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Effectiveness and Implementation Challenges of Malaria Control Interventions Among Children Under Five in Malawi: A Systematic Review

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Abstract

Background: Malaria remains a major cause of morbidity and mortality among children under five years of age in Malawi despite the widespread implementation of insecticide-treated nets (ITNs), indoor residual spraying (IRS), and the RTS,S/AS01 malaria vaccine. However, evidence regarding the effectiveness of these interventions remains fragmented. **Methods:** A systematic review was conducted following the PRISMA 2020 guidelines. PubMed, Scopus, Web of Science, and Embase were searched for studies published between 2015 and 2025 evaluating malaria control interventions among children under five years of age in Malawi. Eight studies met the inclusion criteria and were synthesised narratively due to heterogeneity in study designs and outcome measures. Methodological quality was assessed using study-design-appropriate appraisal tools, including CASP checklists for empirical studies. Five studies were assessed as high quality and three as moderate quality. **Results:** Across the included studies, ITN use was generally associated with lower malaria risk or prevalence, although the magnitude of effect varied due to differences in study design, outcome measures, and study settings. IRS reduced prevalence by up to 20% in sprayed households. Evidence on RTS,S/AS01 indicated protection against clinical malaria that varied with environmental context, while modelling estimated the greatest reductions (65–71%) when vaccination was combined with ITN use. Post-introduction evidence identified no new vaccine safety concerns. Intervention effectiveness was influenced by utilisation, coverage, insecticide resistance, environmental conditions, and socioeconomic factors. Key implementation challenges included inconsistent ITN use, logistical constraints, and inequities in access and uptake. **Conclusions:** Malaria control interventions were generally associated with reductions in the malaria burden among children under five years of age in Malawi, with modelling evidence suggesting additional benefits from combining RTS,S/AS01 vaccination with ITN use. However, evidence on combined interventions was limited and heterogeneous, with the largest estimated benefits derived from modelling. Strengthening integrated delivery strategies, improving adherence, and addressing implementation challenges are essential for achieving sustained reductions in malaria transmission.

Keywords: Malaria; Children under five; Insecticide-treated nets; Indoor residual spraying; vaccine

Introduction

Malaria remains a major public health challenge worldwide and continues to disproportionately affect children under five years of age in sub-Saharan Africa. In 2023, an estimated 263 million malaria cases and 597,000 malaria-related deaths were reported globally, with approximately 95% of deaths occurring in the World Health Organisation (WHO) African Region (WHO, 2024). Children under five account for most of the malaria-related mortality due to their limited immunity and increased susceptibility to severe disease (Ranjha et al., 2023). Despite substantial investments in malaria prevention and control, malaria continues to impose a significant burden on health systems and socioeconomic development across many endemic countries.

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Malawi remains among the countries most affected by malaria, accounting for approximately 2% of reported malaria cases globally (UNICEF, 2024). Malaria transmission occurs year-round, with seasonal peaks during the rainy season, when environmental conditions favour mosquito breeding and parasite development (Megersa et al., 2025). The disease is predominantly caused by Plasmodium falciparum, the most virulent malaria parasite species and a major cause of severe disease and mortality among young children (Gaston and Ramroop, 2020). In Malawi, nearly eight in ten malaria-related deaths occur among children under five years of age, highlighting the substantial vulnerability of this population group (Ranjha et al., 2023). Repeated malaria infections during early childhood are associated with anemia, impaired cognitive development, increased healthcare utilization, and elevated mortality risk (Milner et al., 2020; Ssemata et al., 2023).

To reduce malaria transmission and improve child survival, Malawi has implemented several malaria control interventions aligned with WHO recommendations. Insecticide-treated nets (ITNs) remain the cornerstone of malaria prevention and aim to reduce human–vector contact during sleeping hours. Indoor residual spraying (IRS) has been introduced in selected high-transmission districts to reduce mosquito survival by applying residual insecticides to indoor surfaces (Chilanga et al., 2020). More recently, Malawi became one of the first countries to introduce the RTS,S/AS01 malaria vaccine through routine immunization programmes. Evidence suggests that these interventions can substantially reduce malaria transmission, severe disease, and mortality when effectively implemented and maintained (Duffy et al., 2024).

