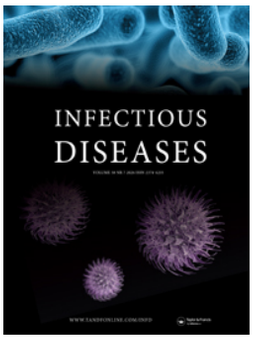

Infectious Diseases

ISSN: 2374-4235 (Print) 2374-4243 (Online) Journal homepage: www.tandfonline.com/journals/infd20

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To cite this article: Gbeminiyi R. Otolorin , María Eugenia. Castellanos , Oyelola A. Adegboye , Himali E. Ratnayake & Emma S. McBryde (14 Jun 2026): Impact of insecticide-treated nets on malaria morbidity and mortality: a systematic review and meta-analysis of randomized controlled trials, Infectious Diseases, DOI: 10.1080/23744235.2026.2666823

To link to this article: https://doi.org/10.1080/23744235.2026.2666823

INFECTIOUS DISEASES
https://doi.org/10.1080/23744235.2026.2666823

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Impact of insecticide-treated nets on malaria morbidity and mortality: a systematic review and meta-analysis of randomized controlled trials

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ABSTRACT

Introduction: This systematic review and meta-analysis examined the efficacy of insecticide-treated nets (ITNs) in reducing malaria incidence and malaria-related mortality among vulnerable populations.

Methodology: A comprehensive search of Scopus, Medline, and CINAHL (up-to-April 2, 2026) identified experimental studies (randomised and cluster-randomised trials) evaluating the effect of ITNs impact for malaria control, and the protocol was registered in PROSPERO (CRD42024609183). Pooled-effect-sizes [rate-ratios(RRs) and odds-ratios (ORs)] were calculated, and meta-regression was conducted to examine study-level sources of variation in effect estimates.

Results: A total of 25 studies were included in the meta-analysis, including 19 assessing malaria-incidence and 6 evaluating malaria-related mortality. Overall, ITNs demonstrated strong protective effects across diverse populations. The pooled-estimate using a random-effects model showed a 29% reduction in malaria incidence among ITNs users in Africa (RR = 0.71; 95% CI: 0.54–0.93; $p = 0.0133$; $I^2 = 64\%$) and 68% in Asia (RR = 0.32; 95% CI: 0.17–0.62; $p = 0.0007$; $I^2 = 89.0\%$). The pooled-odds-ratio for malaria incidence in African studies indicated a 40% reduction in odds (OR = 0.60; 95% CI: 0.44–0.82; $p = 0.0011$; $I^2 = 86.2\%$), whereas the pooled-rate-ratio for malaria-related-mortality in Asia was 0.82 (95% CI: 0.77–0.89; $p < 0.0001$; $I^2 = 0$) from 5 studies, indicating an 18% reduction in mortality. Meta-regression on 17 studies confirmed an overall significant protective effect of ITNs against malaria($\beta = -0.84$; 95% CI: −1.68 to −0.01; $p = 0.05$).

Conclusion: ITNs reduce malaria transmission, though effectiveness varies across regions due to ecological, epidemiological, and implementation differences.

ARTICLE HISTORY
Received 25 October 2025
Revised 8 April 2026
Accepted 24 April 2026

KEYWORDS
Malaria; insecticide-treated nets; malaria incidence; randomised controlled trials; cluster randomised controlled trials; malaria control

Introduction

Malaria is one of the key infectious diseases of global public health significance, with approximately 263 million new cases reported in 2023 across 83 countries, marking an increase from 252 million in 2022. Malaria-related deaths also rose, reaching approximately 597,000 globally in 2023. The heaviest burden is concentrated in the African Region, with approximately 94%of worldwide cases and 95% of malaria-related fatalities [1]. While malaria control programs have successfully prevented over 2.1 billion cases and over 12.5 million deaths since 2000, high-burden countries such as Nigeria, the Democratic Republic of Congo, and Ethiopia still face significant challenges [1]. Malaria occurs when *Plasmodium* parasites, transmitted by *Anopheles* mosquitoes infect a person, with young children and pregnant women at the

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Supplemental data for this article can be accessed online at https://doi.org/10.1080/23744235.2026.2666823.

highest risk [2]. ITNs stand out as a key effective control method, offering personal protection while reducing both mosquito populations and malaria transmission within communities [3].

Experimental studies, particularly Randomised Controlled Trials (RCTs) and Cluster Randomised Controlled Trials (cRCTs), have demonstrated that ITNs effectively reduce malaria. These studies examine the efficacy of ITNs by comparing them to non-ITNs and/or no nets for malaria prevention [4–7]. Major cRCTs in Kenya, Gambia, and India have shown significant reductions in malaria cases and deaths, with the greatest impact observed in the ITNs group, particularly among children under five [8–10]. They assessed ITNs effectiveness by tracking malaria infections and malaria-related mortality rates. However, ITNs effectiveness varies across regions, making it essential to adapt studies to local conditions. Cluster randomised controlled trials are well-suited for this, as they randomise entire communities, allowing researchers to measure ITNs impacts at both individual and community levels in diverse settings [11,12].

ITNs are widely used as a key malaria prevention strategy, with strong evidence demonstrating their protective efficacy compared to untreated nets or no nets [4–7,13]. Major community-based randomised trials conducted in Kenya, The Gambia, India, and Tanzania have demonstrated significant reductions in malaria incidence [8–10,14,15]. However, the effectiveness of ITNs varies across regions, emphasising the importance of tailoring interventions to specific local contexts. These inconsistencies highlight the need for a rigorous synthesis of experimental evidence to improve understanding of ITN performance across different settings. This systematic review and meta-analysis therefore evaluates the efficacy of insecticide-treated nets (ITNs) in reducing malaria incidence and malaria-related mortality using data from randomised controlled trials (RCTs) and cluster randomised controlled trials (cRCTs). The review also examines the potential influence of factors such as geographic region, population characteristics, and study design on the effectiveness of ITNs. The findings aim to provide insights to inform context-specific and regionally tailored malaria control strategies.

While the previous Cochrane review by Pryce et al. [7] provides a comprehensive synthesis of ITN efficacy, the present review complements and extends that work by focusing specifically on studies evaluating the effectiveness of ITNs in real-world settings. This review uniquely focuses on the two most critical public health outcomes: malaria morbidity (incidence) and malaria-related mortality, aligning directly with the global targets that guide malaria control and elimination strategies. Unlike broader reviews that include a range of secondary and indirect outcomes, our review focuses on primary endpoints. This approach reduces clinical and methodological variability and enhances the precision, comparability, and interpretability of the pooled results. Furthermore, we limited inclusion to experimental studies (RCTs and cRCTs) that compared ITNs with no net use. This restriction provides a more accurate estimate of their protective effect, minimising the confounding influence of untreated nets. This rigorous approach offers the clearest possible evidence of the true impact of ITNs scale-up for policymakers and implementers. As a result, our review not only complements but also refines and broadens the existing evidence base, ensuring that its findings are both scientifically robust and practically relevant for decision-making in malaria control programmes. The unique contribution of this review lies in its focused evaluation, limiting inclusion to studies reporting direct malaria morbidity and mortality outcomes, and excluding comparisons involving untreated nets to minimise potential confounding and better attribute observed effects to the insecticidal component of ITNs. By focusing on comparisons that more clearly isolate the effect of ITNs, this review provides a more targeted and methodologically consistent synthesis of their epidemiological impact.

Methods

Search strategy and selection criteria

A systematic literature review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [16], and the completed PRISMA 2020 checklist is provided as Supplementary Material (Appendix 1of the Supplementary Materials). A comprehensive literature search was conducted across Scopus, Ovid MEDLINE, and CINAHL from database inception to April 2, 2026. The search strategy, designed in collaboration with a specialist librarian, encompassed all available studies from the databases' inception to the search date. The review focused exclusively on

peer-reviewed publications relevant to the study objectives. Search terms included: 'Insecticide-treated bednets', and combinations such as (malaria* OR 'marsh fever' OR paludism OR '*plasmodium infection*' OR 'infections' OR 'remittent fever' OR 'black water fever' OR 'black water fevers') and (insecticide-treated net* OR ITN* OR long lasting insecticidal net* OR LLIN*). A complete list of search terms is presented in Appendix 2 (Tables S1A–S1C) of the Supplementary Materials. The articles were compiled in an EndNote 20 library, where they were first screened for duplicates and non-English publications using EndNote's built-in features, followed by a manual check.

In addition to the primary systematic search, a supplementary targeted search was conducted to identify recent evidence on next-generation insecticide-treated nets/long-lasting insecticidal nets (LLINs) in relation to insecticide resistance and malaria control. This additional search was intended to capture emerging literature on resistance-responsive net technologies that may not have been adequately retrieved through broader search strategies focused primarily on conventional insecticide-treated nets (ITNs). The search was performed in Scopus using the title, abstract, and keyword fields.

