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Integrated malaria vector control strategies and their effectiveness in sub-Saharan Africa: a systematic review protocol for interventional studies

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ABSTRACT

Introduction Sub-Saharan Africa has the highest malaria burden in the world. Several vector control strategies are being implemented to reduce mosquito density and protect the most vulnerable populations, such as children under 5 and pregnant women. This systematic review is designed to assess the effectiveness of integrated vector control versus single vector control interventions on malaria incidence and prevalence to guide decisions on controlling malaria vectors in sub-Saharan Africa.

Methods and analyses We will systematically retrieve published and grey literature from electronic databases and clinical trial registries. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines will guide us in applying a systematic approach to screening, reviewing and extracting data. An inclusion criterion will be used to independently assess full-text copies of potentially relevant articles by two review authors. Risk of bias will be assessed using the Cochrane Risk of Bias Tool V.2 for randomised controlled trials and the ROBINS-I (Risk Of Bias In Non-randomised Studies - of Interventions) tool for non-randomised intervention studies. A meta-analysis will be conducted based on studies that have reported a high level of evidence (risk ratios or ORs with 95% CIs). If substantial heterogeneity is encountered, subgroup analyses will be explored.

Ethics and dissemination This review does not require ethical approval. The findings will be shared through open-access publications in peer-reviewed journals and presentations to stakeholders and international policymakers for malaria control.

PROSPERO registration number CRD42024559088.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The protocol follows Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols guidelines, ensuring a structured and transparent approach.
⇒ The inclusion of grey literature and clinical trial registries enhances the comprehensiveness of the evidence base.
⇒ The use of validated tools such as Cochrane's risk of bias assessment and GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology ensures a robust evaluation of study quality and evidence certainty.
⇒ Independent review by two authors at each stage ensures rigour and minimises bias, although subjective interpretation of inclusion criteria remains a potential limitation.
⇒ Potential variability in study designs and outcomes across included studies may pose challenges to synthesising evidence and conducting meta-analyses.

BACKGROUND

Malaria is a life-threatening disease caused by malaria parasites being transmitted to people through the bites of infected female *Anopheles* mosquitoes.[1] In the majority of sub-Saharan Africa regions, malaria remains the main vector-borne disease.[2 3] In 2022, there were an estimated 249 million cases of malaria and 608 000 deaths, whereby sub-Saharan Africa alone accounted for over 94% of cases (233 million) and 95% (580 000) of deaths, particularly among children under 5 years (80%).

Vector control is one of the key evidence-based strategies widely promoted by the WHO and the Roll Back Malaria Partnership for the prevention and reduction of malaria transmission.[2 4 5] Vector control reduces the risk of mosquito bites in humans and thus prevents disease transmission. Traditionally, single-intervention strategies, such as insecticide-treated bed nets (ITNs) and indoor residual spraying (IRS), have been the cornerstone of vector control efforts.[6] While these strategies have led to substantial reductions in malaria burden, there is growing concern about their effectiveness in the face of emerging challenges such as insecticide resistance, changing malaria transmission patterns and community adherence.[2 7–9] Faced with slowing progress in controlling and eliminating malaria, stagnating funding

and the growing complexity of identifying and treating malaria cases,[7 10 11] in 2017, the WHO launched the global vector control response (GVCR) with the goal of integrated vector control (IVC). GVCR offers a toolbox of mosquito control methods to suppress or eradicate malaria vectors.[12] The specific methods recommended in this integrated approach include ITNs; installation of screens on windows, ventilation openings and open roof eaves to prevent mosquitoes from entering homes; closing windows and doors at sunset to reduce mosquito entry into homes; IRS; environmental management and source reduction; larval source management (LSM); topical and spatial mosquito repellents; mosquito coils; and insecticide sprays.[12 13]

Combining different vector control methods can have synergistic effects.[13] For this review, IVC is defined as the use of two or more vector control methods in combination, such as ITN, IRS, LSM or environmental management strategies. This can lead to more significant reductions in mosquito populations and malaria transmission and can address different stages of the mosquito life cycle and various ecological niches, providing more comprehensive control.[6 9 10 14] So far, few data are available synthesising the results of a holistic approach to integrating malaria vector control strategies. This systematic review aims to comprehensively evaluate and synthesise existing research evidence to determine the effectiveness of integrated approaches versus single/isolated vector control interventions in reducing malaria incidence or prevalence in children under 5 years and pregnant women. The relevance of focusing on these two subpopulations lies in their higher vulnerability to adverse outcomes following a malaria infection.

Objective

The objective of this systematic review is to assess the effectiveness of current integrated malaria vector control strategies in reducing malaria incidence or prevalence among children under 5 years and pregnant women in malaria-endemic countries in sub-Saharan Africa. In particular, the review aims to:

- Assess the impact of individual versus combining at least two different malaria vector control methods on malaria prevalence or incidence.
- Explore whether the impact of different vector control interventions varies with the level of malaria transmission (low transmission zone, <50% parasite rate; high transmission zone, >50% parasite rate).

