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Efficacy of Interceptor® G2 Long-Lasting Insecticidal Net Against Pyrethroid-Resistant Malaria Vector *Anopheles gambiae s.l.*: A Systematic Review and Meta-Analysis

Hassan M. Alzain[1], Hassan A. Alkhunaizi[2]

[1]Graduate, Yale School of the Environment, New Haven, United States of America,
[2]Graduate, King Abdullah University of Science and Technology, Thuwal, Saudi Arabia.

Corresponding Author: Hassan M. Alzain, Email: Hassan.Alzain@Yale.edu

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ABSTRACT

Background: Malaria is a major public health issue, primarily in sub-Saharan Africa, where long-lasting insecticidal nets (LLINs) have been compromised by pyrethroid-resistant vectors of the *Anopheles gambiae s.l.* complex. Interceptor® G2 is a new generation alternative that is defined as a dual-insecticide LLIN with alpha-cypermethrin (100 mg/m²) and chlorfenapyr (200 mg/m²) where target-resistant vectors are killed due to a novel mode of action. This is a systematic review and meta-analysis of the entomological efficacy of Interceptor G2 under Phase II WHOPES experimental hut trials.

Methods: A systematic search of PubMed, Scopus, and Web of Science was conducted for articles published between January 1991 and July 2025. Eligible studies were English Phase II WHOPES trials of Interceptor® G2, unwashed and washed 20 times, against pyrethroid-resistant An. gambiae s.l. Comparator arm controls were untreated nets, nets treated solely for chlorfenapyr, and standard Interceptor® (alpha-cypermethrin-only) nets. 72-hour lethality of mosquitoes, blood-feeding inhibition, and mosquito exit were key outcomes. Risk of bias assessment used ROBINS-I. Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were estimated using a random-effects model (DerSimonian–Laird).

Results: Six studies were included, with study locations in Benin, Burkina Faso, Côte d'Ivoire, and Tanzania. Interceptor® G2 (unwashed) had an edge on 72-hour mortality (OR = 47.29; 95% CI: 28.5–78.44) and blood-feeding inhibition (OR = 0.33; 95% CI: 0.21–0.53) compared to untreated ones. Interceptor® G2 washed was significantly effective (OR = 36.23; 95% CI: 21.36–61.45 for mortality). Exiting rates were also significantly enhanced for Interceptor® G2 (unwashed OR = 3.5; 95% CI: 2.49–4.90) use. Results were consistent across studies with very minimal heterogeneity for mortality and exiting outcomes. There was, however, intermediate heterogeneity (I^2 = 62.9%) for blood-feeding inhibition. The overall risk of bias was low to moderate in most studies.

Conclusion: Interceptor® G2 nets have demonstrated significantly greater effectiveness than conventional pyrethroid-only LLINs and chlorfenapyr-only nets in increasing mosquito mortality, reducing blood-feeding, and encouraging mosquito exit behavior. This enhanced performance remains consistent even after 20 washes. These results support the expanded use of

Interceptor® G2 in malaria control programs, especially in areas where mosquitoes are resistant to pyrethroids. However, additional Phase III community-level trials are needed to confirm its public health benefits and cost-effectiveness.

Keywords: Malaria, Interceptor® G2, long-lasting insecticidal nets, pyrethroid resistance, chlorfenapyr, Anopheles gambiae, WHOPES, experimental huts, vector control

INTRODUCTION

Vector-borne infections continue to present a major health risk globally, and of these, malaria remains especially severe in sub-Saharan Africa. In 2020, malaria caused an estimated 627,000 deaths worldwide, the vast majority in low-resource settings where environmental vulnerability and limited infrastructure heighten transmission risk (1). The *Anopheles gambiae* complex, particularly *An. gambiae s.s.* and *An. coluzzii*, is recognized as the primary vector of malaria transmission in Africa (2,3). In the absence of a widely distributed and effective malaria vaccine, the most effective means of reducing disease burden and transmission has been through vector control (4). WHO-recommended core measures include indoor residual spraying (IRS) and long-lasting insecticidal nets (LLINs). Since 2000, malaria morbidity and mortality have declined substantially across sub-Saharan Africa, with cases reduced by 42% and deaths by 66% through the scale-up of multiple interventions, including LLINs, IRS, and improved diagnostics and treatment. Among these, LLINs accounted for the largest share of progress, responsible for an estimated 68% of cases averted between 2000 and 2015 (2). Nevertheless, the effectiveness of LLINs has been increasingly compromised by the emergence of insecticide resistance, particularly to pyrethroids, the only class of insecticides historically licensed for LLINs (5–7).

To address this growing resistance emergen cy, innovative LLIN formulations have been developed to preserve and enhance vector control. One such product is Interceptor® G2 which is a dual-insecticide LLIN that combines chlorfenapyr, a pyrrole-class insecticide (200 mg/m²), with the traditional pyrethroid alpha-cypermethrin (100 mg/m²) (8,9). Chlorfenapyr has a novel mode of action, targeting mitochondrial oxidative phosphorylation pathways, thereby disrupting ATP production in mosquitoes (10,11). This mechanism differs from that of the usual pyrethroids and other conventional insecticides, making the utility of chlorfenapyr its extreme effectiveness against pyrethroid-resistant mosquitoes. Additionally, because of its slow-acting, non-repellent mode of action, its effectiveness is maximized by achieving longer-lasting contact of the mosquito and the net, the main benefit being that of overcoming behavioral avoidance (12,13).

The WHO Global Vector Control Response (GVCR) 2017–2030 emphasizes the urgent need for integrated strategies to address insecticide resistance, climatic forcing of shifts in the epidemiology of infections, and operational limitations of existing tools (14). Climate change, for instance, has been outlined as changing the geographic range, seasonal occurrence, and transmission of malaria vectors (15–17). By modifying temperature, humidity, and rainfall patterns, climate change has direct effects on the survival, breeding, and behavioral response of vectors. This climatic influence reinforces the need for LLINs with long-lasting efficacy across varied ecological settings and resistance profiles. (18) Also, initial tests of Interceptor® G2 under WHOPES Phase II experimental hut trials have been encouraging. These are experimental hut trials under realistic conditions of exposure that give us primary entomological end-points, for example, deaths of mosquitoes, blood-feeding inhibition, and exiting (19–21). Compared to conventional pyrethroid-only nets, Interceptor® G2 has consistently shown higher efficacy against resistant Anopheles species, including An. gambiae, An. funestus, and An. arabiensis, as

evidenced in studies across Benin, Côte d'Ivoire, Tanzania, and Burkina Faso (22,23). Expansion of use of Chlorfenapyr as a first-of-class insecticide is aided by growing literature that presents evidence of its potential for multi-resistant malaria vectors. Some have noted its increased effectiveness as combination LLINs (e.g., Interceptor G2) versus as monotherapies (9,13). Interceptor G2 has also kept its effectiveness after 20 simulated washes, fulfilling the requirements of the WHO for wash-resistance as well as residual activity (20,24). This systematic review and meta-analysis aim to evaluate the entomological efficacy of Interceptor® G2 when applied to LLINs and used against pyrethroid-resistant An. gambiae s.l. in WHOPES Phase II experimental hut trials. Specifically, the analysis compares the performance of Interceptor® G2, both unwashed and after 20 washes, against untreated nets, chlorfenapyr-only nets (200 mg/m²), and standard Interceptor LLINs (200 mg/m² alpha-cypermethrin). The primary entomological outcomes of interest are mosquito exiting rate, blood-feeding inhibition, and 72-hour mortality, that together measure the protective capability of users as well as the control of vectors under conditions of emerging insecticide resistance.