The supplementary search strategy was structured around three core concepts: malaria control, insecticide resistance, and next-generation ITNs technologies. Search terms were selected to reflect both general and product-specific terminology used in the contemporary literature. These included: 'malaria control', 'insecticide resistance', 'next-generation insecticide-treated nets', 'next-generation long-lasting insecticidal nets', and 'dual active ingredient nets'. These terms were applied individually and in combination using Boolean operators to maximise search sensitivity while maintaining conceptual relevance. The principal Scopus search strings included: TITLE-ABS-KEY('malaria control' AND 'insecticide resistance'), TITLE-ABS-KEY('next-generation insecticide-treated nets'), TITLE-ABS-KEY('next-generation long-lasting insecticidal nets'), and TITLE-ABS-KEY('dual active ingredient nets'). Retrieved records were screened initially by title and abstract for relevance. Full texts of potentially eligible studies were then assessed for inclusion based on their relevance to the review objective, with particular emphasis on studies evaluating the role of next-generation LLINs in overcoming insecticide resistance and improving malaria control outcomes. This supplementary search was undertaken to strengthen the evidence base on newer ITN technologies and to ensure that recent developments in resistance-responsive vector control were adequately represented in the review, with the findings incorporated into the discussion section to contextualise the effectiveness of conventional ITNs within the evolving landscape of insecticide resistance and next-generation ITNs strategies. This review was registered with PROSPERO under registration number CRD42024609183.

This systematic review focused exclusively on studies conducted in human populations. The following inclusion criteria were applied (1) only experimental studies assessing the protective efficacy of ITNs or ITNs in human populations; (2) studies that employed either a RCT or cRCT design to ensure methodological rigour; (3) studies evaluating malaria incidence and malaria-related mortality; (4) clearly defined populations with detailed descriptions of both the intervention and control groups; (5) studies that directly compare ITNs with a control group (no nets). In cases where multiple studies utilised the same population, the most up-to-date and complete study was selected to avoid duplication. The following exclusion criteria were applied (1) non-experimental studies, including observational or modelling studies; (2) studies lacking a control group, as this would prevent direct comparison of ITNs effectiveness; (3) studies that did not measure malaria incidence or malaria-related mortality as primary outcomes; and (4) publications in languages besides English.

Data extraction

A structured data extraction table was created using Excel (Version 16.63.1) to systematically categorise, analyse, and document the selected studies. The screening process followed PRISMA guidelines and initially identified 2,088 articles. GO and HR conducted the primary screening, while OA, MC, and EM performed the secondary screening of studies selected for inclusion. Discrepancies were resolved through discussion to reach consensus between the authors; where consensus could not be achieved, EM made the final decision regarding study inclusion. Full-text articles for studies that passed the secondary screening were retrieved and assessed by GO to confirm their eligibility for inclusion in the systematic review. In cases where inconsistencies were found in the assessments of publications, the entire review team engaged in discussions to resolve the issues and ensure accurate extraction.

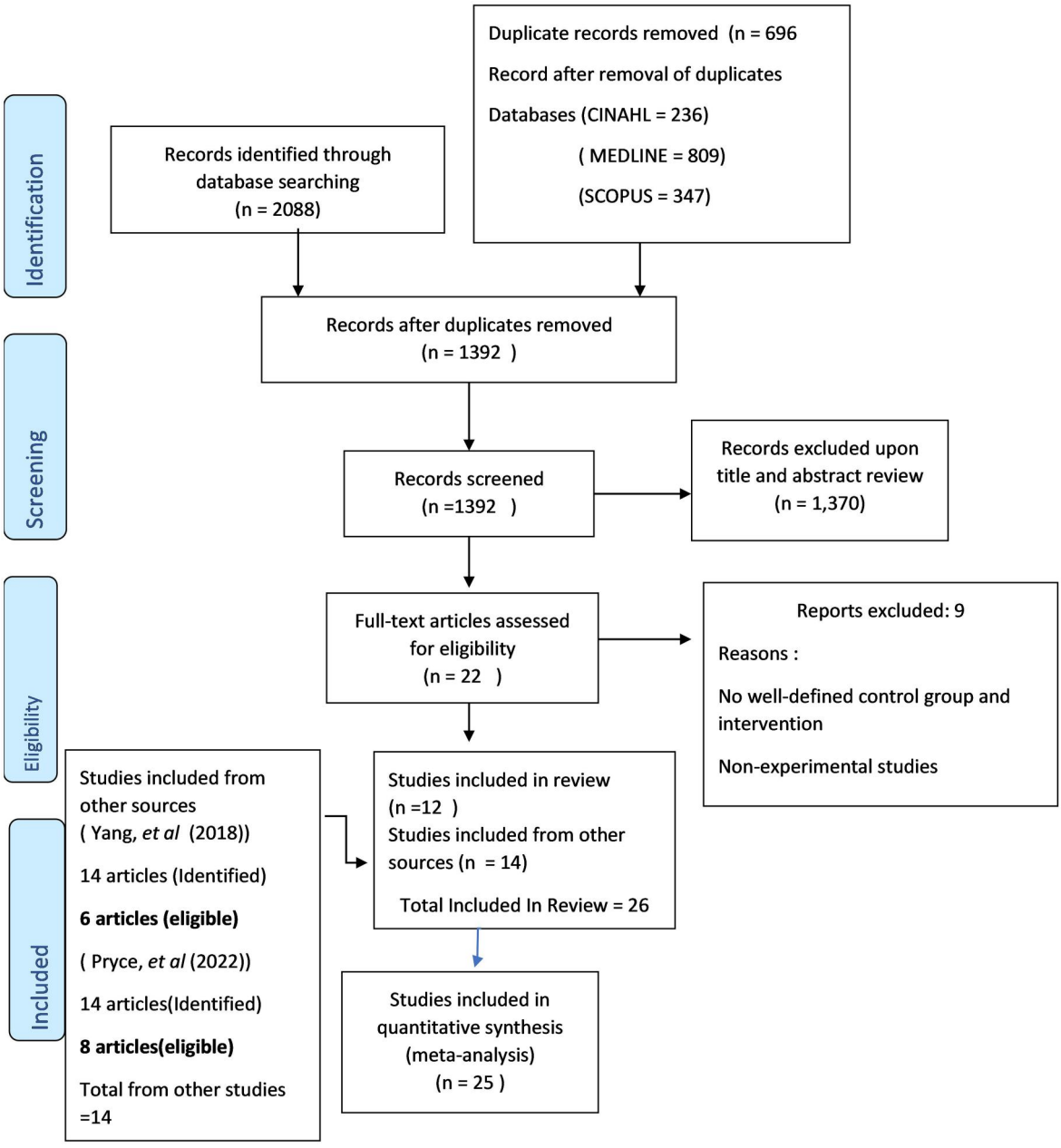

Figure 1. PRISMA diagram for this systematic review on evaluating the effectiveness of insecticide-treated nets (ITNs) in malaria control.

After screening the titles and abstracts, 1,370 articles were removed based on predefined exclusion criteria, including the lack of a well-defined control group, non-experimental study design, or non-inclusion of prespecified outcome data. This resulted in 22 full-text articles being assessed for eligibility. Following a thorough screening and eligibility assessment based on predefined inclusion and exclusion criteria, 12 studies were selected for inclusion in the systematic review.

To enhance the comprehensiveness of the review, additional studies were sourced from systematic reviews by Yang et al. [17] and Pryce et al. [7]. From Yang et al. [17], 14 articles were selected, and 6 of them met the eligibility criteria, while from Pryce et al. [7], 14 articles were screened, with 8 qualifying for inclusion. Combining these 14 externally sourced studies with the 12 selected from the initial search yielded a final dataset of 26 studies (Figure 1).

Quality assessment

The 26 selected studies underwent quality assessment, which was conducted independently by GO, MC, HR and OA. The methodological quality of the included studies was assessed using the Cochrane Risk of Bias Tool Version 1 (RoB v1). Risk of bias was evaluated across nine domains relevant to randomised and cluster-randomised trials: (D1) random sequence generation, (D2) allocation concealment, (D3) baseline outcome measurements, (D4) similarity of baseline characteristics, (D5) incomplete outcome data, (D6) blinding of participants, (D7) protection against contamination between study groups, (D8) selective outcome reporting, and (D9) overall risk of bias judgement. Each domain was rated as low, high, or unclear risk of bias based on the study's methodological quality. Any discrepancies in the evaluation were resolved with input from a fifth researcher (EM). Quality assessment was conducted to ensure that the studies met high methodological rigour and reliability standards, focusing on factors such as study design, data handling, and outcome measurement to accurately assess the efficacy of ITNs in malaria control. Sreehari et al. [8] was identified as having a high risk of bias across multiple domains and excluded from further quantitative meta-analysis to maintain result reliability (Appendix 3: FigureS1of the Supplementary Materials). Of the 26 studies initially included in the systematic review, one study [8] was excluded from the quantitative synthesis due to a high risk of bias. Consequently, 25 studies were included in the meta-analysis to generate pooled effect estimates.

Data analysis

The study assessed the effectiveness of ITNs in malaria control using mainly rate ratios (RRs) and odds ratios (ORs), as primary effect measures. Risk ratios (RRs) and hazard ratios (HRs) were also analysed in some studies. Malaria incidence and malaria-related mortality were the primary outcomes. Differences in study methodologies, effect measures, and population characteristics were anticipated. Therefore, a random-effects model was used to estimate pooled RRs and ORs with corresponding 95% confidence intervals. The results were visualised using separate forest plots for malaria incidence and malaria-related mortality, displaying both individual and pooled estimates. Heterogeneity was assessed using the I^2 statistic and tau^2, allowing for a robust evaluation of variability among the included studies.

To further explore differences in effect estimates across studies, subgroup analyses and meta-regression were conducted. Subgroup forest plots were generated to obtain pooled effect estimates across geographic regions (Africa vs. Asia), study design (RCT vs. cRCT), and population type (children, pregnant women, general population) to determine variations in ITNs effectiveness. Meta-regression was performed to quantify the impact of study characteristics on variation in effect estimates across studies.All analyses were performed in R software (version 4.1.2) [18,19] using the meta [20] and metafor [21] packages.

