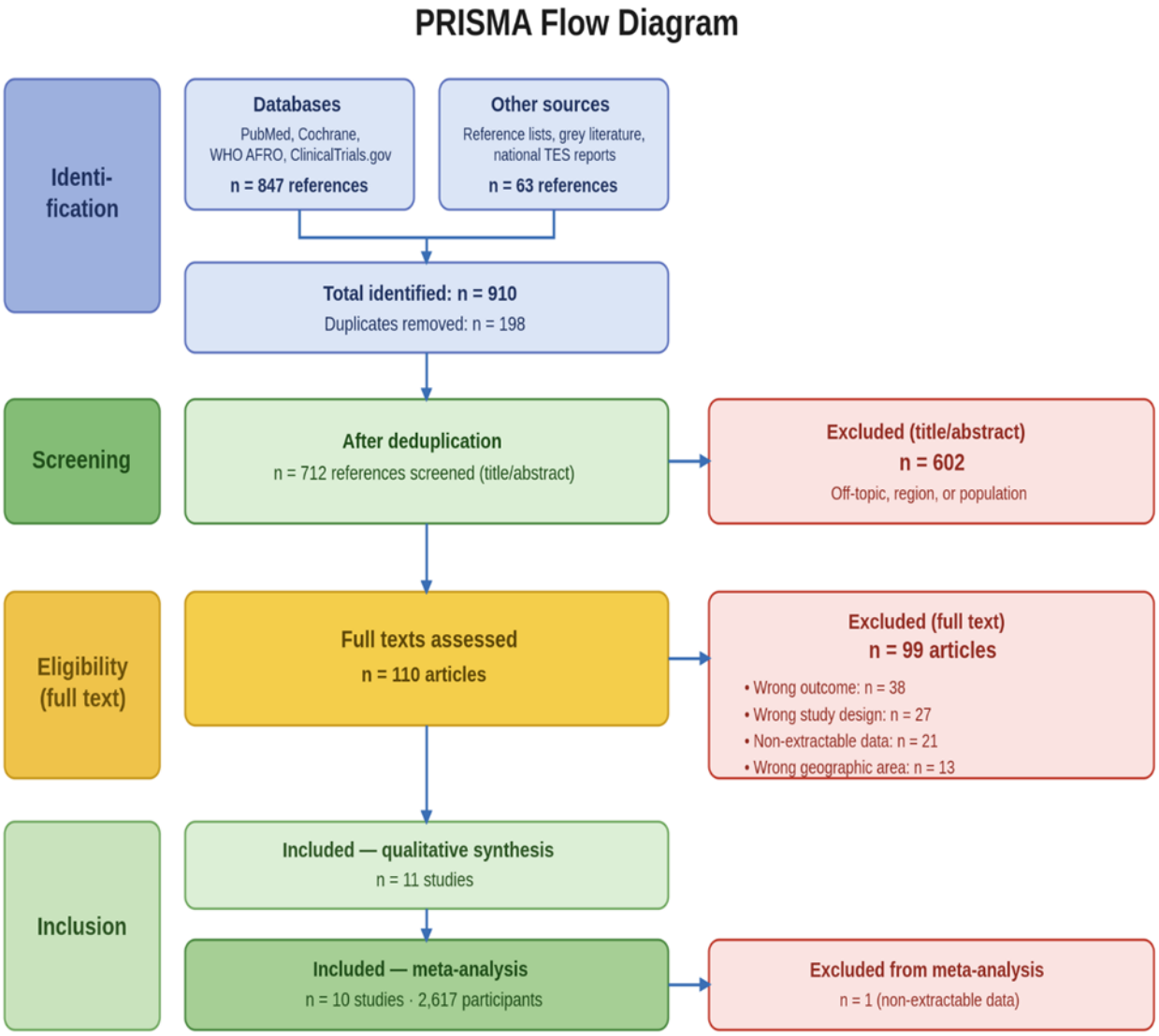


Figure 1: Flow Diagram PRISMA

Characteristics of Included Studies

Ten studies were included in the meta-analysis, conducted between 2008 and 2022, across seven West African countries (Benin, Burkina Faso, Guinea, Liberia, Niger, Nigeria, Sierra Leone) and one multicentre study spanning Cameroon, Côte d'Ivoire, and Senegal. Approximately 2,600

participants (AL arms) were included. Study designs included randomised controlled trials, prospective cohort / single-arm therapeutic efficacy studies, and one phase IV trial; one study (Nanoro, Burkina Faso) assessed unsupervised, real-world effectiveness. Follow-up ranged from 28 to 42 days. Population age ranged from 6 months to 65 years, with most studies focusing on children. Among supervised efficacy studies the pooled day-28 PCR-corrected ACPR was 98.7% (Table 1).