Despite considerable progress, malaria remains highly endemic in Malawi. Between 2016 and 2022, malaria-related mortality declined by approximately 61%, reflecting improvements in prevention and treatment services (Ministry of Health, 2023). However, reductions in malaria prevalence and incidence have slowed, with malaria prevalence among children under five remaining stable at approximately 19–20% between 2015 and 2022 (Mategula et al., 2024). This stagnation suggests that the availability of malaria control interventions alone may be insufficient to achieve sustained reductions in transmission. Several factors, including inconsistent use of interventions, operational limitations, insecticide resistance, environmental conditions, and socioeconomic disparities, may influence the effectiveness of malaria control strategies in real-world settings (Tangena et al., 2023; Nkoka et al., 2019; Chilanga et al., 2020).

Although numerous studies have evaluated individual malaria control interventions in Malawi, the evidence remains fragmented. Most studies have focused on specific interventions or geographic settings, limiting a comprehensive understanding of their overall effectiveness and the factors influencing implementation and uptake. Furthermore, recent Malawi-specific evidence synthesizing multiple interventions and their associated implementation challenges among children under five remains limited. A consolidated assessment is therefore required to inform policy decisions, optimize programme delivery, and support progress towards national and global malaria reduction targets. This systematic review aims to assess the effectiveness of malaria control interventions among children under five years of age in Malawi and to identify key implementation challenges that influence their performance. By synthesizing recent evidence on intervention outcomes and implementation barriers, this review seeks to provide evidence-based insights to support malaria control policy, programme planning, and future research.

Methods

A systematic literature search was conducted in September 2025 in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2021). The review process was further informed by established guidance for conducting systematic reviews in public health research (Kabir et al., 2023). Four electronic databases, namely PubMed, Scopus, Web of Science, and Embase, were searched to identify studies evaluating malaria control interventions among children under five years of age in Malawi.

The search strategy was developed using the Population, Intervention, Control, and Outcome (PICO) framework. The population of interest comprised children under five years of age, while the interventions included ITNs, IRS, and malaria vaccines, particularly RTS,S/AS01. The primary outcomes of interest were malaria incidence, malaria prevalence and intervention effectiveness. Information on intervention uptake, coverage, utilisation, adherence and implementation-related factors was extracted where reported. Boolean operators (AND, OR) were applied to combine search terms. The search was restricted to studies published between 2015 and 2025. This ten-year period was selected to capture the most recent and policy-relevant evidence on malaria control interventions in Malawi, including the introduction and evaluation of newer strategies such as the RTS,S/AS01 malaria vaccine, while ensuring that the review reflected contemporary malaria control practices. Database-specific search strategies were adapted to reflect differences in indexing

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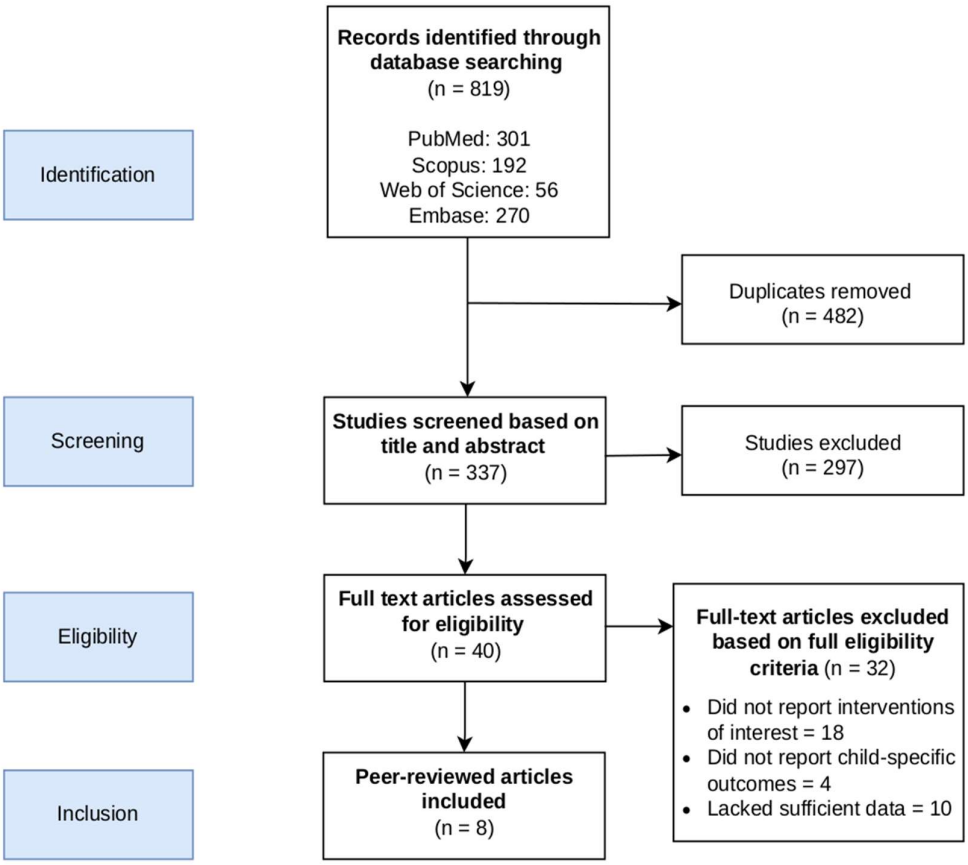
systems and search syntax. The complete search strategies for PubMed, Scopus, Web of Science, and Embase are provided in Appendix A (Supplementary Material).