Results

Systematic review

This review included 26 studies evaluating the effect of ITNs on malaria incidence and mortality compared to no net use. Among them, 14 were cRCTs, and 12 were individual RCTs. The studies were conducted in eight African countries (Gambia, Ghana, Kenya, Sierra Leone, Tanzania, Côte d'Ivoire, Zambia, Burkina Faso) and four Asian countries (India, Myanmar, Cambodia, China) (Figure 2). The populations studied included children under five, pregnant women, and entire households or communities. Follow-up periods ranged from two months to five years, depending on the study (Tables 1–4). Most studies reported malaria incidence as the primary outcome, while others focused on malaria-related mortality. Effect sizes were mostly expressed as rate ratios (15 studies), odds ratios (eight studies), risk ratio (one study), and hazard ratios (two studies) (Tables 1–3).

Most studies ($n = 24$) showed a protective effect of ITNs; for example, Sahu et al. [35] found a rate ratio of 0.14 (95% CI: 0.09–0.23) in tribal villages in India, and Hill et al. [39] reported an odds ratio of 0.09 (95% CI: 0.03–0.28) in Yunnan, China. D'Alessandro et al. [10] reported a rate ratio of 0.75 (95% CI: 0.57–0.98) for malaria-related mortality among children. Bhatt et al. [38] reported a rate ratio of 0.37

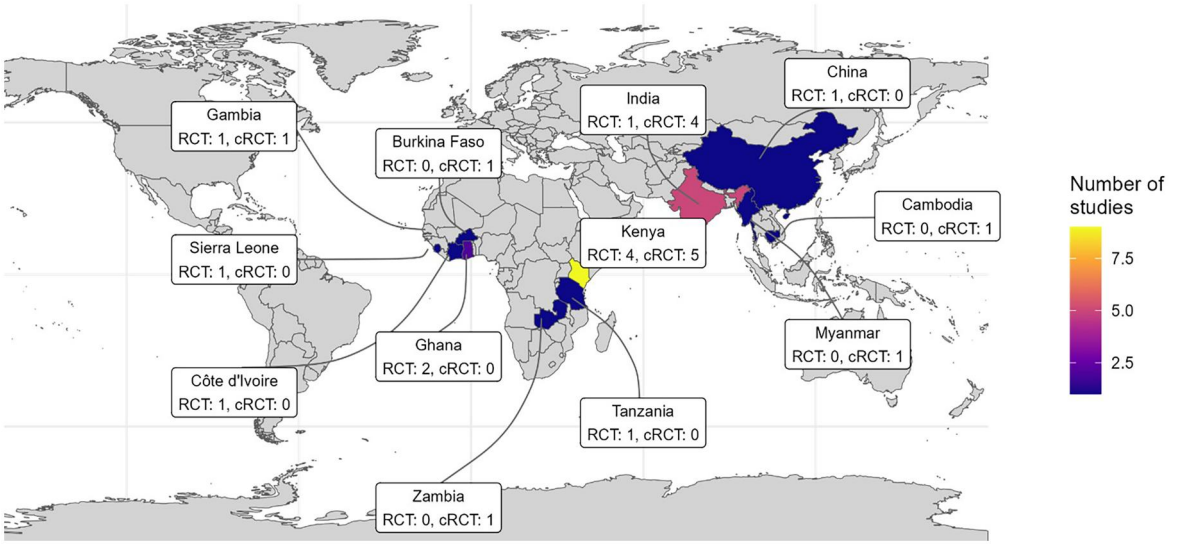

Figure 2. Geographic distribution of included studies.

Table 1. Description of studies included in the systematic review and meta-analysis on malaria incidence in Africa.

Study	Ref	Study design	country	Intervention employed vs. control	Population details	Outcome measures	Effect measures	Value with 95% Confidence Interval	Follow-up duration
Browne et al. (2001)	[22]	RCT	Ghana	ITNs vs. No Nets	Pregnant women in Northern Ghana	Malaria incidence	Odds ratio	0.89[0.73–1.08]	9 months
Phillips-Howard et al. (2003b)	[23]	cRCT	Kenya	ITNsvs.No Nets	Children under 5 years visiting health facilities	Malaria incidence	Rate ratio	0.97[0.66–1.44]	4 years
Shulman et al. (1998)	[24]	RCT	Kenya	ITNs vs. No Nets	Primigravid women in Kenya	Malaria incidence	Risk ratio	0.88[0.50–1.54]	14 months
Ter Kuile et al. (2003a)	[25]	cRCT	Kenya	ITNs vs. No Nets	Pregnant women in Western Kenya	Malaria incidence	Hazard ratio	0.72[0.19–2.78]	2 years
Ter Kuile et al. (2003b)	[26]	cRCT	Kenya	ITNs vs. No Nets	Infants in Western Kenya	Malaria incidence	Rate ratio	0.48[0.33–0.70]	2 years
Hawley et al. 2003	[13]	RCT	Kenya	ITNsvs.No Nets	Households with children in Western Kenya	Malaria Incidence	Odds ratio	0.52[0.33–0.83]	12 months
Henry et al. 2005	[27]	RCT	Côte d'Ivoire	ITNs vs. No Nets	Children aged 0–59 months	Malaria Incidence	Rate ratio	0.43[0.25–0.74)	12 months
Sedlmayr et al. 2013	[28]	cRCT	Zambia	ITNsvs.No Nets	Cotton farming households	Malaria Incidence	Odds ratio	0.51[0.34–0.78]	2 months
Fraser-Hurt et al. 1996	[29]	RCT	Tanzania	ITNs vs. No Nets	Children aged 5–24 months	Malaria Incidence	Rate ratio	1.02[0.71–1.47)	6 months
Marbiah et al. 1998	[30]	RCT	Sierra Leone	ITNs vs. No Nets	Children aged 3 months to 6 28 years	Malaria Incidence	Odds ratio	0.51[0.44–0.58]	12 months
Sexton et al. 1990	[31]	RCT	Kenya	ITNs vs. No Nets	Families in Uriri, Kenya	Malaria Incidence	Rate ratio	0.70[0.48–0.99]	15 weeks
Snow et al. 1988	[32]	RCT	Gambia	ITNs vs. No Nets	Children aged 1–9 years	Malaria Incidence	Rate ratio	0.78[0.52–1.17]	Rainy season

Study design abbreviations: RCT: randomised controlled trial; cRCT: cluster randomised controlled trial.
Intervention: ITNs = Insecticide-Treated Netsused during the study; Control group: No nets used during the study.

(95% CI: 0.29–0.48)and Ter Kuile et al. [26] reported a rate ratio of 0.48 (95% CI: 0.33–0.70), all indicating significant reductions in malaria incidence. However, two studies reported no significant protective effect, with Fraser-Hurt et al. [29] showing a rate ratio of 1.02 (95% CI: 0.71–1.47) and Sahu et al. [41] reporting an odds ratio of 2.77 (95% CI: 1.70–4.52) ((Tables 1–3). Table 3 reports the studies on malaria incidence in Africa, Table 2 details the studies on malaria-related mortality in Africa, and Table 3 outlines the studies on malaria incidence in Asia).

Risk of bias assessment

The risk of bias assessment indicated that 22 out of 25 studies (88%) were rated as low risk for random sequence generation (Figure S1 in Appendix 3 of the Supplementary Materials). Also, all 25 studies (100%) demonstrated a low risk in baseline outcome measurements, protection against contamination,

Table 2. Description of studies included in the systematic review and meta-analysis on malaria-related mortality in Africa.

Study	Ref	Study design	Country	Intervention employed vs. control	Population details	Outcome measures	Effect measures	Value with 95% Confidence Interval	Follow-up duration
D'Alessandro et al. (1995)	[10]	cRCT	Gambia	ITNs vs. No Nets	Children 1–9 years	Malaria-related mortality	Rate ratio	0.75[0.57–0.98]	1 year
Phillips-Howard et al. (2003)	[9]	cRCT	Kenya	ITNs vs. No Nets	Children aged 1–59 months	Malaria-related mortality	Rate ratio	0.84[0.77–0.93]	2 years
Lindblade et al. 2004	[33]	RCT	Kenya	ITNs vs. No Nets	Children under 5 in Asembo and Gem	Malaria-related mortality	Hazard ratio	0.78[0.67–0.90]	60 months
Binka et al. 1996	[4]	RCT	Ghana	ITNs vs. No Nets	Children aged 6 months to 4 years	Malaria-related mortality	Rate ratio	0.83[0.69–1.00]	24 months
Habluetzel et al. 1997	[5]	cRCT	Burkina Faso	ITNs vs. No Nets	Children aged 6–59 months	Malaria-related mortality	Rate ratio	0.85[0.7–1.04]	24 months
Nevill et al. 1996	[34]	cRCT	Kenya	ITNs vs. No Nets	Children under 5 in rural coastal communities	Malaria-related mortality	Rate ratio	0.67[0.49–0.93]	24 months

Study design abbreviations: RCT: randomised controlled trial; cRCT: cluster randomised controlled trial.
Intervention: ITNs = Insecticide-Treated Nets used during the study; Control group: No nets used during the study.

Table 3. Description of studies included in the systematic review and meta-analysis on malaria incidence in Asia.