METHODS AND ANALYSES

The reporting of this systematic review will follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure transparency and completeness in reporting (online supplemental table S1).[15] Registration for this systematic review is now available on the International Prospective Register of Systematic Reviews (PROSPERO; the registration number is CRD42024559088).[16]

Study inclusion and exclusion criteria

To describe the relevant context and highlight key questions for our review, we will use the PICOTS (Patient population, Intervention, Comparison, Outcome, Timing, and Setting)[17] typology of participant/population, intervention, comparator, outcomes, timing and setting/study design.

Participants/population

We will only include human studies involving children under 5 years and pregnant women living in malaria-endemic countries in sub-Saharan Africa according to the WHO in 2023 (online supplemental table S2).

Intervention/exposure/target condition

Any interventions that integrate malaria-specific vector control approaches and which have been evaluated will be considered. This implies a combination of two or more of the following strategies:

- ITNs.
- Installation of screens on windows.
- Ventilation openings and open roof eaves to prevent mosquitoes from entering homes.
- Closing windows and doors at sunset to reduce mosquito entry into homes.
- IRS.
- Environmental management and source reduction.
- LSM.
- Topical and spatial mosquito repellents.
- Mosquito coils.
- Insecticide sprays.

Type of outcome measures

To be eligible for inclusion, studies must report at least one of the following primary outcomes.

Primary outcomes

- Malaria incidence: measured as the number of new cases of malaria diagnosed in a specific population over a given period of time.
- Malaria prevalence: measured as the proportion of surveyed children and pregnant women who are infected with malaria at a specific point in time at the community level.

Comparator

Studies with a comparator or control group using single-intervention strategies or no intervention.

Timing

Studies published over the past 20 years (from 1 January 2004 to 1 May 2024).

Setting and study design

We will consider the following types of studies published between 01 January 2004 and 01 May 2024 for inclusion in this review:

- Cluster-randomised controlled trials (RCTs).

- Cluster-randomised studies using a stepped-wedge design.
- Cluster-randomised cross-over studies.
- Cohort studies (prospective or retrospective).
- Non-randomised cross-over studies.
- Controlled before and after studies.
- Programmatic evaluations.
- Cross-sectional studies.
- Case–control studies.
- Interrupted time series.
- Case series.

Language

Studies that have been published in English or French and are available in full text are eligible for inclusion. Any studies that are published in a language other than English or French will be excluded. The reason for these criteria is the limited resources available for performing this review.

Search strategy

We will use MEDLINE (via PubMed), the Cochrane Central Register of Controlled Trials, Cumulative Index to Nursing and Allied Health (via EBSCO), Global Health (CABI), Web of Science and Embase to search for peer-reviewed articles.[18] A comprehensive search strategy was developed with the support of a librarian (Najoua Ryane) experienced in the field of health sciences at Utrecht University. Additionally, we will conduct forward and backward reference searches to gather the literature relevant to the systematic review question comprehensively. This approach minimises the risk of missing key studies and maximises the robustness and reliability of your findings. We will search Google Scholar and relevant websites such as the WHO, Malaria Consortium and OpenGrey (www.opengrey.eu) for grey literature to identify further potentially eligible articles for inclusion.

Our final search terms include text words; incidence or prevalence; MeSH terms for malaria incidence or prevalence; children under 5 years; malaria with the child filter (birth to 18 years); pregnant women; vector control; malaria vector control strategies; and individual vector control interventions (online supplemental table S3).

Study screening, selection and data extraction

Studies will be considered for inclusion only if they satisfy all the specified inclusion criteria and do not meet any of the exclusion criteria. The abstracts and full-text articles obtained through our search strategy will be imported into Zotero software, where duplicates will be identified and removed. Two reviewers (GK and LD) will be blinded to each other's screening results during this screening process. For any discrepancies between the two reviewers at both the title/abstract screening stage and the full-text review stage, the reviewers will first resolve disagreements through discussion. If consensus cannot be reached, a third author (PN) will be consulted to make the final decision. The data will be extracted by the same two reviewers using predefined criteria. A standardised data extraction form will be developed and piloted to ensure consistency and completeness. The form will include:

- Study identification: study ID, authors, title, journal and year of publication.
- Study characteristics: study design, setting, population demographics and sample size.
- Exposure details: IVC strategy, duration, frequency and implementation details.
- Comparison details: description of comparison group(s) or intervention(s).
- Outcomes measured: specific outcomes related to malaria incidence and prevalence.
- Data collection methods: quantitative, qualitative or mixed approach.
- Methodological quality: results of the quality assessment (the Newcastle-Ottawa Scale).
- Risk of bias: assessment of potential biases in the study.
- Author conclusions: conclusions drawn by the authors of the study.