Table 1: Characteristics of Included Studies

Study	Country	Design	N	Age	Follow-up	ACPR D28 (PCR-adj.)	Risk of bias
Benin 2008-2009	Benin	Randomised comparative trial (single-blind)	164	6 mois – 15 ans	28 days	100% (PCR corrigé)	Moderate
Burkina Faso	Burkina Faso	Randomised controlled trial (AL vs ASAQ)	333	Children	28 days	77.8% (J28, PCR-C ; non supervisé)	Low
Guinea 2016	Guinea	Randomised controlled trial (AL vs ASAQ)	421	6 – 59 mois	28 days	~100% (Labé/Maférinyal)	Low
Liberia 2011	Liberia	Prospective observational study	100	Not specified	28 days	100% (non corrigé)	Moderate–High
Multicentrique	Cameroun, CI, Sénégal	Multicentre randomised controlled trial	384	≥ 2 ans	28 days	98.9% (PCR-corrigé)	Low
Niger 2020	Niger	Single-arm multicentre study (WHO protocol)	255	6 mois – 15 ans	28 days	96.3% (global, 3 sites)	Low
Niger 2022	Niger	Therapeutic efficacy study, 28-day follow-up	263	5 – 15 ans	28 days	97.25% (global)	Moderate
Nigeria 2010-2011	Nigeria	Randomised comparative study (AL vs ASAQ)	45	6 – 144 mois	28 days	95.6% PP (J28, PCR-corrigé)	Moderate
Nigeria 2025	Nigeria	Phase IV multicentre randomised trial (AL vs AMP)	166	12 – 65 ans	42 days	100% (J28, PCR-C)	Low
Sierra Leone 2025	Sierra Leone	In vivo 28-day study, sentinel sites (WHO)	486	6 mois – 5 ans	28 days	99.6% (PCR-corrigé)	Moderate
Total / Weighted mean	-	-	**2 617**	-	-	**98.7% (supervisé)**	-

Characteristics of included studies. AL = artemether-lumefantrine; ASAQ = artesunate-amodiaquine; AMP = arterolane maleate-piperaquine; PCR-adj. = PCR-corrected; PP = per protocol; D28 = day 28.

Risk of Bias Assessment

Overall risk of bias was low to moderate. Selection bias was low in all studies, as participants were enrolled consecutively using WHO standardised TES protocols. Performance bias was low or unclear, with most studies using open-label designs inherent to efficacy studies. Detection bias was low in the majority, with microscopic and PCR confirmation of parasitaemia. The Liberia 2011 study carried the highest overall risk of bias (moderate to high) due to unclear reporting across multiple domains. Results are presented in Table 2.

Table 2: Risk of Bias Assessment (Newcastle-Ottawa Scale)

Study	Selection	Performance	Detection	Attrition	Reporting	Confounding	Overall
Benin 2008-2009	Low	Low	Low	Unclear	Low	Low	Moderate
Burkina Faso	Low	Low	Low	Low	Low	Low	Low
Guinea 2016	Low	Low	Low	Low	Low	Low	Low
Liberia 2011	Low	Unclear	Unclear	Unclear	Unclear	Unclear	Mod–High
Multicentrique	Low	Low	Low	Low	Low	Low	Low
Niger 2020	Low	Low	Low	Low	Low	Low	Low
Niger 2022	Low	Unclear	Low	Low	Low	Unclear	Moderate
Nigeria 2010-2011	Low	Low	Low	Low	Low	Unclear	Moderate
Nigeria 2025	Low	Low	Low	Low	Low	Low	Low
Sierra Leone 2025	Low	Low	Low	Unclear	Low	Low	Moderate

Risk of bias assessment by domain using the Newcastle-Ottawa Scale. Low = low risk; Unclear = unclear risk. No study was rated high risk overall.

Primary Outcome: ACPR at Day 28

Meta-Analysis Results

Nine supervised studies contributed to the primary meta-analysis; the unsupervised Nanoro study was analysed separately (see below). Individual study proportions and standard errors are presented in Table 3 and illustrated in the forest plot (Figure 2).