Study	Ref	Study design	Country	Intervention employed vs. control	Population details	Outcome measures	Effect measures	Value with 95% Confidence Interval	Follow-up duration
Sahu et al. (2008)	[35]	cRCT	India	ITNs vs. No Nets	Tribal villages, Orissa, India	Malaria incidence	Rate ratio	0.14[0.09–0.23]	19 months
Smithuis et al. (2013)	[36]	cRCT	Myanmar	ITNsvs.No Nets	Children under 10 years, Myanmar	Malaria incidence	Odds ratio	0.67[0.92–1.21]	10 months
Sochantha et al. (2006)	[37]	cRCT	Cambodia	ITNs vs. No Nets	Children in 34 villages under 5 years in Cambodia	Malaria incidence	Rate ratio	0.72[0.47–1.08]	10 months
Bhatt et al. (2012)	[38]	RCT	India	ITNsvs.No Nets	Tribal populations villages in Chhattisgarh, India	malaria incidence	Rate ratio	0.37[0.29–0.48]	3 years
Hill et al. 2014	[39]	RCT	China	ITNs vs. No Nets	Households in Yunnan, China	Malaria Incidence	Odds ratio	0.09[0.03–0.28]	Six monthly surveys
Study	Ref	Study design	Country	Intervention employed vs. control	Population details	Outcome measures	Effect measures	Value with 95% Confidence Interval	Follow-up duration
Sreehari et al. (2007)	[8]	cRCT	India	ITNs vs. No Nets	Rural villages in India	Malaria incidence	Odds ratio	0.04[0.02-0.007]	2 years
Sharma et al. 2009	[40]	cRCT	India	ITNs vs. No Nets	Tribal population in Sundargarh District, Orissa	Malaria incidence	Rate ratio	0.27[0.16–0.45]	1 year

Study design abbreviations: RCT: randomised controlled trial; cRCT: cluster randomised controlled trial.
Intervention: ITNs = Insecticide-Treated Nets used during the study; Control group: No nets used during the study.

Table 4. Meta-regression of intervention effect estimates by country, study design, and population type.

Moderator (reference category)	Estimate β	SE	z-value	p-value	95 % CI
Intercept (Country = Africa; Design = RCT; Population = General population)	−0.837	0.432	−1.935	0.053	[−1.68–0.011]
Country: Asia (vs. Africa)	−0.355	0.467	−0.759	0.448	[−1.270–0.561]
Study design: cRCT (vs. RCT)	0.336	0.412	0.817	0.414	[−0.471–1.144]
Population: Children (vs. General population)	0.336	0.432	0.777	0.437	[−0.511–1.182]
Population: Pregnant women (vs. General population)	0.720	0.842	0.855	0.392	[−0.930–2.370]

RCT: randomised controlled trial; cRCT: cluster-randomised controlled trial; SE: Standard Error.

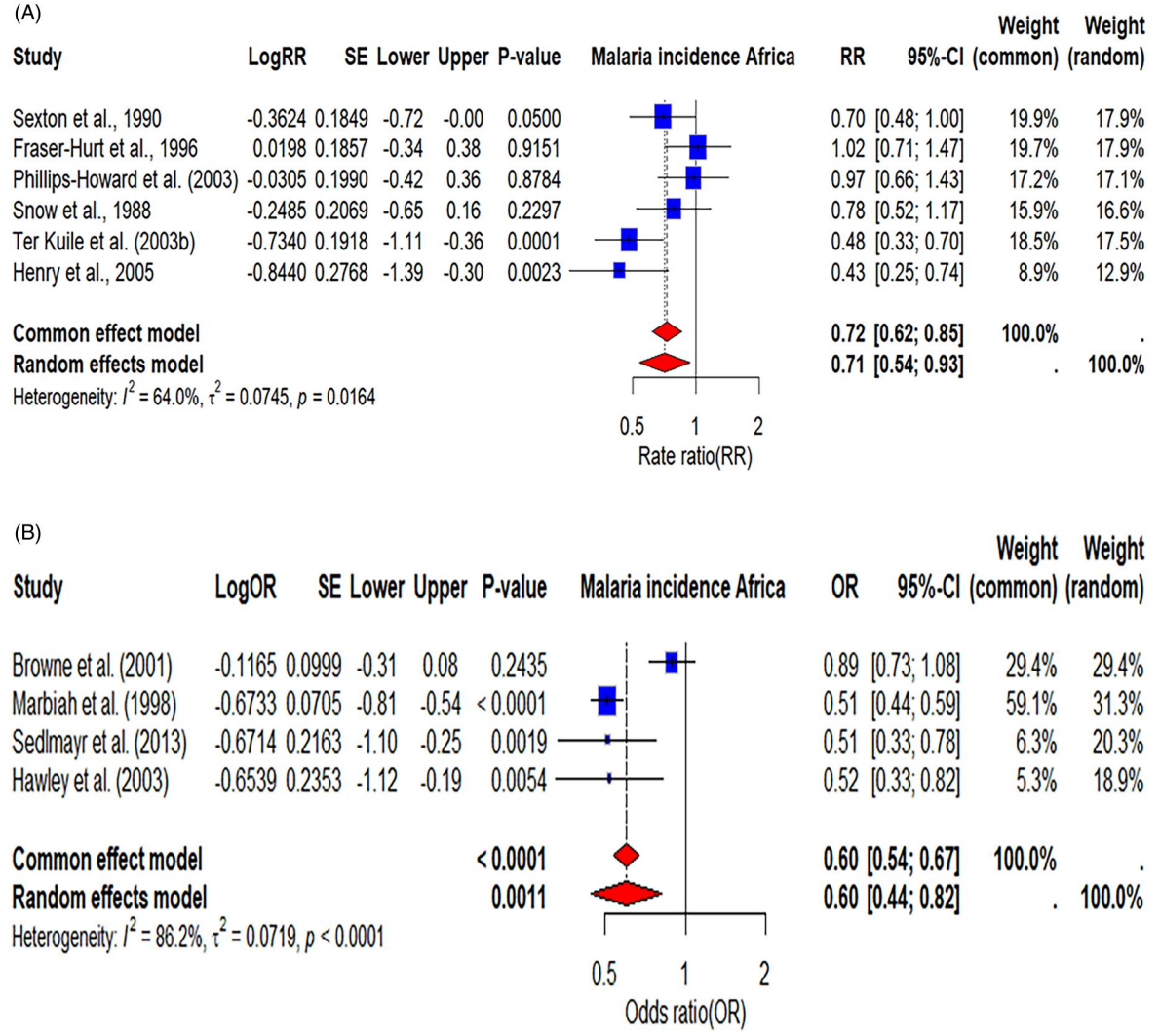

Figure 3. A. Forest plot showing the effect of ITNs on malaria incidence in Africa (Rate Ratio). B. Forest plot showing the effect of insecticide-treated nets ITNs on malaria incidence in Africa (Odds Ratio).

and selective outcome reporting. Additionally, 20 out of 25 studies (80%) were rated as low risk for incomplete outcome data. However, unclear risk was noted in allocation concealment and blinding of outcome assessment, primarily due to limited reporting. Despite some methodological concerns, the overall study quality was robust.

Meta-analysis of ITNs impact on malaria incidence and mortality

In Africa, six (6) studies reporting rate ratios revealed a 29% reduction in malaria incidence (RR = 0.71; 95% CI: 0.54–0.93; I^2 = 64.0%), while four (4) studies reporting odds ratios showed a 40% reduction (OR = 0.60; 95% CI: 0.44–0.82; I^2 = 86.2%) (Figures 3(A and B)). In Asia, four (4) studies reporting rate ratios demonstrated a 68% reduction in malaria incidence (RR = 0.32; 95% CI: 0.17–0.62; I^2 = 89.0%). However,