Eligibility Criteria and Study Selection

Studies were eligible for inclusion if they were peer-reviewed journal articles published in English between 2015 and 2025, conducted in Malawi, focused on children under five years of age, and evaluated at least one malaria control intervention, including ITNs, IRS, or malaria vaccines. Studies reporting malaria incidence, prevalence, or intervention effectiveness were considered eligible. Information on intervention uptake, coverage, utilisation, adherence, and implementation-related factors was extracted where reported within eligible studies. Given the objective of this review to evaluate malaria control interventions at both the individual and population levels, quantitative modelling studies were also considered eligible when they provided Malawi-specific estimates of intervention impact.

Figure 1: PRISMA flow diagram of the literature search and study selection process.



Studies were excluded if they were non-peer-reviewed publications (e.g., editorials, commentaries, conference abstracts, or opinion articles); conducted outside Malawi without reporting Malawi-specific findings; focused on populations other than children under five years of age; did not evaluate malaria control interventions; or lacked sufficient methodological or outcome information.

All retrieved records were imported into Zotero reference management software for organization and duplicate removal. Titles and abstracts were screened against the predefined eligibility criteria, followed by full-text assessment of potentially relevant studies. The database search identified 819 records. After duplicate removal and title and abstract screening, 40 studies were assessed for full-text eligibility. Of these, 32 studies were excluded because they did not report child-specific outcomes, did not evaluate the malaria control interventions of interest, or lacked sufficient data for analysis; eight studies met the inclusion criteria and were retained for the final review.

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Data Extraction and Quality Assessment

Data were extracted using a standardized extraction form to ensure consistency across studies. Information collected included authorship, publication year, study design, sample characteristics, intervention type, outcome measures, principal findings, and implementation-related factors. Particular attention was given to information describing barriers and facilitators influencing intervention effectiveness and uptake.

Table 1: Characteristics and principal findings of the studies included in the systematic review.

Author/ Year	Study Design	Study setting	Sample size (age)	Intervention (s) evaluated	Outcome measure(s)	Key findings
Tangena *et al*. (2023)	Cross-Sectional	Malawi; nationally representative MIS data covering urban and rural areas	n=10,358; 6-59 months	ITNs	Malaria prevalence (blood-smear microscopy) ; ITN access and use	Consistent ITN use significantly reduced malaria prevalence among children under five, though spatial heterogeneity persisted across regions
Chilanga *et al*. (2020)	Cross-sectional	Rural Dowa District, Central Malawi; six postnatal clinics	n=523; 2-59 months	ITNs, IRS	Malaria infection/prevalence (RDT); factors associated with malaria infection	Malaria prevalence remained high among children of local farmers. ITN use and IRS were associated with lower malaria prevalence, although effectiveness was influenced by spray coverage and timing, and environmental conditions
Nkoka *et al*. (2019)	Cross-sectional (DHS 2010 and 2015–16)	Malawi; nationally representative 2010 and 2015–16 DHS, urban and rural households	n=22,574; Under five	ITNs	ITN use among children under five	ITN use increased from 57.8% (2010) to 69.5% (2015–16). Use was higher in wealthier, urban, and educated households, but gaps persisted among rural and poorer families despite ownership
Zamawe *et al*. (2016)	Cross-sectional	Malawi; nationally representative MIS data, urban and rural areas	n=4193; 6-59 months	ITNs	Malaria prevalence (blood-smear testing); ITN coverage and use	The universal ITN campaign greatly increased ownership but did not significantly reduce malaria infection among children under five. Poor utilization, rural residence, and insecticide resistance likely limited effectiveness
Bell *et al*. (2020a)	Quantitative modelling study using Phase III trial data	Urban/peri-urban Lilongwe, Malawi; modelling extended to rural settings	n=693; 5–17 months	RTS,S/AS01 and ITNs	Malaria incidence/cases averted; vaccine and combined vaccine–ITN effectivenes	RTS,S/AS01 vaccination was estimated to reduce malaria incidence, with efficacy of 53.08% during the first 18 months and 43.08% following the fourth