A structured data extraction form will facilitate the systematic collection and synthesis of information from each included study, ensuring a comprehensive analysis of the evidence on integrated malaria vector control in sub-Saharan Africa. Pilot testing of the data extraction form on a few studies will be done to ensure it captures all relevant information and to enable any necessary adjustments. Two reviewers will independently extract data from each included study. Differences will first be resolved through discussion. If a consensus cannot be reached, a third author (PN) will be consulted to make the final decision. A database or spreadsheet will be used to organise and manage the extracted data (as quantitative data for the meta-analysis and as qualitative data for a narrative synthesis).[19] Zotero will be used to manage the references included (store, organise, cite).

Assessment of risk of bias and grading strength of evidence

The two reviewers will independently assess and score the quality of selected studies. Technical experts (content experts) will be consulted when needed. The risk of bias for RCTs was assessed using the Cochrane Risk of Bias Tool (V.1) (online supplemental table S4) for earlier studies and the revised Risk of Bias Tool (V.2) (online supplemental table S5) for more recent trials. These tools evaluate biases across key domains, ensuring the reliability and validity of the results. For non-randomised studies, the ROBINS-I tool was employed to assess biases related to confounding, selection and reporting. This systematic approach ensures a comprehensive evaluation of study quality across diverse methodologies. Any discrepancies among the raters will be resolved through consensus, with the involvement of a third rater if necessary. Certainty of proof will be confirmed using the GRADE methodology. Publication bias will be assessed using funnel plot asymmetry. We will compile a summary of findings and create detailed tables for each outcome, also highlighting areas that require further research: 'high' or 'unclear' and summarised in graphs.

Data synthesis and statistical analysis

We will create a PRISMA flow chart that displays every step of the review process. Our first step is to use descriptive statistics and forest plots to summarise the included studies and conduct the structured synthesis of data. If the result is dichotomous, we will compare intervention and control data, using (preferably) HRs or ORs. We will present the mean difference for continuous data, and for count or rate data, we will use rate ratios. We will use adjusted effect measures to summarise the effects of interventions from non-randomised studies. We will present all results with their associated 95% CIs. The meta-analysis will be conducted using the Cochrane Collaboration Review Manager Software package.[20] The heterogeneity will be evaluated by visually examining the overlapping CIs of the studies and applying the χ^2 and I^2 statistics. A χ^2 test result with a p value <0.1 indicates significant heterogeneity. The interpretation of I^2 will follow the classification[21]:

- 25%–49%: moderate heterogeneity.
- 50%–74%: substantial heterogeneity.
- 75%–100%: considerable heterogeneity.

If we observe substantial or considerable heterogeneity, we will perform further subgroup analysis.[21] Where appropriate, we will explore the clinical and methodological aspects of the study, examining trial populations, methods and interventions and visualising study results. A narrative synthesis will be conducted to summarise the findings.[22] This will involve organising studies by type of intervention (or single intervention) and summarising results related to best practices.

Dealing with missing data

To ensure the robustness and validity of the results, several essential steps must be taken when dealing with missing data in a meta-analysis. If there are gaps in the data, we need to determine the extent and nature of them in each study and comprehend how they were filled by the original studies. Determine if data are missing at random or not and assess the risk of bias. We will employ appropriate methods such as multiple imputation or maximum likelihood to randomly miss data and conduct sensitivity analyses to verify the reliability of our results. If it is feasible, we could ask the authors of the studies to provide additional information to fill any gaps.

DISCUSSION

Although the integrated use of malaria vector control measures is effective, summary evidence of these interventions on malaria incidence or prevalence in endemic countries in sub-Saharan Africa is lacking/needed. This systematic review will contribute to updating knowledge on the impact of the integration of malaria vector control interventions. We will use a rigorous methodology to select and assess the quality of the studies and also to extract the data. The results will be presented in accordance with the PRISMA declaration. However, the certainty of the evidence of this systematic review may be limited if there are a limited number of studies available and if there is a possible low quality of (some) individual studies.

Patient and public involvement

Patients and the public were not directly involved in the design, conduct, reporting or dissemination plans of this protocol for a systematic review and meta-analysis.

ETHICS AND DISSEMINATION

We will not seek ethical approval as this is a systematic review protocol. We will synthesise the literature on integrated malaria vector control approaches. As this research is based on previously published data, there will be no patient and public involvement in the design, interpretation or dissemination of study findings. The results of this study will be shared electronically and in print at peer-reviewed conferences and publications, to inform scientists in the development of guidelines for effective and sustainable malaria control in malaria-endemic countries in sub-Saharan Africa.

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Contributors GK designed the protocol. MvdS corrected and advised. LD, PN, DEG and KA-MS provided guidance and reviewed. All review authors read and approved the final protocol draft. GK acted as a guarantor and is responsible for the accuracy of the manuscript.

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