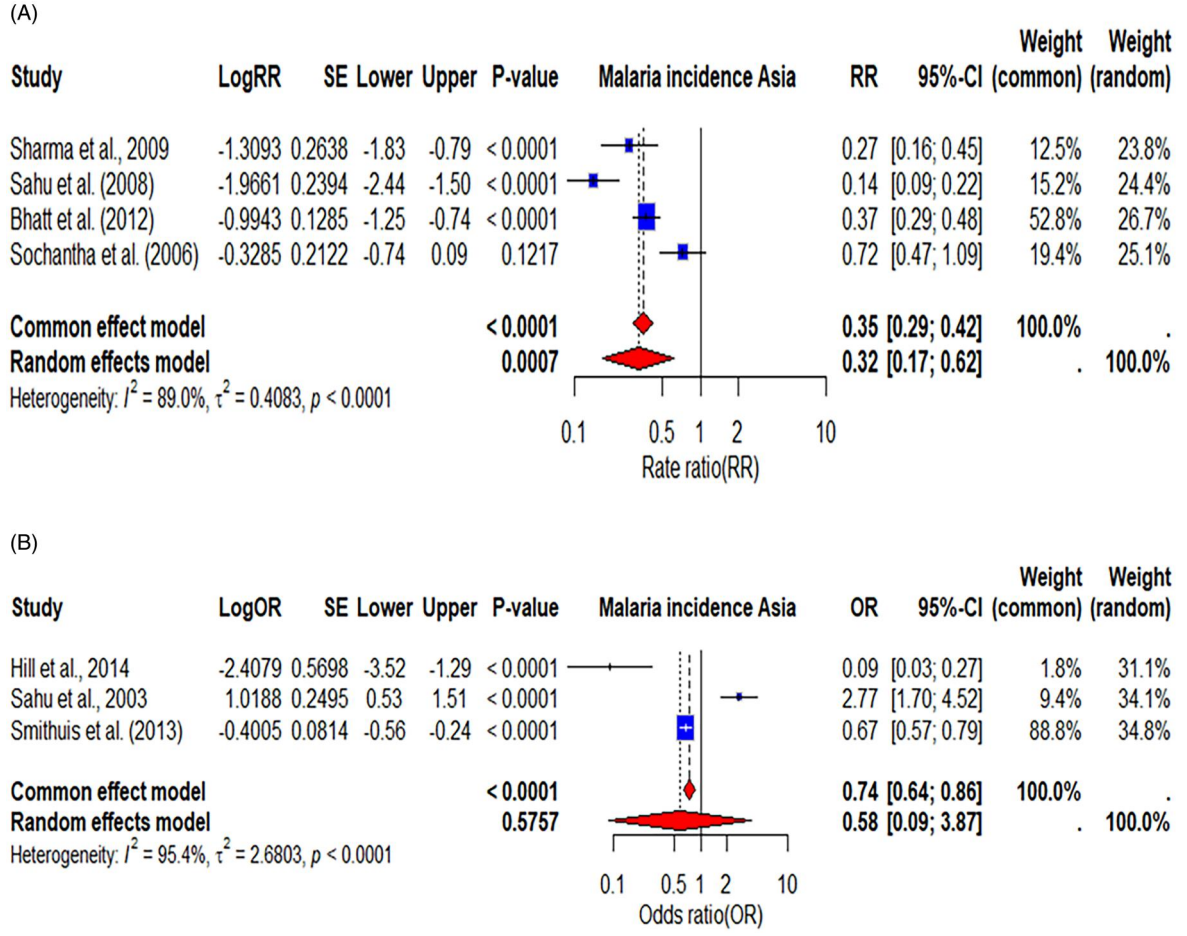

Figure 4. A. Forest plot showing the effect of ITNs on malaria incidence in Asia (Rate Ratio). B. Forest plot showing the effect of insecticide-treated nets ITNs on malaria incidence in Asia (Odds Ratio).

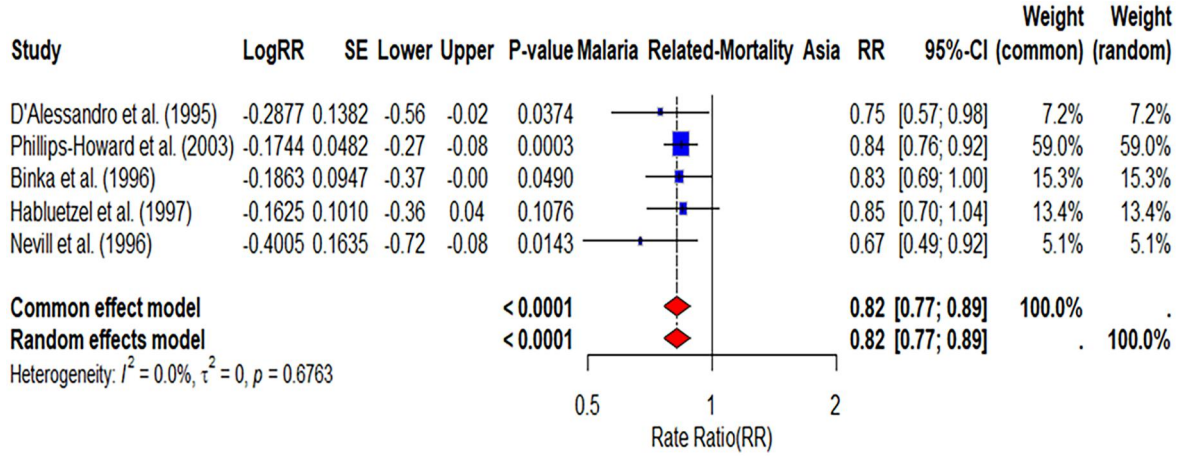

Figure 5. Meta-analysis of effects (Rate Ratio) ITNs interventions on malaria-related mortality in Asia.

the three (3) Asian studies that reported odds ratios showed substantial inconsistency in their effect estimates and no statistically significant pooled effect (OR = 0.58; 95% CI: 0.09–3.87; I^2 = 95.4%) (Figures 4(A and B)). Meta-Analysis of Rate Ratio of Malaria-Related Mortality in Asia Evaluating ITNs Interventions:

The meta-analysis showed a rate ratio (RR) of 0.82 (95% CI: 0.77–0.89; I^2 = 0%), indicating an 18% reduction in malaria-related mortality associated with ITN use, with consistent findings across the included studies (Figure 5). Three(3) studies reported effect measures of hazard ratios and a risk ratio,

that were not pooled due to the limited number of studies per metric. Lindblade et al. (2004) found a significant protective effect of ITNs on malaria-related mortality using a hazard ratio (HR = 0.78; 95% CI: 0.67–0.90; $p = 0.0010$). In contrast, Ter Kuile et al. [25] reported a non-significant effect on malaria incidence using a hazard ratio (HR = 0.72; 95% CI: 0.19–2.78; $p = 0.62$), with a wide confidence interval indicating high uncertainty. Similarly, Shulman et al. [24] reported no significant impact of ITNs on malaria incidence using a risk ratio (RR = −0.13; 95% CI: −0.69 to 0.43; $p = 0.66$). Given that each metric was represented by only one study, no pooled meta-analysis was conducted.

Effect modifiers of ITNs effectiveness

A meta-regression was conducted on 17 included studies to assess the influence of key moderators; geographic region (Africa vs. Asia), study design (RCT vs. cRCT), and population type (children, pregnant women, general population) on the effectiveness of the intervention. The meta-regression analysis (Table 4) showed a marginally significant intercept ($\beta = -0.84$; 95% CI −1.68 to −0.01; $p = 0.053$), indicating that at the reference levels (studies conducted in Africa, randomised controlled trial design, and general population), the intervention was associated with a protective effect against malaria outcomes. The dispersion in effect estimates across studies was not substantially explained by the examined moderators, with geographic region ($\beta = -0.35$; $p = 0.44$), study design ($\beta = 0.33$; $p = 0.41$), and population subgroups, including children ($\beta = 0.33$; $p = 0.44$) and pregnant women ($\beta = 0.72$; $p = 0.39$), showing no meaningful association with effect size. These findings suggest that the protective effect of the intervention was relatively consistent across study regions, designs, and population groups, and that the dispersion in effect estimates across studies was not substantially explained by the examined moderators. Meta-regression was not conducted for studies reporting malaria-related mortality outcomes, as the study findings were highly consistent across studies ($I^2 = 0\%$), indicating consistency across these studies. Similarly, studies that reported HRs and RRs were excluded from the meta-regression due to their small number and incompatibility with log-transformed odds and rate ratio metrics.

Publication bias assessment

Publication bias was evaluated using Doi plots and the Luis Furuya-Kanamori (LFK) index across the four(4) subgroups. The Doi plots and LFK indices, which are graphical and numeric tools for detecting and quantifying asymmetry in meta-analyses and detecting publication bias, indicated no significant publication bias for most subgroups. Specifically, the LFK index revealed minor asymmetry in malaria incidence, measured as rate ratios in Africa (LFK = −1.42) and Asia (LFK = −1.16), as well as odds ratios in Asia (LFK = −1.24), indicating limited concern for publication bias in these analyses. However, the odds ratio subgroup for malaria incidence in Africa showed minor-to-major asymmetry (LFK = +1.82), approaching the threshold for major asymmetry and indicating potential publication bias in that subgroup (Appendix 4 of the (Supplementary Materials Figures S2A–S2D)).

Discussion

This systematic review and meta-analysis shows strong evidence that ITNs, are effective in reducing malaria cases and deaths. By focusing only on randomised controlled trials (RCTs and cluster-RCTs) with clearly defined intervention and control groups, the review ensured reliable results. Studies conducted in Africa and Asia demonstrated that pooled estimates from the meta-analysis revealed a 29% reduction in malaria incidence in Africa and a 68% reduction in Asia. Additionally, ITNs were associated with an 18% reduction in malaria-related mortality in Asia, reinforcing their critical role in malaria prevention across diverse endemic regions. These findings are consistent with previous systematic reviews. For example, Pryce et al. [7] provided robust evidence supporting the efficacy of ITNs in reducing child mortality and malaria incidence, particularly for *Plasmodium. falciparum*. The reductions in malaria mortality and incidence observed in our research align with these results, reinforcing the high-certainty benefits of ITNs in malaria control. Similarly, the 41% reduction in malaria prevalence reported by Yang et al. [17] is consistent with the findings of our research, further validating the effectiveness of ITNs in reducing malaria

transmission across different regions. Recent studies, including those by Barker et al. [42] and Koppula *et al*. [43], further confirmed the significant protective effect of ITNs in reducing malaria transmission. Collectively, this growing body of evidence highlights the robust efficacy of ITNs and supports their continued prioritisation in global malaria control efforts. Our findings on the efficacy of ITNs are further supported by Wangdi et al. [44], who identified ITNs as the only malaria control strategy with statistically significant effectiveness in their analysis. Their study concluded that, when prioritising resource allocation, ITNs should be favoured. Hence, reinforcing their role as a key intervention in malaria prevention efforts.

Significant heterogeneity was observed in the subgroup analyses, particularly among studies conducted in Asia, indicating that the effectiveness of ITNs varies across different settings. This variability may stem from underlying ecological and management approaches, such as vector species diversity, patterns of insecticide resistance, and community compliance with net usage. Despite heterogeneity in effect estimates across studies, meta-regression demonstrated a significant overall protective effect of ITNs against malaria. However, the analysis did not identify any single study-level characteristic, such as region, study design, or population type, as a statistically significant source of the observed variation. These results suggest that while ITNs are broadly effective, their impact is influenced by complex and context-specific factors that conventional study-level covariates may not fully capture. Similar findings to this were reported by Yang et al. [17]. Meta-regression was not performed on studies evaluating malaria-related mortality, as the effect estimates were highly consistent across studies, indicating a consistent mortality-reducing effect of ITNs across diverse contexts. This highlights the importance of tailoring malaria control interventions to the local epidemiological context and investing in further research to identify additional underlying factors contributing to the dispersion in effect estimates across studies.