METHODS

Study Design and Ethical Considerations

This study is a systematic review and meta-analysis conducted in accordance with the PRISMA 2020 guidelines. It aimed to evaluate the comparative efficacy of Interceptor® G2 long-lasting insecticidal nets (LLINs) against pyrethroid-resistant Anopheles gambiae sensu lato in Phase II experimental hut trials approved under the WHO Pesticide Evaluation Scheme (WHOPES). Since the analysis relied solely on published data, no ethics approval was required.

Data Sources and Search Strategy

A systematic search of PubMed, Scopus, and Web of Science Core Collection databases was conducted for English-language articles published between January 1991 and July 2025. The search combined Medical Subject Headings (MeSH) and free-text terms including "chlorfenapyr," "alpha-cypermethrin," "cypermethrin," "Interceptor® G2," "malaria," "Anopheles gambiae," and "pyrethroid-resistant vector." The Boolean strategy used was: ("chlorfenapyr" OR "alpha-cypermethrin" OR "cypermethrin" OR "Interceptor® G2") AND ("malaria" OR "Anopheles gambiae" OR "pyrethroid-resistant vector"). Reference lists of included studies were also screened manually to identify additional eligible trials.

Study Selection

All documents that resulted from the search strategy were transferred to Endnote; then removed duplicate articles from the file. The remaining documents were then passed through a title- and abstract-screening step, followed by a full-text-screening step, and finally were read carefully to evaluate their suitability for this study's intended inclusion and exclusion criteria. The PRISMA flow chart explains the included and omitted studies and the grounds for exclusion (Figure 1).

Eligibility Criteria

The included studies were English-language science publications from 1991 to July 2025. All studies evaluated the effectiveness of Interceptor® G2 applied on LLINs to protect against pyrethroid-resistant malaria species (*An. gambiae s.l.*) in phase II WHOPES trials using experimental huts. In terms of species, we included pyrethroid-resistant *An. gambiae s.l.* In terms of interventions, we included all studies that evaluated the efficacy of Interceptor® G2 (200 mg/m^2 chlorfenapyr added to 100 mg/m^2 alpha-cypermethrin), both unwashed and after 20 washes, in comparison with untreated nets, nets treated with chlorfenapyr 200 mg/m^2, and nets treated with standard Interceptor (200 mg/m^2 alpha-cypermethrin), both unwashed and after 20 washes. We included only studies that addressed the efficacy of

Interceptor® G2 applied to LLINs in experimental huts.

We excluded studies that evaluated only one active component separately (rather than the Interceptor® G2 mixture as a whole); studies that evaluated the Interceptor® G2 mixture against susceptible or non-resistant An. gambiae, or resistant *Anopheles* other than pyrethroid-resistant *An. gambiae s.l.*; studies that evaluated Interceptor® G2 efficacy using methods other than long-lasting insecticidal nets; studies that evaluated Interceptor® G2 in phases other than WHOPES phase II experimental huts; studies not containing the intended outcomes; reviews; protocols; letters to the editor; meeting abstracts; phase I laboratory studies; and studies in languages other than English. We included all studies that addressed the percentage of exiting, blood feeding, and mortality after 72 hours.

Data Extraction

Two independent reviewers extracted data using a standardized Excel template. Extracted information included author name, publication year, study region, trial duration, mosquito species, net type, wash status, comparator arms, and outcome measures. When data were not presented in tables, values were extracted from graphs.

Outcome Measures

The exiting rate was defined as the proportion of mosquitoes caught in exit traps, reflecting behavioral avoidance. The blood-feeding inhibition rate referred to the proportion of mosquitoes that did not blood-feed, representing the personal protective efficacy of the LLIN. The 72-hour mortality rate measured the percentage of mosquitoes that died within 72 hours of exposure, indicating insecticidal potency.

Risk of Bias Assessment

Risk of bias was evaluated using the ROBINS-I tool for non-randomized studies. Domains assessed included confounding, participant selection, classification of interventions, deviations from intended interventions, missing data, outcome measurement, and selective reporting. As shown in Figures 2 and 3, two studies were classified as having a low overall risk of bias, two had moderate risk, and two were judged to have serious risk due to confounding and poor reporting. Inter-reviewer agreement was high, and discrepancies were resolved through discussion.

STATISTICAL ANALYSIS

Meta-analyses were performed using R software (version 4.1.1). Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using a random-effects model (DerSimonian–Laird). Analyses were stratified by net washing status (unwashed vs. washed 20 times). Heterogeneity was assessed using Cochran's Q test and quantified using the I^2 statistic. A p-value less than 0.05 or I^2 greater than 60% was considered indicative of substantial heterogeneity. Network meta-analysis was not performed due to limited overlap of interventions; pairwise random-effects meta-analyses were conducted for each comparison. All treatment comparisons used untreated nets as the reference. The certainty of evidence was not formally graded due to the small number of studies.

RESULTS

Search Strategy Results

A total of 2,014 records were retrieved from electronic databases including PubMed (n = 657), Scopus (n = 800), and Web of Science (n = 557). After removal of duplicates (n = 871), ineligible articles flagged by automation tools (n = 143), and other irrelevant records (n = 22), 978 articles remained for title and abstract screening. Of these, 10 full-text articles were assessed for eligibility, with 4 excluded due to design or outcome mismatch. Ultimately, six studies were included in the final meta-analysis. The study selection process is illustrated in Figure 1.