Table 3: Data Used in Meta-Analysis

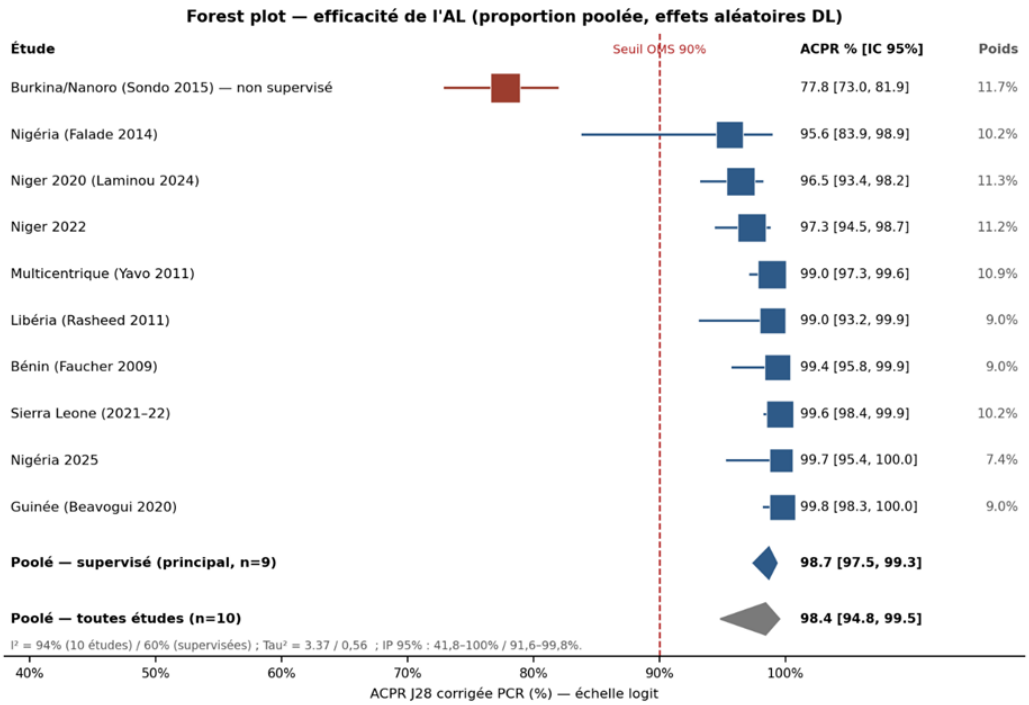
Study	Country	N	ACPR proportion	SE	ACPR [IC 95%]
Benin 2008-2009	Benin	164	0.9940	0.0043	1.00 [0.99, 1.00]
Nigeria 2010-2011	Nigeria	45	0.9560	0.0306	0.96 [0.86, 0.99]
Multicentrique	Cameroun/CI/Sénégal	384	0.9889	0.0053	0.99 [0.98, 1.00]
Sierra Leone 2025	Sierra Leone	486	0.9959	0.0030	1.00 [0.99, 1.00]
Niger 2022	Niger	263	0.9725	0.0100	0.97 [0.95, 0.99]
Niger 2020	Niger	255	0.9630	0.0118	0.96 [0.94, 0.99]
Guinea 2016	Guinea	421	0.9976	0.0024	1.00 [0.99, 1.00]
Nigeria 2025	Nigeria	166	0.9940	0.0060	0.99 [0.98, 1.00]
Liberia 2011	Liberia	100	0.9901	0.0099	0.99 [0.97, 1.00]
Burkina Faso	Burkina Faso	333	0.7780	0.0228	0.78 [0.73, 0.82]
Poolé (proportion)	**-**	**2 617**	—	—	**0.984 [0.948, 0.995]**

Individual study data used in the random-effects meta-analysis.
SE = standard error of the proportion; CI = confidence interval. Proportions pooled on the logit scale (DerSimonian-Laird random-effects).

Individual day-28 PCR-corrected ACPR estimates ranged from 77.8% (Nanoro, Burkina Faso; unsupervised effectiveness) and 95.6% (Ibadan, Nigeria) to 99.8% (Guinea). Among the nine supervised efficacy studies, the pooled ACPR was 98.7% (95% CI: 97.5–99.3%; P < 0.001), with a 95% prediction interval of 91.6–99.8%. The two Nigerien studies returned the lowest supervised estimates (96.3% and 97.3%). When the unsupervised Nanoro study was added, the pooled estimate was 98.4% (95% CI: 94.8–99.5%), but heterogeneity rose sharply and the prediction interval widened to 41.8–100% (see below).