					s; cost-effectiveness	dose. Combining vaccination with ITN use was estimated to provide greater protection, with efficacy of 71.23% during the first 18 months and 65.10% during the second 18 months, with potential cost-effectiveness benefits.
Bell *et al*. (2020b)	Secondary analysis of a phase III randomized controlled trial	Lilongwe District, Central Malawi	n=757; 5–17 months	RTS,S/AS01	Clinical malaria incidence; vaccine efficacy and modification by environmental factors	Increased vegetation cover was associated with higher efficacy of the three-dose RTS,S/AS01 series during the first 18 months but lower efficacy during the subsequent 18 months without the fourth dose. Background malaria prevalence and roof type did not significantly modify vaccine efficacy, and vegetation cover did not significantly modify fourth-dose efficacy
Hajison *et al*. (2018)	Case Control	Zomba District, southern Malawi; lakeshore and highland areas	n=765; Under five	ITNs	Malaria infection (mRDT); individual and household risk factors	ITN use was associated with lower odds of malaria infection among children under five. Children from households without ITNs, and those in lakeshore areas, had significantly higher malaria risk
Haine *et al*. (2025)	Phase 4 prospective cohort event-monitoring study	Ghana, Kenya and Malawi; routine immunization settings under MVIP	n=44,912 overall (12,929 Malawi); <18 months	Malaria vaccine (RTS,S/AS01)	Vaccine safety outcomes, including adverse events, meningitis, cerebral malaria, mortality and hospitalization	No new safety concerns were identified up to one year after the third RTS,S/AS01E dose. Vaccine implementation was associated with an 8% reduction in all-cause child mortality and a 14% reduction in malaria-related mortality during 12 months of follow-up

The methodological quality of included studies was assessed using study-design-appropriate appraisal tools. CASP checklists were used for relevant empirical studies, while the Philips et al. (2004) checklist for decision-analytic modelling studies was used to assess the quantitative modelling study (Long et al., 2020; Kabir et al., 2023; Philips et al., 2004). The appraisal considered study design, sampling procedures, outcome measurement, analytical methods, reporting quality, and potential sources of bias, as applicable to each study design. Based on the assessment, studies were categorized as being of low, moderate, or high methodological quality. Quality assessment findings were used to inform the interpretation of the evidence but were not used as criteria for study exclusion.

Data Synthesis

Given the heterogeneity in study designs, interventions, and outcome measures, a quantitative meta-analysis was not feasible. Therefore, findings were synthesized narratively. The heterogeneity arose from differences in study designs (cross-sectional, case-control, cohort, randomized controlled trials, and modelling studies), as well as variation in outcome measures and effect estimates, including malaria prevalence, incidence, infection status, odds ratios, and percentage reductions. Further heterogeneity was introduced by differences in follow-up periods, population characteristics, and intervention delivery contexts, which limited the comparability of results across studies. As no quantitative pooling was performed, the I^2 statistic was not calculated.

The synthesis was organized according to the intervention category, namely ITNs, IRS, and malaria vaccines. Quantitative findings relating to malaria incidence, prevalence, and intervention effectiveness were summarised descriptively, while qualitative findings were synthesised to identify implementation barriers and contextual factors influencing intervention performance. Comparisons across studies were undertaken to identify recurring patterns, differences in effectiveness, and common implementation challenges affecting malaria control interventions among children under five years of age in Malawi.

Results

The systematic review included eight studies conducted in Malawi and published between 2015 and 2025. The studies comprised diverse methodological designs, including four cross-sectional studies, one case–control study, one prospective cohort study, one secondary analysis of Phase III randomized controlled trial data, and one modelling study. Malawi-specific sample sizes ranged from 523 to 22,574 participants. The interventions evaluated included ITNs, IRS, and the RTS,S/AS01 malaria vaccine, either as standalone interventions or in combination. The characteristics and principal findings of the included studies are summarized in Table 1.