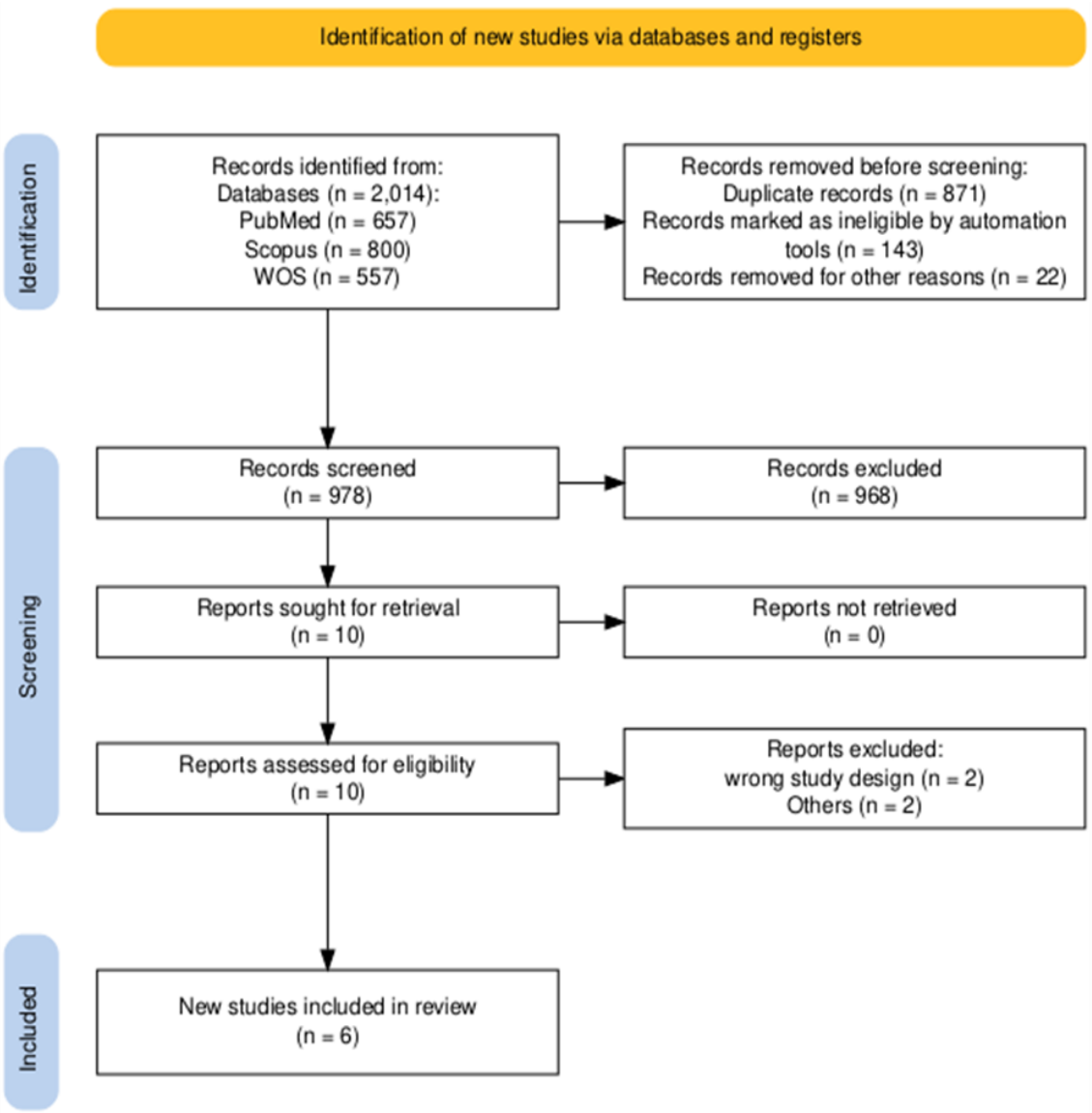

Figure 1. PRISMA 2020 flow diagram of study screening and selection. Numbers in each box match those reported in the Results ("Search Strategy Results").

General Characteristics of the Included Studies

The six included experimental hut trials were conducted in West and East Africa, specifically in Benin (two studies), Burkina Faso (one study), Côte d'Ivoire (one study), and Tanzania (two studies). All studies employed WHOPES Phase II experimental hut designs to evaluate the efficacy of Interceptor® G2 long-lasting insecticidal nets (LLINs) against pyrethroid-resistant Anopheles gambiae s.l. or related species. Across studies, the intervention arms commonly included untreated nets, chlorfenapyr-only nets (200 mg/m²), Interceptor LN (alpha-cypermethrin 200 mg/m²), and Interceptor® G2 (chlorfenapyr 200 mg/m² + alpha-cypermethrin 100 mg/m²), tested both unwashed and after 20 washes. Additional LLIN brands such as Royal Guard® and PermaNet® 3.0 were included in the Sovegnon et al. study. (25)

Study durations ranged from 6 to 10 weeks, with mosquito species tested including *An. gambiae s.l.*, *An. coluzzii*, *An. arabiensis*, *An. funestus s.s.*, and *Culex (Cx.) quinquefasciatus*. Most studies confirmed high baseline resistance to pyrethroids among vector populations. Supplementary Table 1 summarizes the detailed study characteristics.

Table 1. Study characteristics of included Phase II experimental hut trials (location, species, arms, wash status, outcomes).

Study ID	Study Design	Duration	Study Site	Comparison Arms	Insecticide Concentration	Anopheles Species	Study Outcomes
Sovegnon et al., 2024 (25)	Experimental Huts	2 rounds	Za-Kpota, Benin	Interceptor® G2, Royal Guard®, PermaNet® 3.0 (new and aged), Untreated, PermaNet 2.0	Varied per net: see document, e.g., IG2 100 mg/m² alpha-cypermethrin + 200 mg/m² chlorfenapyr	An. gambiae s.s., An. coluzzii	IG2 highest mortality (90%), Royal Guard highest feeding inhibition (5.6%)
Kibondo et al., 2022 (24)	Experimental Huts, Cone Tests, Tunnel Tests, I-ACT	20 nights per modality	Bagamoyo (lab), Lupiro (field), Tanzania	Interceptor® G2 (unwashed, 20x washed), Interceptor® (unwashed, 20x washed), SafNet (untreated)	100 mg/m² alpha-cypermethrin, 200 mg/m² chlorfenapyr	An. arabiensis, An. gambiae s.s., Cx. quinquefasciatus	IG2 superior in hut, tunnel, I-ACT vs Interceptor; cone test less predictive.
Tungu et al., 2021 (23)	Experimental Huts (Phase II)	54 nights (Trial 1), 36 nights (Trial 2)	Zeneti, Tanzania	Interceptor® G2 (unwashed, 20x washed), Interceptor® (unwashed, 20x washed), Chlorfenapyr net, Untreated net	100 mg/m² alpha-cypermethrin, 200 mg/m² chlorfenapyr	An. funestus s.s.	IG2 mortality consistently higher; no wash effect; chlorfenapyr drove mortality.
Camara et al., 2018 (4)	Experimental Huts (semi-field)	6 weeks	M'Bé, Côte d'Ivoire	Interceptor® G2 (unwashed, 20x washed), Interceptor® (unwashed, 20x washed), Chlorfenapyr net, Untreated net	100 mg/m² alpha-cypermethrin, 200 mg/m² chlorfenapyr	An. gambiae s.s.	IG2 mortality 82-87%; blood-feeding inhibition 34-42%; met WHOPES Phase III criteria.
Bayili et al., 2017 (19)	WHOPES Phase II Experimental Huts	8 weeks	Vallée du Kou, Burkina Faso	Interceptor® G2 (unwashed, 20x washed), Interceptor® (unwashed, 20x washed), Chlorfenapyr net, Untreated net	100 mg/m² alpha-cypermethrin, 200 mg/m² chlorfenapyr	An. gambiae s.l.	Mixture nets killed 76-78% vs. 10-17% for alpha-cypermethrin alone. Improved protection post-wash.
N'Guessan et al., 2016 (22)	Experimental Huts	72 nights	Cove, Benin	Interceptor® G2 (unwashed, 15x, 20x washed), Interceptor® (unwashed, 15x, 20x washed), Chlorfenapyr net, Untreated net	100 mg/m² alpha-cypermethrin, 200 mg/m² chlorfenapyr	An. gambiae s.l., An. coluzzii	IG2 mortality ~65-71% post wash vs 20% alpha-cypermethrin only; improved durability confirmed.