The lowest day-28 estimates were the unsupervised Nanoro study (77.8%) and the two Nigerien efficacy studies (Niger 2020: 96.3%; Niger 2022: 97.3%); the supervised studies all remained above the WHO 90% efficacy threshold, whereas the unsupervised Nanoro study fell below it.

Figure 2: Forest plot of the random-effects meta-analysis of the Adequate Clinical and Parasitological Response (ACPR) rate at day 28 following artemether-lumefantrine treatment across ten studies in West Africa



Effect sizes are pooled proportions (day-28 PCR-corrected ACPR) on the logit scale, back-transformed to percentages, under a DerSimonian-Laird random-effects model (inverse-variance weighting). Square sizes are proportional to study weight; the diamond represents the pooled estimate. Primary analysis (nine supervised studies): pooled ACPR = 98.7% (95% CI: 97.5–99.3%); I^2 = 60%; Tau^2 = 0.56; 95% prediction interval 91.6–99.8%. Including the unsupervised Nanoro study (ten studies): pooled ACPR = 98.4% (95% CI: 94.8–99.5%); I^2 = 94%; Tau^2 = 3.37; 95% prediction interval 41.8–100%.

Heterogeneity

Between-study heterogeneity was substantial and, contrary to the initial analysis, not attributable merely to a ceiling effect. Among the nine supervised studies, I^2 = 60% with Tau^2 = 0.56; including the unsupervised Nanoro study, I^2 = 94% with Tau^2 = 3.37. The non-zero Tau^2 indicates genuine between-study variance in true efficacy. The principal driver was the unsupervised Nanoro effectiveness study (77.8%) and, secondarily, the two Nigerien efficacy studies (96.3% and 97.3%), likely reflecting higher transmission intensity and multi-site variability. The wide prediction interval shows that high efficacy cannot be assumed uniform across all West African settings and conditions of use.

Publication Bias

Funnel plot inspection (Figure 3) shows the studies clustered at high ACPR with low standard errors, with one clear outlier: the unsupervised Nanoro effectiveness study at 77.8%. With only ten studies, and given that supervised efficacy and unsupervised effectiveness measure different constructs, the plot should be interpreted cautiously and is not a reliable basis for inferring selective non-publication. Formal quantitative assessment of asymmetry by Egger's regression test was not undertaken, as it is uninformative and potentially misleading with so few studies. The possibility of publication bias attributable to non-reporting of studies with lower ACPR cannot be excluded and is acknowledged as a limitation.