ITNs were the most frequently investigated intervention, appearing in six studies, while three studies evaluated the RTS,S/AS01 malaria vaccine and one study evaluated IRS as part of an integrated malaria control strategy. Methodological quality was assessed using study-design-appropriate appraisal tools. The individual quality appraisal results are summarized in Table 2.

Overall, five studies were assessed as high quality and three as moderate quality. Most studies demonstrated clearly defined objectives, appropriate study designs, valid outcome measures, and suitable analytical methods. Two of the moderate-quality studies were primarily limited by sampling representativeness, reliance on self-reported measures of intervention use, and potential residual confounding. The modelling study by Bell et al. (2020a), also rated as moderate quality, was limited by assumptions regarding baseline malaria transmission, bed-net effects, and the generalizability of modelled estimates. No studies were excluded based on the quality assessment.

Effectiveness of Malaria Control Interventions

Insecticide-Treated Nets

Six studies examined the effectiveness of ITNs among children under five years of age in Malawi (Tangena et al., 2023; Nkoka et al., 2019; Zamawe et al., 2016; Chilanga et al., 2020; Hajison et al., 2018; Bell et al., 2020a). Overall, ITN use was generally associated with lower malaria risk or prevalence, although findings varied across studies. Tangena et al. (2023) reported a significant protective effect of regular ITN use, while Hajison et al. (2018) found that children from households without ITNs had significantly higher odds of malaria infection. Despite improvements in ownership following national distribution campaigns, several studies reported that utilization remained inconsistent. Nkoka et al. (2019) observed that ITN use was higher among wealthier and more educated households, whereas Zamawe et al. (2016) found limited reductions in malaria prevalence despite widespread ownership. These findings suggest that utilization and adherence are critical determinants of ITN effectiveness.

Indoor Residual Spraying

Only one included study evaluated IRS. Chilanga et al. (2020) reported approximately 20% lower malaria prevalence among children living in sprayed households compared with those living in unsprayed households. However, the effectiveness of IRS varied with spray coverage, application timing, environmental conditions, and vector ecology. The reviewed evidence suggests that IRS can provide additional protection when

implemented alongside other malaria control interventions, although its effectiveness depends heavily on operational quality and program coverage.

Table 2: Summary of the methodological quality assessment of included studies using study-design-appropriate appraisal tools.

Study	Quality appraisal tool	Appraisal summary	Overall quality
Bell et al. (2020b)	CASP RCT	Secondary analysis of an individually randomized, double-blind phase III malaria vaccine trial, with appropriate follow-up, clearly defined outcomes, and appropriate statistical analyses. Potential limitations include secondary analysis of trial data and possible detection/surveillance bias.	High
Bell et al. (2020a)	Philips et al. (2004) checklist for decision-analytic models	Clear study objectives and data sources, with modelling methods and sensitivity analyses reported. Limitations relate to assumptions concerning baseline malaria transmission, bed-net effects, and generalization of intervention effects.	Moderate
Hajison et al. (2018)	CASP Case-Control	Appropriate matched case-control design with laboratory-confirmed malaria diagnosis and adjustment for confounding: possible recall bias and limited mRDT sensitivity.	High
Zamawe et al. (2016)	CASP Cohort (adapted for cross-sectional studies)	Nationally representative survey with objective malaria outcomes and propensity score adjustment. Limited by observational design, self-reported ITN use, and residual confounding.	Moderate
Chilanga et al. (2020)	CASP Cohort (adapted for cross-sectional studies)	Systematic sampling with objective malaria testing and appropriate regression analyses. Limited by clinic-based recruitment, seasonal coverage, and inability to infer causality.	Moderate
Nkoka et al. (2019)	CASP Cohort (adapted for cross-sectional studies)	Large nationally representative DHS dataset with standardized data collection and multivariable analyses. Limited by cross-sectional design and self-reported ITN use.	High
Tangena et al. (2023)	CASP Cohort (adapted for cross-sectional studies)	Large representative sample with reliable malaria measurements and appropriate analyses. Limited by recall bias and inability to establish causality.	High
Haine et al. (2025)	CASP Cohort	Large prospective cohort with active surveillance, clearly defined safety outcomes, and appropriate statistical analyses. Limitations include the cluster-level implementation design, potential residual confounding, and imprecision for rare safety outcomes.	High