Laboratory Bioassays in Included Studies

Cone bioassays were conducted in all studies, while tunnel tests were performed in four studies. In general, tunnel tests were more predictive of field efficacy than cone tests, especially for chlorfenapyr-containing nets. For example, Camara et al. reported mortality ranging from 82–87% and blood-feeding inhibition of 34–42% using Interceptor® G2. (4) N'Guessan et al. showed consistent mortality around 65–71% even after 20 washes (22). Bayili et al. also demonstrated high durability of mixture-treated nets, with mortality sustained at 76–78% after washing. (19)

Kibondo et al. and Tungu et al. conducted comprehensive assessments including Ifakara Ambient Chamber Test (IACT) and field assays, showing that Interceptor® G2 consistently outperformed standard Interceptor nets and chlorfenapyr alone in terms of both blood-feeding inhibition and delayed mortality. (23,24) Chemical analysis of net samples was performed in Bayili et al. and N'Guessan et al., confirming the stability of insecticide content after washing and field use. (19,22) CDC bottle bioassays were conducted in Camara et al. and N'Guessan et al. to determine resistance intensity (4,22).

Quality Assessment

Risk of bias was assessed using the ROBINS-I tool. None of the studies clearly reported blinding collectors or sleepers. Randomization and rotation of nets and sleepers were confirmed in four studies. Three studies followed WHOPES-standard washing procedures. Laboratory bioassays were performed before and after trials in all studies. Chemical content validation of insecticides was performed in two studies. Figures 2 and 3 summarize risk-of-bias findings across studies and bias domains.

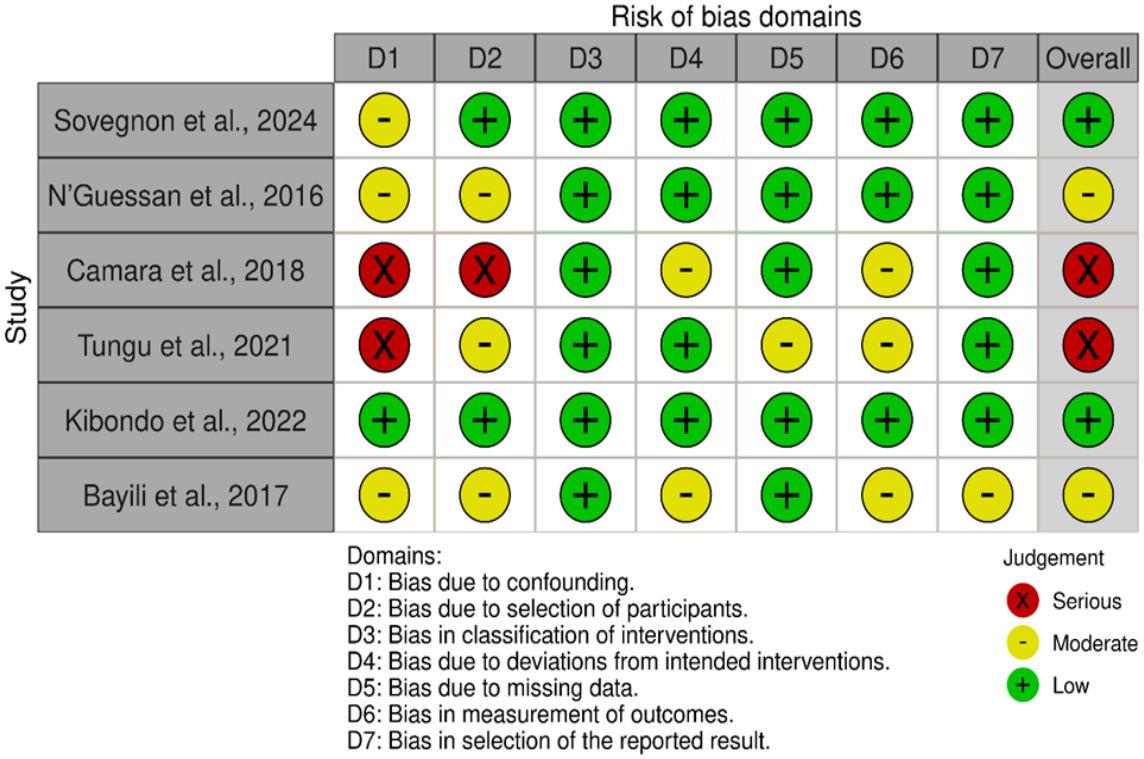

Figure 2. ROBINS-I risk-of-bias summary across included studies.

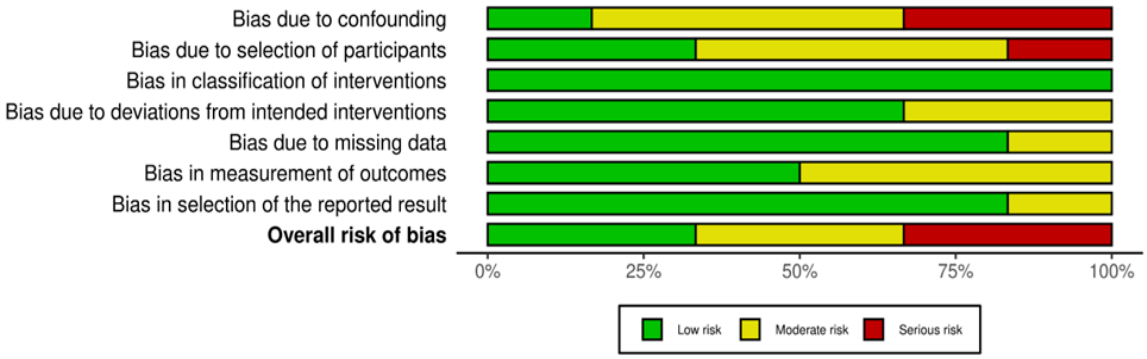

Figure 3. ROBINS-I traffic-light plot by study and domain.

Mosquito Capture Data in Experimental Huts

Across all trials, the total number of An. gambiae s.l. mosquitoes collected was as follows: 2,447 in the untreated nets arm, 1,670 in the chlorfenapyr arm, 1,580 in the unwashed Interceptor LN arm, 2,496 in the Interceptor LN after 20 washes arm, 1,879 in the unwashed Interceptor G2 arm, and 2,326 in the Interceptor G2 after 20 washes arm.