The implications of these findings for malaria prevention practice, policy, and future research are substantial. Although ITNs demonstrate undeniable effectiveness, their observed variability suggests that malaria control strategies relying solely on ITNs may be inadequate, particularly in areas with insecticide resistance. Therefore, integrated vector management (IVM) strategies, including indoor residual spraying (IRS), larval source management, and dual-active ingredient ITNs, are essential complements. Recent literature supports this integrative approach; for example, Demissie et al. [45,46] strongly advocate for the combination of ITNs with IRS and novel vector control methods to overcome resistance and adapt to changing vector behaviour. Future research should emphasise operational studies evaluating long-term net durability, community compliance, and insecticide resistance trends. Expanding the geographical scope of future trials and incorporating observational research is crucial to enhance the real-world relevance and generalisability of findings. Continued investment in innovative net technologies, tailored interventions, and sustainable distribution strategies will be critical to achieving sustained malaria control and progressing towards global malaria elimination.

To the best of our knowledge, this is one of the very few meta-analyses that exclusively includes randomised experimental studies, specifically RCTs and cRCTs, focusing on ITNs as the intervention and control groups without nets. The uniqueness of our review lies in its rigorous methodological approach, assessing ITNs effectiveness using two key malaria control indicators: malaria incidence and malaria-related mortality. By limiting the analysis to experimental studies with well-defined intervention and control groups, this review ensures a high level of scientific rigour, providing robust evidence of ITNs' impact on malaria prevention. Through meta-analysis, we systematically evaluated pooled data from RCTs and cRCTs, highlighting both the strengths and limitations of these studies while exploring how factors such as geography, transmission intensity, and study design influence the effectiveness of insecticide-treated nets (ITNs). This focused approach enhances the reliability of findings and provides valuable evidence to guide malaria control strategies and inform targeted interventions. However, an important consideration in interpreting these results is the potential role of insecticide resistance in mosquito vector populations, which may act as a confounding or effect-modifying factor. Resistance to commonly used pyrethroids has been increasingly reported across malaria-endemic regions [47]and may reduce the protective efficacy of ITNs by lowering mosquito mortality and changing vector behaviour. Since most of the included studies did not systematically measure or adjust for insecticide resistance, its impact could not be formally evaluated within this review. As a result, variations in ITN effectiveness observed across

studies may partly reflect underlying differences in resistance profiles, which should be taken into account when interpreting the pooled estimates.

Despite the ongoing significance of long-lasting insecticidal nets (LLINs) for malaria prevention, their effectiveness is increasingly compromised by the expansion and intensification of pyrethroid resistance in Anopheles populations [48,49]. Pyrethroid resistance was confirmed in 48 of 53 countries that reported monitoring data between 2020 and 2024, according to the World malaria report 2025 [50], and is mediated through multiple mechanisms, including knockdown resistance (kdr) mutations in the voltage-gated sodium channel; particularly *L995F/L995S*, previously reported as *L1014F/L1014S*; as well as enhanced metabolic detoxification mediated by cytochrome P450 enzymes such as *CYP6P3*, *CYP6M2*, and *CYP9K1* [49,51]. A systematic review and meta-analysis from India similarly demonstrated widespread resistance to Dichlorodiphenyltrichloroethane (DDT) and pyrethroids in *Anopheles culicifacies* and *Anopheles stephensi*, with notable regional heterogeneity, emphasising insecticide resistance as a significant and growing threat to the efficacy of conventional pyrethroid-only LLINs as the primary malaria prevention strategy [52].

In response to this challenge, new-generation LLINs with dual active ingredients have been developed to improve control in areas where standard pyrethroid-only nets are losing effectiveness [53,54]. The main types include pyrethroid-piperonyl butoxide (PBO) nets, such as PermaNet® 3.0, Olyset® Plus, and VEERALIN®, which combine a pyrethroid with the synergist PBO to block detoxification enzymes involved in pyrethroid resistance; pyrethroid-chlorfenapyr nets, like Interceptor® G2, which combine a pyrethroid with chlorfenapyr, a pro-insecticide that is activated in the insect and disrupts cellular energy production; and pyrethroid-pyriproxyfen nets, such as Royal Guard®, which combine a pyrethroid with the insect growth regulator pyriproxyfen that reduces mosquito reproduction and fertility [53,55–57]. This move from single-active pyrethroid nets to resistance-responsive combinations reflects the growing realisation that sustaining LLIN effectiveness now depends not only on maintaining the physical barrier of nets but also on restoring insecticidal action against resistant mosquito populations [58].

Our findings continue to support the effectiveness of insecticide-treated nets as a key malaria control tool because nets still decrease human-vector contact, limit blood feeding, and reduce transmission at both individual and community levels [56,58]. In routine deployment settings, the use of newer-generation LLINs in Uganda was linked with a decrease in malaria incidence from 827 to 538 cases per 1000 person-years, representing an estimated 23% reduction within the first 12 months after distribution [59]. Entomological evidence from Burkina Faso further demonstrated that pyrethroid-only, pyrethroid-chlorfenapyr, and pyrethroid-PBO nets had different impacts on mosquito density, sporozoite infection rates, and entomological inoculation rates over time, showing that the current effectiveness of LLINs increasingly depends on the local resistance profile and whether nets maintain adequate insecticidal activity under operational conditions [58,60]. The strongest current evidence suggests that pyrethroid-chlorfenapyr nets may offer the most consistent entomological benefit in highly resistant areas: in south-western Burkina Faso, Interceptor® G2 was linked with an 88.7% decline in Anopheles density over three years, whereas mosquito density increased again by year 3 under the pyrethroid-only net Interceptor® G1 and remained relatively stable under the pyrethroid-PBO net PermaNet® 3.0 [60]. Similarly, in Benin, the pyrethroid-chlorfenapyr net showed the most consistent superiority across new and field-aged nets, with higher mortality than comparator nets at all time points, whereas the additional benefit of the pyrethroid-PBO net decreased after ageing and the fertility-reducing effect of the pyrethroid-pyriproxyfen net diminished over time [54]. These observations align with modelling data indicating that the overall effectiveness of next-generation LLINs depends not only on entomological potency but also on functional survival, insecticidal durability, ITN use, and the synchronisation of human sleeping behaviour with mosquito biting patterns [58]. Overall, these findings show that ITNs remain effective, but maintaining that efficacy in resistant environments increasingly relies on deploying pyrethroid-chlorfenapyr, pyrethroid-PBO, or pyrethroid-pyriproxyfen LLINs with stronger and more durable insecticidal profiles. It also remains essential to consider that long-term impact will continue to be influenced by product durability, operational use, and residual transmission ecology [54,58–60].

Limitation of study

Several limitations concerning the evidence reviewed must be acknowledged. Variability in study designs, length of follow-up periods (ranging from two (2) months to five (5) years), and studied populations (e.g. children under five, pregnant women, and general communities) may limit the generalisability of the pooled findings. Publication bias could also influence the results, given the higher likelihood that studies reporting positive outcomes are published. However, no evidence of publication bias was detected for malaria incidence outcomes. Publication bias was not formally assessed for mortality outcomes due to the limited number of studies reporting mortality, which should be considered when interpreting these findings. Furthermore, compliance with ITN use at the community-level, which is often not fully captured under controlled RCT conditions, may contribute to differences between trial efficacy and real-world effectiveness [45]. Factors such as net durability, correct and consistent use, and replacement rates may influence the sustained impact of ITNs in routine programmatic settings, a limitation similarly noted in previous systematic reviews [4,17,44]. In addition, the included studies were conducted primarily in Africa and Asia, which may limit the generalisability of the findings to other malaria-endemic regions. Finally, a general limitation of this study is the potential for conflicts of interest linked to ITN manufacturers in studies evaluating specific ITN products. Although this was not formally examined in the present review, industry involvement through funding, product provision, or technical collaboration may influence study design, conduct, reporting, and interpretation, and should therefore be considered when interpreting the broader evidence base. Additionally, only studies published in English were included, which may have introduced language bias and led to the exclusion of relevant evidence published in other languages. Furthermore, most of the included studies were conducted in Asia and Africa, primarily in moderate- to high-transmission settings, which may restrict the applicability of the findings to low-transmission or elimination settings where malaria epidemiology, vector behaviour, and intervention efficacy may differ.