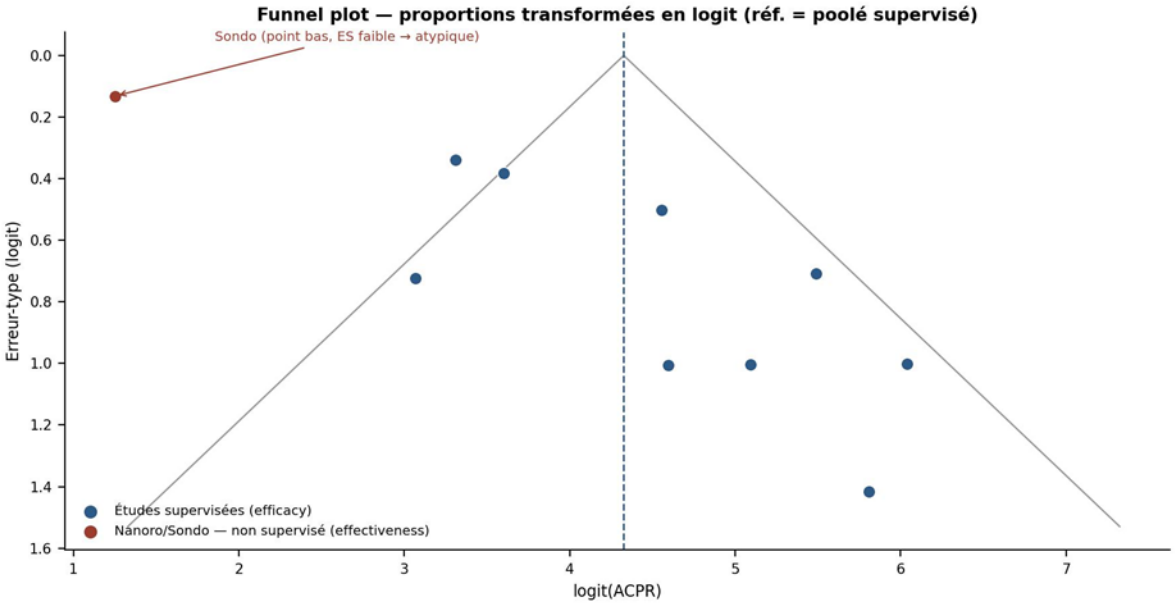


Figure 3: Funnel plot for the assessment of publication bias in the random-effects meta-analysis of ACPR at day 28 following artemether-lumefantrine treatment (n = 10 studies)

All studies show high ACPR with low standard errors except the unsupervised Nanoro effectiveness study (77.8%), which appears as an outlier. With only ten studies and a mix of supervised efficacy and unsupervised effectiveness designs, the plot is not a reliable basis for assessing publication bias.

Sensitivity Analyses

Sensitivity analyses were conducted to assess the robustness of the pooled estimate. Results are summarised in Table 4. The single most influential factor was whether the unsupervised Nanoro effectiveness study was included.

Excluding the unsupervised Nanoro study (Burkina Faso) — which measures real-world effectiveness rather than supervised efficacy — yielded a pooled ACPR of 98.7% (95% CI: 97.5–99.3%) with I^2 = 60% and Tau^2 = 0.56; this is our primary analysis. Excluding the multicentre study (Cameroon, Côte d'Ivoire, Senegal) while retaining Nanoro gave 98.4% (95% CI: 94.3–99.5%; I^2 = 94%); excluding both gave 98.7% (95% CI: 97.2–99.4%; I^2 = 62%). Excluding the Liberia study gave 98.4% (95% CI: 94.3–99.5%; I^2 = 95%). The pooled estimate is therefore stable around 98–99% across exclusions, but the magnitude of heterogeneity depends almost entirely on whether the unsupervised Nanoro study is included.

Across analyses, the pooled estimate remained between 98.3% and 98.7%. However, heterogeneity was driven overwhelmingly by the unsupervised Nanoro study: with it, $I^2 \approx 94\%$ and $Tau^2 \approx 3.4$; without it, $I^2 \approx 60\%$ and $Tau^2 \approx 0.56$. This confirms that the heterogeneity is genuine and concentrated in the difference between supervised efficacy and unsupervised real-world effectiveness, rather than being a statistical artifact.

Table 4: Sensitivity Analyses — Summary of Results

Analysis	Studies (N)	Pooled proportion (95% CI)	Z	P	I^2 (%)	Tau^2
All studies, incl. Nanoro (n = 10)	10 (2,617)	0.984 [0.948, 0.995]	—	<0.001	94%	3.37
Primary — supervised studies only (n = 9)	9 (2,284)	0.987 [0.975, 0.993]	—	<0.001	60%	0.56
Excl. Multicentre (non-ECOWAS site)	9 (2,233)	0.984 [0.943, 0.995]	—	<0.001	94%	3.26
Excl. Nanoro + Multicentre	8 (1,900)	0.987 [0.972, 0.994]	—	<0.001	62%	0.66
Excl. Liberia (non-PCR-corrected)	9 (2,517)	0.984 [0.943, 0.995]	—	<0.001	95%	3.36

Summary of pre-specified sensitivity analyses

Safety and Adverse Events

Adverse event data were available for all eleven qualitative synthesis studies. Across studies, no serious adverse event (SAE) attributable to AL

was reported. The Nigeria 2025 study (AL arm n=166; Phase IV) explicitly confirmed zero SAEs. The Liberia 2011 study reported 10% mild-to-moderate adverse events (nausea, dizziness, vomiting) with no deaths. The Benin 2008-2009 study reported AL as well-tolerated with no major adverse events. Cardiac adverse events (QTc prolongation) were not systematically measured across most studies.

Overall, AL demonstrated an excellent tolerability profile across diverse West African populations and age groups. Treatment discontinuation due to adverse events was rare (< 1% where reported).