Meta-analysis Outcomes

Exiting Rate

Compared to untreated nets, unwashed Interceptor® G2 LN exhibited the highest increase in mosquito exiting (OR = 3.5; 95% CI: 2.49–4.90), followed by Interceptor® G2 LN after 20 washes (OR = 2.59; 95% CI: 1.85–3.62), unwashed Interceptor LN (OR = 2.46; 95% CI: 1.76–3.44), chlorfenapyr (OR = 2.42; 95% CI: 1.73–3.39), and Interceptor LN after 20 washes (OR = 1.83; 95% CI: 1.31–2.56). All interventions significantly increased exiting compared to untreated nets. Heterogeneity was low ($Q = 8.76$, $I^2 = 0\%$, $P = 0.55$). Figure 4 presents the forest plot of exiting rate.

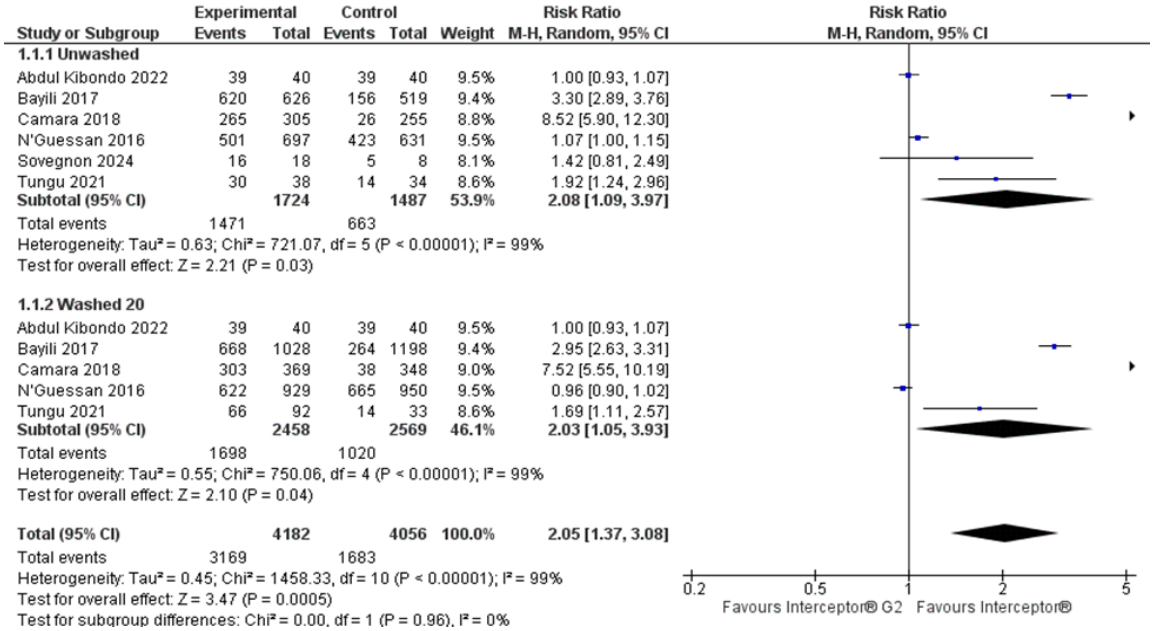

Figure 4. Forest plot of exiting rate for Interceptor® G2 versus comparator nets, stratified by wash status (pooled OR with 95% CI; random-effects).

Blood-Feeding Inhibition

Unwashed Interceptor® G2 achieved the greatest reduction in blood feeding (OR = 0.33; 95% CI: 0.21–0.53), followed by chlorfenapyr (OR = 0.37; 95% CI: 0.22–0.63), Interceptor® G2 LN after 20 washes (OR = 0.39; 95% CI: 0.23–0.66), unwashed Interceptor LN (OR = 0.42; 95% CI: 0.26–

0.68), and Interceptor LN after 20 washes (OR = 0.54; 95% CI: 0.32–0.91). All interventions were significantly better than untreated nets. Moderate heterogeneity was observed (Q = 32.35, I^2 = 62.9%, P < 0.01). Results are shown in Figure 5.

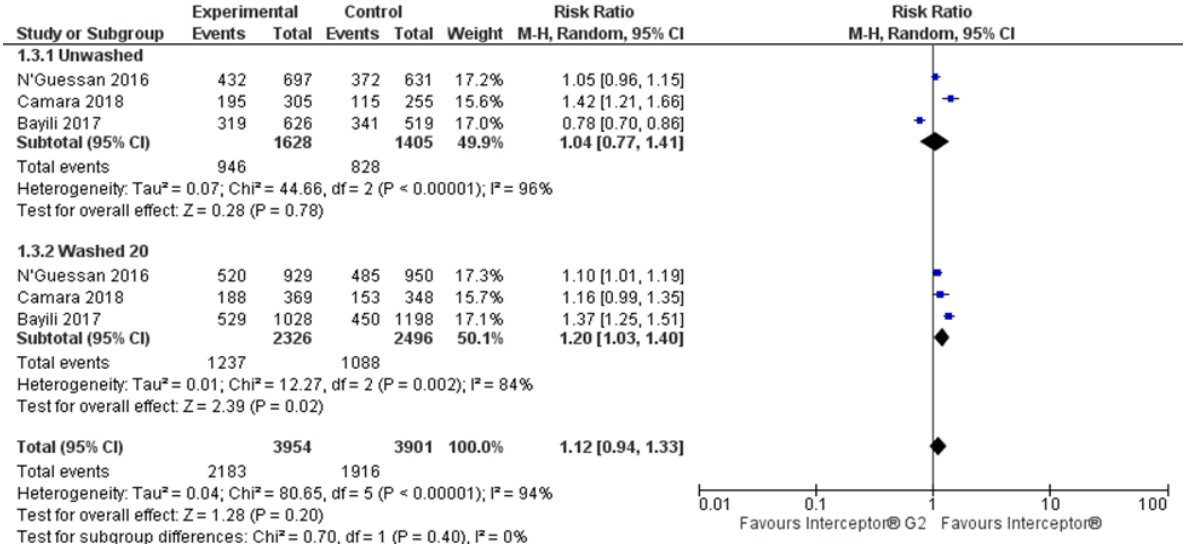

Figure 5. Forest plot of blood-feeding inhibition (pooled OR with 95% CI; random-effects).

72-Hour Mosquito Mortality

For delayed mortality at 72 hours, chlorfenapyr showed the highest efficacy (OR = 66.72; 95% CI: 37.89–117.48), followed by unwashed Interceptor® G2 (OR = 47.29; 95% CI: 28.5–78.44), Interceptor® G2 after 20 washes (OR = 36.23; 95% CI: 21.36–61.45), unwashed Interceptor LN (OR = 3.70; 95% CI: 2.26–6.06), and Interceptor LN after 20 washes (OR = 2.66; 95% CI: 1.56–4.54). All intervention arms resulted in significantly higher mortality than untreated nets. Heterogeneity was low (Q = 19.49, I^2 = 27.2%, P = 0.17). The forest plot is displayed in Figure 6.