Conclusion

This review provided strong evidence that the use of ITNs led to significant reductions in both malaria incidence and malaria-related mortality across various endemic settings. This review provides a comprehensive assessment of the protective effect of insecticide-treated nets (ITNs) under field conditions, and the robustness and credibility of its findings are strengthened by the rigorous inclusion criteria applied throughout the study. The studies included in this meta-analysis demonstrated substantial reductions in malaria incidence in both Africa and Asia, as well as a significant reduction in malaria-related mortality in Asia. These findings reinforce the continued importance of ITNs as a cornerstone intervention for malaria prevention across endemic settings. However, sustaining and enhancing these gains may require continued innovation in vector control. In particular, emerging evidence from the broader literature suggests that next-generation insecticide-treated nets, including pyrethroid-piperonyl butoxide (PBO) nets and other dual-active-ingredient ITNs, may help address the growing challenge of insecticide resistance, although these products were not included in the primary studies included in the present meta-analysis. It also requires the integration of ITNs into broader integrated vector management (IVM) strategies [54,61]. Such approaches may include complementary interventions, such as indoor residual spraying (IRS), larval source management, and insecticidal wall linings. Emerging vector control tools, including attractive targeted sugar baits, genetically modified mosquitoes, and green-synthesized metallic nanoparticles, are also being explored as more environmentally sustainable options. Integrating multiple vector control strategies may help address persistent challenges related to insecticide resistance, vector behavioural adaptation, and residual transmission. Although ITNs remain a cornerstone of malaria prevention, their optimal impact is likely to be achieved when they are implemented as part of broader integrated vector management approaches, particularly in settings where insecticide resistance is established. However, high heterogeneity and emerging insecticide resistance warrant combination strategies and continued surveillance. Taken together, these findings underscore the need for sustained investment in ITN distribution, alongside ongoing monitoring and evaluation, to optimise their long-term effectiveness in malaria control efforts.

Acknowledgments

GO, EM, MEC, OA conceived and designed the study; GO conducted the analysis; EM,MEC,OA verified the analysis and provided critical feedback; GO wrote the first draft; MEC, EM,OA, and HR revised the manuscript. All authors reviewed successive drafts and approved the final manuscript.

Ethical standards

Not applicable

Consent for publication

Not applicable.

Author contributions

CRediT: **Gbeminiyi R. Otolorin**: Conceptualization, Data curation, Formal analysis, Methodology, Writing – original draft, Writing – review & editing; **María Eugenia. Castellanos**: Data curation, Methodology, Supervision, Writing – review & editing; **Oyelola A. Adegboye**: Methodology, Supervision, Writing – review & editing; **Himali E. Ratnayake**: Methodology, Writing – review & editing; **Emma S. McBryde**: Conceptualization, Methodology, Supervision, Writing – review & editing.

Manuscript preparation

Grammarly for Windows (Grammarly, Inc.; https://www.grammarly.com) was used to assist with proofreading and language correction during manuscript preparation. All scientific content, interpretation, and final wording were reviewed and approved by the authors.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Data availability statement

All data analysed during this study are included in this article.

References

[1] World Health Organization. World malaria report 2024: addressing inequity in the global malaria response. Geneva: WHO; 2024. [cited 2025 May 12]. Available from: https://www.who.int/publications/i/item/9789240104440.

[2] Centers for Disease Control and Prevention. How malaria spreads; 2024. [cited 2025 May 12]. Available from: https://www.cdc.gov/malaria/causes/index.html.

[3] World Health Organization. Insecticide-treated nets to reduce the risk of malaria in pregnant women; 2023. [cited 2024 Aug 9]. Available from: https://www.who.int/tools/elena/interventions/bednets-malaria-pregnancy.

[4] Binka FN, Kubaje A, Adjuik M, et al. Impact of permethrin impregnated bed nets on child mortality in Kassena-Nankana district, Ghana: a randomized controlled trial. Trop Med Int Health. 1996;1(2):147–154. doi: 10.1111/j.1365-3156.1996.tb00020.x.

[5] Habluetzel A, Diallo DA, Esposito F, et al. Do insecticide-treated curtains reduce all-cause child mortality in Burkina Faso? Tropical Med Int Health. 1997;2(9):855–862. doi: 10.1046/j.1365-3156.1997.d01-413.x.

[6] Gimnig JE, Vulule JM, Lo TQ, et al. Impact of permethrin-treated bed nets on entomologic indices in an area of intense year-round malaria transmission. Am J Trop Med Hyg. 2003;68(4_suppl):16–22. doi: 10.4269/ajtmh.2003.68.16.

[7] Pryce J, Richardson M, Lengeler C. Insecticide-treated nets for preventing malaria. Cochrane Database Syst Rev. 2018;11(11):CD000363. doi: 10.1002/14651858.CD000363.pub3.

[8] Sreehari U, Razdan RK, Mittal PK, et al. Impact of Olyset® Nets on malaria transmission in India. J Vect Borne Dis. 2007;44(2):137–144.

[9] Phillips-Howard PA, Nahlen BL, Kolczak MS, et al. Efficacy of permethrin-treated bed nets in the prevention of mortality in young children in an area of high perennial malaria transmission in western Kenya. Am J Trop Med Hyg. Hyg2003;68(4_suppl):23–29. doi: 10.4269/ajtmh.2003.68.23.
[10] D'Alessandro U, Olaleye BO, McGuire W, et al. Mortality and morbidity from malaria in Gambian children after introduction of an impregnated bednet programme. Lancet. 1995;345(8948):479–483. doi: 10.1016/S0140-6736(95)90582-0.
[11] Barker D, McElduff P, D'Este C, et al. Stepped wedge cluster randomised trials: a review of the statistical methodology used and available. BMC Med Res Methodol. 2016;16(1):69. doi: 10.1186/s12874-016-0176-5.
[12] Corrigan N, Bankart MJG, Gray LJ, et al. Changing cluster composition in cluster randomised controlled trials: design and analysis considerations. Trials. 2014;15(1):184. doi: 10.1186/1745-6215-15-184.
[13] Hawley WA, Phillips-Howard PA, Ter-Kuile FO, et al. Community-wide effects of permethrin-treated bed nets on child mortality and malaria morbidity in western Kenya. Am J Trop Med Hyg. 2003;68(4 Suppl):121–127. doi: 10.4269/ajtmh.2003.68.121.
[14] Soremekun S, Maxwell C, Zuwakuu M, et al. Measuring the efficacy of insecticide-treated bednets: the use of DNA fingerprinting to increase accuracy of protection estimates in Tanzania. Trop Med Int Health. 2004;9(6): 664–672. doi: 10.1111/j.1365-3156.2004.01250.x.
[15] Fegan GW, Noor AM, Akhwale WS, et al. Effect of expanded insecticide-treated bednet coverage on child survival in rural Kenya: a longitudinal study. Lancet. 2007;370(9592):1035–1039. . doi: 10.1016/S0140-6736(07)61477-9.
[16] Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi: 10.1136/bmj.n71.
[17] Yang G, Kim D, Pham A, et al. A meta-regression analysis of the effectiveness of mosquito nets for malaria control: the value of long-lasting insecticide nets. Int J Environ Res Public Health. 2018;15(3):546. doi: 10.3390/ijerph15030546.
[18] R Core Team. R: a language and environment for statistical computing (Version 4.1.2). R Foundation for Statistical Computing; 2021. Available from: https://www.R-project.org.
[19] RStudio Team. RStudio: Integrated development for R (Version 1.4.1717). RStudio, PBC; 2020. Available from: https://rstudio.com.
[20] Schwarzer G. meta: General package for metaanalysis Version 6.00). CRAN; 2022. Available from: https://CRAN.R-project.org/package = meta
[21] Viechtbauer W. Conducting meta-analyses in R with the metafor package. J Stat Soft. 2010;36(3):1–48. doi: 10.18637/jss.v036.i03.
[22] Browne ENL, Maude GH, Binka FN. The impact of insecticide-treated bednets on malaria and anaemia in pregnancy in Kassena-Nankana district, Ghana: a randomized controlled trial. Trop Med Int Health. 2001;6(9):667–676. doi: 10.1046/j.1365-3156.2001.00759.x.
[23] Phillips-Howard PA, Nahlen B, Wannemuehler K, et al. Impact of permethrin-treated bed nets onthe incidence of sick child visits to peripheral health facilities. Am J Trop Med Hyg. 2003;68(4_suppl):38–43. doi: 10.4269/ajtmh.2003.68.38.
[24] Shulman CE, Dorman EK, Talisuna AO, et al. A community randomized controlled trial of insecticide-treated bednets for the prevention of malaria and anaemia among primigravid women on the Kenyan coast. Trop Med Int Health. 1998;3(3):197–204. doi: 10.1046/j.1365-3156.1998.00214.x.
[25] Ter Kuile FO, Terlouw DJ, Kariuki SK, et al. Impact of permethrin-treated bed nets on malaria and all-cause morbidity in young children in an area of intense perennial malaria transmission in western Kenya: cross-sectional survey. Am J Trop Med Hyg. 2003;68(4_suppl):100–107. doi: 10.4269/ajtmh.2003.68.100.
[26] Ter Kuile FO, Terlouw DJ, Kariuki SK, et al. Impact of permethrin-treated bed nets on malaria, anemia, and growth in infants in an area of intense perennial malaria transmission in western Kenya. Am J Trop Med Hyg. 2003;68(4_suppl):68–77. doi: 10.4269/ajtmh.2003.68.68.
[27] Henry MC, Assi SB, Rogier C, et al. Protective efficacy of lambda-cyhalothrin treated nets in *Anopheles gambiae*pyrethroid resistance areas of Côte d'Ivoire. Am J Trop Med Hyg. 2005;73(5):859–864. doi: 10.4269/ajtmh.2005.73.859.
[28] Sedlmayr R, Fink G, Miller JM, et al. Health impact and cost-effectiveness of a private sector bed net distribution: experimental evidence from Zambia. Malar J. 2013;12(1):102. doi: 10.1186/1475-2875-12-102.
[29] Fraser-Hurt N, Felger I, Edoh D, et al. Effect of insecticide-treated bed nets on haemoglobin values, prevalence and multiplicity of infection with *Plasmodium falciparum* in a randomized controlled trial in Tanzania. Trans R Soc Trop Med Hyg. 1999;93 Suppl 1(1):47–51. doi: 10.1016/s0035-9203(99)90327-9.
[30] Marbiah NT, Petersen E, David K, et al. A controlled trial of lambda-cyhalothrin-impregnated bed nets and/or dapsone/pyrimethamine for malaria control in Sierra Leone. Am J Trop Med Hyg. 1998;58(1):1–6. doi: 10.4269/ajtmh.1998.58.1.
[31] Sexton JD, Ruebush TK, Brandling-Bennett AD, et al. Permethrin-impregnated curtains and bed-nets prevent malaria in western Kenya. Am J Trop Med Hyg. 1990;43(1):11–18. doi: 10.4269/ajtmh.1990.43.11.