RTS,S/AS01 Malaria Vaccine

Three studies evaluated the RTS,S/AS01 malaria vaccine among children in Malawi (Bell et al., 2020b; Bell et al., 2020a; Haine et al., 2025). Bell et al. (2020a) modelled the potential impact and cost-effectiveness of RTS,S/AS01 vaccination alone and in combination with bed nets, Bell et al. (2020b) conducted a secondary analysis of Phase III randomized controlled trial data to examine environmental modifiers of vaccine efficacy, whereas Haine et al. (2025) primarily assessed vaccine safety following routine program implementation. Bell et al. (2020a) estimated reductions in malaria incidence and cases averted under different vaccination and bed-net scenarios, while Bell et al. (2020b) found that environmental context, particularly vegetation cover, modified RTS,S/AS01 vaccine efficacy. Haine et al. (2025) reported no new safety concerns up to one year

following the third vaccine dose. The available evidence indicates that RTS,S/AS01 outcomes may vary according to environmental context and implementation conditions. However, these factors were not evaluated consistently across the included studies and should therefore be interpreted cautiously.

Combined Interventions and Implementation Challenges

The included evidence on combined malaria control interventions was limited. Chilanga et al. (2020) examined ITNs and IRS, while Bell et al. (2020a), a quantitative modelling study, specifically evaluated the potential impact of combining RTS,S/AS01 vaccination with ITNs. Overall, the limited evidence suggests that combining malaria control interventions may provide complementary protection; however, the small number of studies and differences in study designs and outcomes make it difficult to conclude that combined interventions are more effective than individual interventions. The quantitative modelling study by Bell et al. (2020a), using a modelling analysis based on phase III RTS,S/AS01 trial data from Lilongwe, Malawi, estimated that combining four-dose RTS,S/AS01 vaccination with insecticide-treated bed nets could reduce clinical malaria by 71.23% during the first 18 months and 65.10% during the second 18 months. The modelling analysis also indicated that the combined vaccination and bed-net strategy was cost-effective compared with vaccination alone.

Several implementation challenges were identified across the included studies and influenced intervention effectiveness. Behavioral barriers were the most frequently reported, primarily involving inconsistent ITN use despite high ownership levels. Factors contributing to poor utilization included heat discomfort, cultural practices, sleeping arrangements, poor net maintenance, and limited awareness of the importance of nightly use (Tangena et al., 2023; Nkoka et al., 2019; Zamawe et al., 2016). Environmental barriers included insecticide resistance, poor housing conditions, and proximity to mosquito breeding sites, all of which reduced the effectiveness of vector-control interventions (Tangena et al., 2023; Hajison et al., 2018; Chilanga et al., 2020).

Quality assessment indicated that five studies were of high quality and three were of moderate quality. Common sources of bias included self-reported measures of ITN ownership and utilization, geographically restricted sampling, and residual confounding related to socioeconomic and environmental factors. Nevertheless, the included studies provided generally consistent evidence regarding the effectiveness of malaria control interventions among children under five years of age in Malawi, supporting the robustness of the overall findings.

Discussion

This systematic review assessed the effectiveness of malaria control interventions among children under five years of age in Malawi and identified key factors influencing their implementation and uptake. The findings indicate that ITNs, IRS, and the RTS,S/AS01 malaria vaccine may contribute to reducing malaria burden among young children, although intervention effectiveness varied across studies and was influenced by behavioral, environmental, and operational factors. Evidence directly evaluating combined interventions was limited and heterogeneous. The largest estimated reduction in malaria cases (65–71%) was derived from the quantitative modelling study by Bell et al. (2020a), which assessed the potential impact of combining RTS,S/AS01 vaccination with ITN use. These estimates therefore represent projected rather than directly observed effects and should not be interpreted as demonstrating the superiority of combined interventions. Overall, the findings suggest that integrated malaria control strategies may offer complementary protection, but further empirical evidence is needed to determine their comparative effectiveness.

ITNs remained the most widely evaluated intervention and were generally associated with lower malaria risk, although findings varied across studies. Nevertheless, their effectiveness depended heavily on utilization rather than ownership alone. Although Malawi has achieved substantial improvements in ITN coverage through universal distribution campaigns, several studies reported persistent gaps in utilization, particularly among rural and low-income households (Nkoka et al., 2019; Zamawe et al., 2016). Similar findings have been reported elsewhere in sub-Saharan Africa, where behavioral factors, household conditions, and socioeconomic constraints continue to limit the effectiveness of ITN programs despite high ownership levels (Biset et al., 2022; Lutambi et al., 2025). These findings suggest that increasing access alone is insufficient and that greater attention should be directed towards sustained utilization and behavioral adherence. The inconsistency in ITN effectiveness across studies is therefore likely explained by differences in usage behavior, net condition, and socioeconomic conditions across study settings.