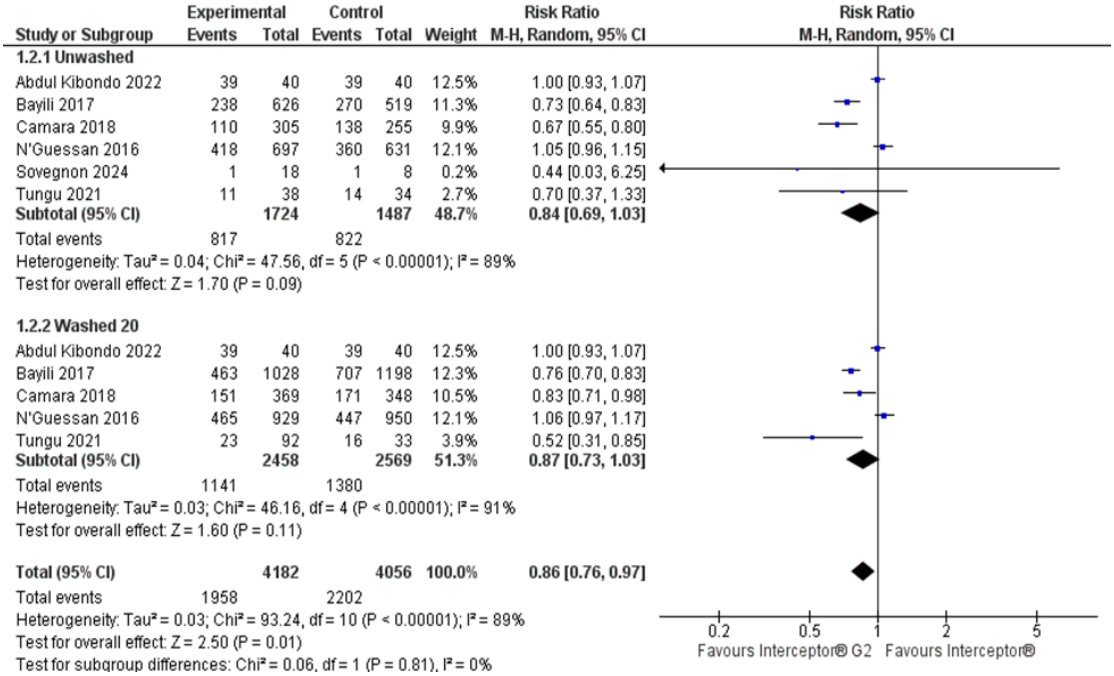

Figure 6. Forest plot of 72-hour mortality (pooled OR with 95% CI; random-effects).

DISCUSSION

Sub-Saharan Africa has a high rate of pyrethroid-resistant malaria vectors. Because the experimental hut trial is the gold-standard method for assessing the effectiveness of LNs in controlled settings, this systematic review and meta-analysis evaluated the efficacy of Interceptor® G2 long-lasting insecticidal nets (LLINs) against pyrethroid-resistant Anopheles gambiae s.l. vectors using Phase II WHOPES experimental hut trials. (26,27) The analysis demonstrated that Interceptor® G2 significantly outperformed standard pyrethroid-only LLINs and chlorfenapyr-only nets across all primary outcomes: 72-hour mortality, blood-feeding inhibition, and mosquito exiting rates. These outcomes are especially important in the context of escalating pyrethroid resistance, which threatens to undermine the global progress made in malaria control over the past two decades (1,28).

The analysis revealed that Interceptor® G2, unwashed and after 20 washes, caused significantly greater mortality (OR = 47.29 and OR = 36.23, respectively) than controls of conventional alpha-cypermethrin nets or of nets of only chlorfenapyr. These findings are consistent with previous reports suggesting that the synergistic combination of chlorfenapyr and alpha-cypermethrin provides dual-action efficacy by combining rapid knockdown from the pyrethroid with the delayed, lethal mitochondrial disruption of chlorfenapyr (19,22,29). Unlike other insecticides, chlorfenapyr does not act on the nervous system but instead disrupts oxidative phosphorylation, which not only overcomes resistance mechanisms but also ensures lasting toxicity even against pyrethroid-tolerant mosquitoes (10).

Also, blood-feeding inhibition results confirm the protective effectiveness of Interceptor® G2. While a very mild irritant or repellent effect is possessed by chlorfenapyr alone, the excito-repellent of the net, alpha-cypermethrin, presents substantial reductions of mosquito-feeding (4). Lower percentages of blood-feeding that were achieved for unwashed as well as washed Interceptor® G2 nets indicate that these nets offer both personal protection and vector control. This combination effectively reduces both mosquito survival and host-vector contact. The observed efficacy remained high even after 20 standard washes, also supporting recommendations of the WHO for long-lasting bioefficacy. These had a greater effect than that of chlorfenapyr alone or of typical pyrethroid nets (24). With induced exiting behavior, Interceptor® G2 also outperformed all of its comparator arms, most noticeably when unwashed, thus establishing its behavioral effect as well as its kill. This implies that the net not only kills but also does not give mosquitoes even an attempt to feed, an additional measure of protection. Both active compounds are also most likely to cause increased irritant reaction and behavioral avoidance, an additional risk reduction of malaria transmission (23). Our results also indicate that wash had no perceivable reduction of net performance, once again supporting the wash durability of the product as well as WHOPES guideline use (30). The study's findings align with prior evaluations conducted across diverse ecological settings in sub-Saharan Africa, where Interceptor® G2 showed sustained efficacy against multiple resistant Anopheles species, including An. arabiensis, An. coluzzii, and An. funestus s.s. (20,23,24) Such findings have great public health advantages. Interceptor® G2 introduction could, to some degree, compensate for the effects of general insecticide resistance, most emblematically in sub-Saharan Africa, where sub-Saharan mosquitoes have practically entrenched pyrethroid resistance (5). Nevertheless, as the most scalable and inexpensive preventive for malaria, under realistic conditions, the effectiveness of LLINs is of highest significance, as they still constitute the most scalable and inexpensive preventive for malaria.

However, the study also has limitations. First, although Phase II hut trials provide strong evidence of entomological efficacy, they are not designed to measure clinical outcomes such as malaria incidence or

prevalence. Therefore, even as Interceptor G2 demonstrates effectiveness for population reduction of vectors as well as prevention of mosquito-human contact, its direct epidemiological impact still requires validation through community-level Phase III cluster randomized trials (31,32).