[32] Snow RW, Rowan KM, Lindsay SW, et al. A trial of bed nets (mosquito nets) as a malaria control strategy in a rural area of The Gambia, West Africa. Trans R Soc Trop Med Hyg. 1988;82(2):212–215. doi: 10.1016/0035-9203(88)9041.
[33] Lindblade KA, Eisele TP, Gimnig JE, et al. Sustainability of reductions in malaria transmission and infant mortality in Western Kenya with use of insecticide-treated bednets: 4 to 6 years of follow-up. JAMA. 2004;291(21): 2571–2580. doi: 10.1001/jama.291.21.2571.
[34] Nevill CG, Some ES, Mung'ala VO, et al. Insecticide-treated bednets reduce mortality and severe morbidity from malaria among children on the Kenyan coast. Trop Med Int Health. 1996;1(2):139–146. doi: 10.1111/j.1365-3156.1996.tb00019.x.
[35] Sahu SS, Vijayakumar T, Kalyanasundaram M, et al. Impact of lambdacyhalothrin capsule suspension treated bed nets on malaria in tribal villages of Malkangiri district, Orissa, India. Indian J Med Res. 2008;128(3):262–270.
[36] Smithuis FM, Kyaw MK, Phe UO, et al. The effect of insecticide-treated bed nets on the incidence and prevalence of malaria in children in an area of unstable seasonal transmission in western Myanmar. Malar J. 2013; 12(1):363. doi: 10.1186/1475-2875-12-363.
[37] Sochantha T, Hewitt S, Nguon C, et al. Insecticide-treated bednets for the prevention of *Plasmodium falciparum* malaria in Cambodia: a cluster-randomized trial. Trop Med Int Health. 2006;11(8):1166–1177. doi: 10.1111/j.1365-3156.2006.01673.x.
[38] Bhatt RM, Sharma SN, Uragayala S, et al. Effectiveness and durability of Interceptor® long-lasting insecticidal nets in a malaria endemic area of central India. Malar J. 2012;11(1):189. doi: 10.1186/1475-2875-11-189.
[39] Hill N, Zhou HN, Wang P, et al. A household randomized, controlled trial of the efficacy of 0.03% transfluthrin coils alone and in combination with long-lasting insecticidal nets on the incidence of *Plasmodium falciparum* and *Plasmodium vivax* malaria in Western Yunnan Province, China. Malar J. 2014;13(1):208. doi: 10.1186/1475-2875-13-208.
[40] Sharma SK, Tyagi PK, Upadhyay AK, et al. Efficacy of permethrin treated long-lasting insecticidal nets on malaria transmission and observations on the perceived side effects, collateral benefits and human safety in a hyperendemic tribal area of Orissa, India. Acta Trop. 2009;112(2):181–187. doi: 10.1016/j.actatropica.2009.07.022.
[41] Sahu SS, Jambulingam P, Vijayakumar T, et al. Impact of alphacypermethrin-treated bed nets on malaria in villages of Malkangiri district, Orissa, India. Acta Trop. 2003;89(1):55–66. doi: 10.1016/j.actatropica.2003.07.002.
[42] Barker TH, Stone JC, Hasanoff S, et al. Effectiveness of dual active ingredient insecticide-treated nets in preventing malaria: a systematic review and meta-analysis. PLoS One. 2023;18(8):e0289469. doi: 10.1371/journal.pone.0289469.
[43] Koppula DT, Shriram AN, Ramasamy A, et al. Evaluation of long lasting insecticidal nets in experimental huts and WHO PQT/VCP compliance: a systematic review. PLoS One. 2025;20(3):e0318673. doi: 10.1371/journal.pone.0318673.
[44] Wangdi K, Furuya-Kanamori L, Clark J, et al. Comparative effectiveness of malaria prevention measures: a systematic review and network meta-analysis. Parasit Vectors. 2018;11(1):210. doi: 10.1186/s13071-018-2783-y.
[45] Demissie DB, Fetensa G, Desta T(2025).), et al. Effectiveness and efficacy of long-lasting insecticidal nets for malaria control in Africa: systematic review and meta-analysis of randomized controlled trials. Int J Environ Res Public Health. 2025;22(7):1045. doi: 10.3390/ijerph22071045.
[46] Otolorin GR, Castellanos ME, Adegboye OA, et al. Integrated vector management for malaria control: a review of approaches and effectiveness. Trans R Soc Trop Med Hyg. 2025;119(11):1223–1232. doi: 10.1093/trstmh/traf084.
[47] Implications of Insecticide Resistance Consortium. Implications of insecticide resistance for malaria vector control with long-lasting insecticidal nets: trends in pyrethroid resistance during a WHO-coordinated multi-country prospective study. Parasit Vectors. 2018;11(1):550. doi: 10.1186/s13071-018-3101-4.
[48] Cleanclay WD, Bajepade TI, Folamade JK, et al. Molecular and metabolic mechanisms of pyrethroid resistance in Anopheles gambiae complex (Diptera: culicidae) in West Africa: a systematic review. J Med Entomol. 2026; 63(2):tjag034. doi: 10.1093/jme/tjag034.
[49] Tazokong HR, Tchouakui M, Wondji M, et al. Four-year monitoring of the malaria vector Anopheles funestus in central-west Cameroon reveals an escalation of pyrethroid resistance combined with high malaria transmission. BMC Infect Dis. 2026;26(1):418. doi: 10.1186/s12879-026-12708-w.
[50] World Health Organization(WHO). World malaria report 2025. [cited 2026 Apr 8]. Available from: https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2025.
[51] Silva AP, Santos JM, Martins AJ. Mutations in the voltage-gated sodium channel gene of anophelines and their association with resistance to pyrethroids: a review. Parasit Vectors. 2014;7(1):450. doi: 10.1186/1756-3305-7-450.
[52] Mullick R, Yadav CP, Singhal R. Spatio-temporal trends of insecticide resistance in Indian malaria vectors (2000–2024): a systematic review and meta-analysis. BMC Public Health. 2025;26(1):326. doi: 10.1186/s12889-025-25977-y.

[53] Sih C, Protopopoff N, Koffi AA, et al. Efficacy of chlorfenapyr-pyrethroid and piperonyl butoxide-pyrethroid long-lasting insecticidal nets (LLINs) compared to pyrethroid-only LLINs for malaria control in Côte d'Ivoire: a three group, cluster randomised trial. Trials. 2024;25(1):151. doi: 10.1186/s13063-024-07969-2.
[54] Agbevo A, Syme T, Fagbohoun J, et al. The experimental hut efficacy of next-generation insecticide-treated nets against pyrethroid-resistant malaria vectors after 12, 24 and 36 months of household use in Benin. Malar J. 2024;23(1):388. doi: 10.1186/s12936-024-05199-0.
[55] Accrombessi M, Cook J, Ngufor C, et al. Assessing the efficacy of two dual-active ingredients long-lasting insecticidal nets for the control of malaria transmitted by pyrethroid-resistant vectors in Benin: study protocol for a three-arm, single-blinded, parallel, cluster-randomized controlled trial. BMC Infect Dis. 2021;21(1):194. doi: 10.1186/s12879-021-05879-1.
[56] World Health Organization. Guidelines for malaria. 15th ed. Geneva: World Health Organization; 2025 [accessed 2026 Feb 17]. Available from: https://iris.who.int/server/api/core/bitstreams/26a6af2d-060c-4449-8207-1f25e63c6cc3/content.
[57] Oruni A, Menze BD, Fotso-Toguem YG, et al. Chlorfenapyrbednets effectively overcome pyrethroid resistance escalation in highly resistant *Anopheles* malaria vectors in Uganda. Sci Rep. 2026;16(1):4292. doi: 10.1038/s41598-025-34493-3.
[58] Champagne C, Lemant J, Assenga A, et al. Cascades of effectiveness of next-generation insecticide-treated nets against malaria, from entomological trials to real-life conditions. Nat Commun. 2025;16(1):11162. doi: 10.1038/s41467-025-66130-y.
[59] Epstein A, Gonahasa S, Namuganga JF, et al. Evaluating the impact of two next-generation long-lasting insecticidal nets on malaria incidence in Uganda: an interrupted time-series analysis using routine health facility data. BMJ Glob Health. 2025;10(3):e017106. doi: 10.1136/bmjgh-2024-017106.
[60] Tapsoba M, Guelbeogo WM, Sanou A, et al. Three-year trends in malaria transmission parameters under deployment of Interceptor®G1, Interceptor®G2 and PermaNet®3.0 insecticide-treated bed nets in South-Western Burkina Faso. Malar J. 2025;25(1):45. doi: 10.1186/s12936-025-05732-9.
[61] World Health Organization. Expanded use of new dual-insecticide nets offers hope for malaria control efforts in Africa [Internet]. Geneva: World Health Organization; 2025. [cited 2026 Mar 17]. Available from: https://www.who.int/news-room/feature-stories/detail/expanded-use-of-new-dual-insecticide-nets-offers-hope-for-malaria-control-efforts-in-africa.