Discussion

This meta-analysis indicates that, under supervised conditions, AL maintains high day-28 efficacy (pooled 98.7%, 95% CI 97.5–99.3%) against uncomplicated P. falciparum malaria in West Africa, consistent with WHO guidance (WHO Malaria Policy Advisory Group, 2022; World Health Organization, 2015). Two findings, however, temper the picture of uniformly near-perfect efficacy. First, between-study heterogeneity is genuine ($Tau^2 > 0$), not an artifact of proportions approaching unity. Second, real-world effectiveness under unsupervised treatment was markedly lower (77.8% in Nanoro; Sondo, 2015), falling below the WHO 90% threshold; the 95% prediction interval for supervised studies (91.6–99.8%) has a lower bound close to that threshold.

The heterogeneity requires careful interpretation. Among supervised studies the ACPR range is clinically narrow (95.6–99.8%) and all remain above the WHO 10% failure threshold; here the moderate I^2 (60%) reflects sensitivity to small absolute differences when proportions approach 1.0. The unsupervised Nanoro study (77.8%) is the exception and the main source of overall heterogeneity. Clinically meaningful sources of variation include differences in study population age, site-level transmission intensity (high in Niger), variability in PCR-correction methodology, supervised versus unsupervised administration, and design differences between single-arm TES and comparative RCTs.

The two Nigerien studies (Niger 2020: 96.3%, Laminou, 2024; Niger 2022: 97.25%, Laminou, 2025) consistently produced the lowest ACPR estimates. Niger has among the highest malaria transmission intensities globally (World Health Organization, 2023), and high transmission increases the risk of new infections during follow-up that may be misclassified as recrudescence without PCR correction (World Health Organization, 2009). Continued vigilance in Niger, including PCR-corrected TES and molecular surveillance for kelch13 mutations (Uwimana, 2020), is warranted.

The safety findings are reassuring. Across eleven studies spanning over fifteen years of AL use in West Africa, no serious drug-related adverse

event or death was attributed to AL. Mild adverse events (nausea, vomiting, dizziness, headache) were reported in a minority of patients and resolved spontaneously. This profile is consistent with global pharmacovigilance data on AL (Bakshi, 2000) and supports its continued use across age groups, including children under five — the highest-risk population.

AL should be retained as first-line treatment for uncomplicated *P. falciparum* malaria across West African national malaria control programmes. The supervised efficacy evidence, extending through 2026, shows no clear erosion over time; however, the lower real-world effectiveness observed under unsupervised treatment, and the lower prediction-interval bound approaching the WHO threshold, warrant vigilance. The following are recommended: (i) systematic TES at sentinel sites every two years per WHO protocol (World Health Organization, 2009); (ii) integration of molecular markers of artemisinin partial resistance (kelch13) into routine surveillance (Ashley, 2014; Uwimana, 2020); (iii) strengthened pharmacovigilance with standardised adverse-event reporting; (iv) attention to treatment adherence and to administration of AL with fatty food (Sondo, 2015); and (v) particular attention to Niger, which showed the lowest supervised ACPR rates in this analysis.

Strengths: broad geographic coverage across seven countries and one multicentre site; strict PRISMA 2020 methodology; use of PCR-corrected ACPR as primary outcome; random-effects model appropriate for the observed heterogeneity; inclusion of studies spanning 2008–2026 allowing temporal trends to be assessed; four pre-specified sensitivity analyses confirming robustness of the primary estimate across different study exclusion scenarios.

Limitations: single-arm design of most included studies limits causal inference; inconsistent PCR correction across studies may introduce heterogeneity; adverse event reporting was not standardised; the Liberia 2011 study had moderate-to-high risk of bias; potential publication bias cannot be fully excluded; and the multicentre study (Cameroon, Côte d'Ivoire, Senegal) includes sites partially outside the strict ECOWAS West Africa definition.

Conclusions

Under supervised conditions, artemether-lumefantrine retains high day-28 efficacy against uncomplicated Plasmodium falciparum malaria in West Africa (pooled ACPR 98.7%, 95% CI 97.5–99.3%), and can be retained as first-line treatment. The drug is well-tolerated, with no serious adverse events attributed to AL in any included study.

Between-study heterogeneity is genuine rather than a statistical artifact, and is concentrated in the contrast between supervised efficacy and

unsupervised real-world effectiveness (77.8% in Nanoro). Because the lower bound of the prediction interval approaches the WHO action threshold, regular protocol-standardised efficacy monitoring — complemented by molecular resistance surveillance and attention to treatment adherence — remains essential to detect any future decline at the earliest stage.

Conflict of Interest: The authors reported no conflict of interest.

Data Availability: All data are included in the content of the paper.

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