Second, variations in mosquito species composition, resistance mechanisms, and environmental conditions vary between study sites, allowing for a potential heterogeneity. Although we observed low statistical heterogeneity in some outcomes (e.g., mortality and exiting), blood-feeding inhibition showed moderate heterogeneity (I^2 = 62.9%), suggesting that some results may be context-dependent. Additionally, the limited availability of raw data and the lack of blinding in some studies may have introduced bias, despite rigorous risk-of-bias assessment (33). Another possible limitation of these 72 hr surrogate endpoints of mosquito mortality following exposure is that they might not sufficiently represent delayed sub-lethal events that develop over days or terminal-stage changes of mosquito comportment. Cost-effectiveness of scale-up as well as operational usability of incorporating Interceptor® G2 into national malaria control programs is an area under investigation (9,14). Despite these limitations, our findings highlight the substantial entomological benefit of Interceptor® G2, especially in areas where conventional LLINs have diminished effectiveness due to resistance. Its unique combination of rapid and delayed toxicity, wash durability, and broad-spectrum efficacy makes it a strong candidate for next-generation vector control tools. As pyrethroid resistance continues to threaten malaria control gains, Interceptor® G2 emerges as a promising tool to sustain and enhance vector control efficacy (20,34). Future research should focus on head-to-head comparisons of Interceptor® G2 with other dual-insecticide LLINs such as Royal Guard® or PermaNet® 3.0, and on community trials that quantify their epidemiological impact in terms of malaria incidence, transmission dynamics, and cost-effectiveness (35,36).

CONCLUSION

In conclusion, Interceptor® G2 represents a significant advancement in LLIN technology and offers a promising solution to the challenge of pyrethroid resistance. Its dual active components provide a potent and durable response against resistant malaria vectors and support its broader integration into global malaria elimination strategies.

Availability of data and materials

All study data and materials are published in the manuscript.

Author Contributions

All authors contributed to the study design, data extraction, analysis, and manuscript preparation. The corresponding author finalized the manuscript and approved the submission.

Declaration by Authors

Ethical Approval: No ethics approval or consent to participate is required for this study.

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Conflict of Interest: The authors declare there is no conflict of interest regarding the publication of this paper.

REFERENCES

1. World Health Organization. World malaria report 2021. Geneva: World Health Organization; 2021. Available from: https://iris.who.int/handle/10665/350147
2. Bhatt S, Weiss DJ, Cameron E, et al. The effect of malaria control on Plasmodium falciparum in Africa between 2000 and 2015. Nature. 2015;526(7572):207–211. doi:10.1038/nature15535
3. Rossati A, Bargiacchi O, Kroumova V, Zaramella M, Caputo A, Garavelli PL. Climate, environment and transmission of

malaria. Le infezioni in medicina. 2016;24(2):93–104. Available from: https://pubmed.ncbi.nlm.nih.gov/27367318/

4. Camara S, Alou LPA, Koffi AA, Clegban YCM, Kabran JP, Koffi FM, et al. Efficacy of Interceptor® G2, a new long-lasting insecticidal net against wild pyrethroid-resistant Anopheles gambiae s.s. from Côte d'Ivoire: a semi-field trial. Parasite. 2018;25:42. Available from: https://doi.org/10.1051/parasite/2018042
5. Edi CV, Koudou BG, Jones CM, Weetman D, Ranson H. Multiple-insecticide resistance in Anopheles gambiae mosquitoes, Southern Côte d'Ivoire. Emerging Infectious Diseases. 2012;18(9):1508–1511. Available from: https://wwwnc.cdc.gov/eid/article/18/9/12-0262_article
6. Mosha JF, Kulkarni MA, Messenger LA, Rowland M, Matowo N, Pitt C, et al. Protocol for a four parallel-arm, single-blind, cluster-randomised trial to assess the effectiveness of three types of dual active ingredient treated nets compared to pyrethroid-only long-lasting insecticidal nets to prevent malaria transmitted by pyrethroid insecticide-resistant vector mosquitoes in Tanzania. BMJ Open. 2021;11(3):e046664. Available from: https://bmjopen.bmj.com/content/11/3/e046664
7. Mosha JF, Kulkarni MA, Lukole E, Matowo NS, Pitt C, Messenger LA, et al. Effectiveness and cost-effectiveness against malaria of three types of dual-active-ingredient long-lasting insecticidal nets (LLINs) compared with pyrethroid-only LLINs in Tanzania: a four-arm, cluster-randomised trial. The Lancet. 2022;399(10331):1227–1241. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02499-5/fulltext
8. N'Guessan R, Boko P, Odjo A, Knols B, Akogbeto M, Rowland M, et al. Control of pyrethroid-resistant Anopheles gambiae and Culex quinquefasciatus mosquitoes with chlorfenapyr in Benin. Tropical Medicine & International Health. 2009;14(4):389–395. Available from: https://doi.org/10.1111/j.1365-3156.2009.02244.x
9. Ngufor C, Fongnikin A, Hobbs N, Gbegbo M, Kiki L, Odjo A, et al. Indoor spraying with chlorfenapyr (a pyrrole insecticide) provides residual control of pyrethroid-resistant malaria vectors in southern Benin. Malaria Journal. 2020; 19:249. Available from: https://malariajournal.biomedcentral.com/articles/10.1186/s12936-020-03325-2
10. Black BC, Hollingworth RM, Ahammadsahib KI, Kukel CD, Donovan S. Insecticidal action and mitochondrial uncoupling activity of AC-303,630 and related halogenated pyrroles. Pesticide Biochemistry and Physiology. 1994;50(2):115–128. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0048357584710649
11. Oxborough RM, N'Guessan R, Jones R, Kitau J, Ngufor C, Malone D, et al. The activity of the pyrrole insecticide chlorfenapyr in mosquito bioassay: towards a more rational testing and screening of non-neurotoxic insecticides for malaria vector control. Malaria Journal. 2015; 14:124. Available from: https://malariajournal.biomedcentral.com/articles/10.1186/s12936-015-0639-x
12. Oliver SV, Kaiser ML, Wood OR, Coetzee M, Rowland M, Brooke BD. Evaluation of the pyrrole insecticide chlorfenapyr against pyrethroid resistant and susceptible Anopheles funestus (Diptera: Culicidae). Tropical Medicine & International Health. 2010;15(1):127–131. Available from: https://doi.org/10.1111/j.1365-3156.2009.02416.x
13. Verma V, Elamathi N, Velamuri PS, Sreehari U, Agrawal OP, Raghavendra K. Chlorfenapyr: Irritant effect compared to other insecticides and its intrinsic toxicity in multiple-insecticide-susceptible and -resistant Anopheles stephensi (Diptera: Culicidae). Journal of Vector Borne Diseases. 2015;52(1):99–103. Available from: https://journals.lww.com/jvbd/fulltext/2015/52010/chlorfenapyr__irritant_effect_compared_to_other.14.aspx
14. World Health Organization, UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases. Global vector control response 2017-2030. Geneva: World Health Organization; 2017. Available from: https://iris.who.int/handle/10665/259205
15. Caminade C, McIntyre KM, Jones AE. Impact of recent and future climate change

on vector-borne diseases. Annals of the New York Academy of Sciences. 2019;1436(1):157–173. Available from: https://doi.org/10.1111/nyas.13950