Evidence relating to IRS indicated moderate effectiveness in reducing malaria transmission, particularly in areas of high endemicity. However, the impact of IRS was highly dependent on operational factors such as spray coverage, timing, and insecticide selection. Previous studies in Malawi have also reported increasing insecticide resistance among malaria vectors, which may reduce the long-term effectiveness of vector-control interventions (Riveron et al., 2015). However, the variability in reported effectiveness across studies may also reflect differences in intervention coverage, implementation conditions, housing characteristics, and local transmission settings (Damien et al., 2023).

The RTS,S/AS01 malaria vaccine demonstrated clinically meaningful protection against malaria in the randomized evidence included in this review. Bell et al. (2020b), a secondary analysis of a phase III randomized controlled trial, examined environmental factors that modified vaccine efficacy and provided empirical evidence of vaccine performance in Malawi. In contrast, Bell et al. (2020a) was a quantitative modelling study that estimated the potential impact and cost-effectiveness of RTS,S/AS01 vaccination, including its combination with ITNs. The modelling evidence suggested that combining vaccination with ITNs could provide greater protection against clinical malaria than vaccination alone, although these estimates represent projected rather than observed effects. Haine et al. (2025) primarily assessed the safety of RTS,S/AS01 following routine program implementation and did not estimate vaccine effectiveness. Therefore, Haine et al. (2025) should be interpreted primarily as evidence supporting the safety of RTS,S/AS01 in routine program settings rather than as evidence of vaccine effectiveness.

Overall, the findings of this review suggest the potential value of combining malaria control interventions. Integrated approaches may offer complementary protection by targeting multiple pathways of malaria transmission; however, the limited and heterogeneous evidence prevents firm conclusions regarding their comparative effectiveness. Differences in study design and methodological quality likely contribute to variation in reported effect sizes. Observational studies of ITNs and IRS are more susceptible to selection bias, information bias, and confounding, which may lead to overestimation of effectiveness. Evidence derived from randomized trial data is less susceptible to some of these biases, although the vaccine evidence included in this review also comprised secondary analysis and modelling evidence. Therefore, the magnitude of reported effects should be interpreted with caution across intervention types.

The potential benefits of integrated interventions may reflect their ability to target multiple stages of malaria transmission simultaneously. While ITNs and IRS reduce vector–human contact, vaccination provides direct protection against malaria infection and disease progression. Integrated approaches may therefore offer additional protection by addressing multiple components of malaria transmission, although the limited and heterogeneous evidence prevents firm conclusions about their comparative effectiveness.

Policy and Implementation Implications

The findings have important implications for malaria control policy and program implementation in Malawi. First, the evidence suggests that national malaria control efforts should continue prioritizing integrated intervention strategies rather than relying on single interventions. The potential complementary benefits of integrated malaria control strategies support coordinated delivery approaches consistent with Malawi's National Malaria Strategic Plan.

Second, the review highlights the limitations of relying solely on coverage-based indicators when evaluating program success. Although ownership of ITNs and uptake of malaria vaccination have increased substantially, intervention effectiveness ultimately depends on utilization, adherence, and sustained protection. Future monitoring frameworks should therefore complement coverage indicators with measures that capture actual intervention use and program performance under real-world conditions.

Third, the findings highlight persistent socioeconomic and geographic inequities in malaria protection. Several studies reported lower intervention utilization and higher malaria burden among children living in rural and lower-income households. To reduce these disparities, malaria control programs should adopt equity-focused implementation strategies, including targeted home-visit programs delivered by community health workers for high-risk households, integrating malaria education into routine under-five and immunization clinics, and prioritizing outreach activities in underserved rural communities. These strategies may strengthen caregiver health literacy, improve the correct and consistent use of insecticide-treated nets, increase malaria vaccine uptake, and promote more equitable access to malaria prevention services among vulnerable populations.