16. Mordecai EA, Ryan SJ, Caldwell JM, Shah MM, LaBeaud AD. Climate change could shift disease burden from malaria to arboviruses in Africa. The Lancet Planetary Health. 2020;4(9):e416–e423. Available from: https://www.thelancet.com/journals/lanplh/article/PIIS2542-5196(20)30178-9/fulltext
17. Ryan SJ, Lippi CA, Zermoglio F. Shifting transmission risk for malaria in Africa with climate change: a framework for planning and intervention. Malaria Journal. 2020; 19:170. Available from: https://doi.org/10.1186/s12936-020-03224-6
18. Semenza JC, Rocklöv J, Ebi KL. Climate Change and Cascading Risks from Infectious Disease. Infectious Diseases and Therapy. 2022; 11:1371–1390. Available from: https://link.springer.com/article/10.1007/s40121-022-00647-3
19. Bayili K, N'do S, Namountougou M, Sanou R, Ouattara A, Dabiré RK, et al. Evaluation of efficacy of Interceptor® G2, a long-lasting insecticide net coated with a mixture of chlorfenapyr and alpha-cypermethrin, against pyrethroid resistant Anopheles gambiae s.l. in Burkina Faso. Malaria Journal. 2017; 16:190. Available from: https://link.springer.com/article/10.1186/s12936-017-1846-4
20. Hien AS, Soma DD, Maiga S, Coulibaly D, Diabaté A, Belemvire A, et al. Evidence supporting deployment of next generation insecticide treated nets in Burkina Faso: bioassays with either chlorfenapyr or piperonyl butoxide increase mortality of pyrethroid-resistant Anopheles gambiae. Malaria Journal. 2021; 20:406. Available from: https://doi.org/10.1186/s12936-021-03936-3
21. Ngufor C, N'Guessan R, Boko P, Odjo A, Vigninou E, Asidi A, et al. Combining indoor residual spraying with chlorfenapyr and long-lasting insecticidal bed nets for improved control of pyrethroid-resistant Anopheles gambiae: an experimental hut trial in Benin. Malaria Journal. 2011; 10:343. Available from: https://malariajournal.biomedcentral.com/articles/10.1186/1475-2875-10-343
22. N'Guessan R, Odjo A, Ngufor C, Malone D, Rowland M. A Chlorfenapyr Mixture Net Interceptor® G2 Shows High Efficacy and Wash Durability against Resistant Mosquitoes in West Africa. PLOS ONE. 2016;11: e0165925. Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0165925
23. Tungu PK, Michael E, Sudi W, Kisinza WW, Rowland M. Efficacy of interceptor® G2, a long-lasting insecticide mixture net treated with chlorfenapyr and alpha-cypermethrin against Anopheles funestus: experimental hut trials in north-eastern Tanzania. Malaria Journal. 2021; 20:180. Available from: https://link.springer.com/article/10.1186/s12936-021-03716-z
24. Kibondo UA, Odufuwa OG, Ngonyani SH, Mpelepele AB, Matanilla I, Ngonyani H, et al. Influence of testing modality on bioefficacy for the evaluation of Interceptor® G2 mosquito nets to combat malaria mosquitoes in Tanzania. Parasites & Vectors. 2022; 15:124. Available from: https://doi.org/10.1186/s13071-022-05207-9
25. Sovegnon PM, Akoton R, Stopard IJ, Churcher TS, McCall PJ, Ranson H, et al. Efficacy of Interceptor G2, Royal Guard and PermaNet 3.0 against pyrethroid-resistant Anopheles gambiae s.l. from Za-Kpota, southern Benin: an experimental hut trial. Parasites & Vectors. 2024; 17:300. Available from: https://doi.org/10.1186/s13071-024-06372-9
26. Degarege A, Fennie K, Degarege D, Chennupati S, Madhivanan P. Improving socioeconomic status may reduce the burden of malaria in sub-Saharan Africa: a systematic review and meta-analysis. PLOS ONE. 2019;14(1):e0211205. Available from: https://doi.org/10.1371/journal.pone.0211205
27. Sharp BL, Ridl FC, Govender D, Kuklinski J, Kleinschmidt I. Malaria vector control by indoor residual insecticide spraying on the tropical island of Bioko, Equatorial Guinea. Malaria Journal. 2007; 6:52. Available from: https://doi.org/10.1186/1475-2875-6-52
28. Ochomo E, Chahilu M, Cook J, Kinyari T, Bayoh NM, West P, et al. Insecticide-Treated Nets and Protection against Insecticide-Resistant Malaria Vectors in Western Kenya. Emerging Infectious Diseases. 2017;23(5):758–764. Available from: https://doi.org/10.3201/eid2305.161315

29. Ngufor C, Fagbohoun J, Critchley J, N'Guessan R, Todjinou D, Malone D, et al. Which intervention is better for malaria vector control: insecticide mixture long-lasting insecticidal nets or standard pyrethroid nets combined with indoor residual spraying? Malaria Journal. 2017; 16:340. Available from: https://malariajournal.biomedcentral.com/articles/10.1186/s12936-017-1987-5
30. World Health Organization, WHO Pesticide Evaluation Scheme. Guidelines for laboratory and field-testing of long-lasting insecticidal nets. 2nd ed. Geneva: World Health Organization; 2013. Available from: https://iris.who.int/handle/10665/80270
31. Hemingway J, Ranson H, Magill A, Kolaczinski J, Fornadel C, Gimnig J, et al. Averting a malaria disaster: will insecticide resistance derail malaria control? The Lancet. 2016;387(10029):1785–1788. Available from: https://doi.org/10.1016/S0140-6736(15)00417-1
32. Monroe A, Williams NA, Ogoma S, Karema C, Okumu F. Reflections on the 2021 World Malaria Report and the future of malaria control. Malaria Journal. 2022; 21:154. Available from: https://doi.org/10.1186/s12936-022-04178-7
33. Gleave K, Lissenden N, Chaplin M, Choi L, Ranson H. Piperonyl butoxide (PBO) combined with pyrethroids in insecticide-treated nets to prevent malaria in Africa. Cochrane Database of Systematic Reviews. 2021;5:CD012776. Available from: https://doi.org/10.1002/14651858.CD012776.pub3
34. Raghavendra K, Barik TK, Sharma P, Bhatt RM, Srivastava HC, Sreehari U, et al. Chlorfenapyr: a new insecticide with novel mode of action can control pyrethroid resistant malaria vectors. Malaria Journal. 2011; 10:16. Available from: https://doi.org/10.1186/1475-2875-10-16
35. Mbewe NJ, Rowland MW, Snetselaar J, Azizi S, Small G, Nimmo DD, et al. Efficacy of bednets with dual insecticide-treated netting (Interceptor® G2) on side and roof panels against Anopheles arabiensis in north-eastern Tanzania. Parasites & Vectors. 2022; 15:326. Available from: https://doi.org/10.1186/s13071-022-05454-w
36. Oxborough RM, Kitau J, Matowo J, Feston E, Mndeme R, Mosha FW, et al. ITN mixtures of chlorfenapyr (pyrrole) and alphacypermethrin (pyrethroid) for control of pyrethroid resistant Anopheles arabiensis and Culex quinquefasciatus. PLOS ONE. 2013;8(2):e55781. Available from: https://doi.org/10.1371/journal.pone.0055781

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