Public health officers, nurses, and community health workers also play a critical role in translating malaria control policies into effective community practice. Routine child health and immunization services provide

important opportunities to strengthen caregiver health literacy by demonstrating the correct hanging and consistent use of insecticide-treated nets, reinforcing malaria prevention practices, addressing misconceptions that contribute to poor intervention uptake, including vaccine hesitancy, and promoting timely care-seeking for febrile illness. Community-based health education delivered through trusted frontline health workers may improve adherence to malaria control interventions, increase community engagement, and enhance the effectiveness of integrated malaria control programs among children under five years of age. Finally, effective delivery of integrated malaria interventions requires adequate health-system capacity. Strengthening program delivery and ensuring sustained access to malaria prevention interventions will therefore remain important for translating potential benefits into population-level impact.

Strengths and Limitations

This review has several strengths. It followed the PRISMA 2020 guidelines and employed a transparent and systematic approach to literature identification, screening, and synthesis. The review incorporated evidence from multiple study designs and focused specifically on Malawi, providing contextually relevant insights into malaria control among children under five years of age. Furthermore, the inclusion of recent studies enabled assessment of emerging interventions, particularly the RTS,S/AS01 malaria vaccine.

Several limitations should be acknowledged. First, the review protocol was not prospectively registered in PROSPERO or another systematic review registry. Although predefined eligibility criteria, search methods, and quality appraisal procedures were established before the review was conducted, prospective registration would have enhanced transparency and reduced the potential risk of selective reporting. Secondly, the review was restricted to peer-reviewed studies published in English and may therefore have excluded relevant evidence from grey literature, program reports, and non-English publications. The small number of eligible studies and substantial heterogeneity in study design, outcome measures, and analytical methods limited direct comparison across studies and precluded quantitative meta-analysis. In addition, several included studies relied on self-reported measures of intervention utilization, which may have introduced reporting bias. These limitations should be considered when interpreting the findings. Overall, despite these limitations, the reviewed studies provided generally consistent evidence regarding the effectiveness of malaria control interventions among children under five years of age in Malawi and offer valuable insights for future malaria control policy and program implementation.

Most observational studies evaluating ITNs and IRS were subject to selection bias due to non-representative sampling and information bias resulting from reliance on self-reported intervention use, which may have led to overestimation of coverage and effectiveness. In addition, confounding by socioeconomic and environmental factors may have influenced observed associations, particularly in non-randomized studies. In contrast, evidence from randomized controlled trials evaluating the RTS,S/AS01 vaccine is less affected by these biases, providing greater confidence in estimates of vaccine effect. Overall, while the direction of effect is consistent across studies, the magnitude of effectiveness, particularly for ITNs and IRS should be interpreted with caution due to methodological limitations.

Although the overall direction of evidence was consistent across the included studies, the magnitude of the reported intervention effects, particularly for ITNs and IRS, should be interpreted with caution because of differences in study design, methodological quality, and potential bias. Higher-quality randomized studies provided more robust evidence than observational studies, which were inherently more vulnerable to bias and confounding.

Conclusions

This systematic review suggests that malaria control interventions, including insecticide-treated nets, indoor residual spraying, and malaria vaccination, may contribute to reductions in malaria burden among children under five years of age in Malawi, based on the available evidence from a limited number of studies and a narrative synthesis without quantitative meta-analysis. While each intervention appeared to reduce malaria risk within the included studies, the limited evidence on combined interventions suggests that they may provide complementary or additional protection compared with individual interventions; however, the available evidence is insufficient to conclude that combined interventions are more effective. The largest estimated reduction (65–71%) was derived from a quantitative modelling study and therefore represents a projected rather than directly observed effect. Intervention effectiveness was influenced by behavioural, environmental, and operational factors, including inconsistent utilization, insecticide resistance, socioeconomic disparities, and programme delivery challenges. The findings support strengthening the integrated delivery of insecticide-treated nets and malaria vaccination through routine child health services, alongside community-based

caregiver education and equitable access to malaria prevention interventions. Addressing these implementation barriers may help achieve sustained reductions in malaria burden and support progress towards national and global malaria control targets.

Statements

Funding Statement: This research received no external funding.

Ethical Considerations: Ethical approval was not required because this systematic review used data from previously published and publicly available studies and did not involve human participants or identifiable personal data.

Data Availability: All data analyzed in this systematic review were obtained from the published studies included in the review.

Conflict of Interest Statement: The authors declare no conflicts of interest.

CRediT role of authors: Eneles Chisonga: Conceptualization, Methodology, Investigation, Data Curation, Formal Analysis, Writing – Original Draft. Russell Kabir: Supervision, Validation, Writing – Review & Editing.

Declaration of Generative Artificial Intelligence (AI): The authors declare that generative artificial intelligence was not used in the preparation of this manuscript.

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