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Housing interventions for preventing malaria (Protocol)

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Housing interventions for preventing malaria.
Cochrane Database of Systematic Reviews 2019, Issue 8. Art. No.: CD013398.
DOI: 10.1002/14651858.CD013398.

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[Intervention Protocol]

Housing interventions for preventing malaria

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Editorial group: Cochrane Infectious Diseases Group.
Publication status and date: Edited (no change to conclusions), published in Issue 8, 2019.

Citation: Furnival-Adams J, Olanga EA, Napier M, Garner P. Housing interventions for preventing malaria. *Cochrane Database of Systematic Reviews* 2019, Issue 8. Art. No.: CD013398. DOI: 10.1002/14651858.CD013398.

ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

Primary

To assess the effects of different structural house modifications on malaria disease burden.

Secondary

To explore whether effects vary with level of transmission.

BACKGROUND

Description of the condition

Preventing malaria

Malaria is a life-threatening parasitic disease caused by *Plasmodium* species and is transmitted by female *Anopheles* mosquitoes (WHO 2018). *Plasmodium falciparum* is responsible for most malaria deaths and 93% of those deaths occur in Africa. Although malaria can be prevented, progress in malaria control to date appears to have plateaued for the first time since the turn of the century (WHO 2017a; WHO 2018). In 2017, there were an estimated 219 million cases worldwide (8 million more cases than estimated in 2015), with 80% of cases occurring in sub-Saharan African countries and India. In sub-Saharan Africa, malaria primarily affects rural communities, due to the breeding site preferences of the major malaria vectors, *An gambiae* s.l. and *An funestus* s.l. These vectors are endophilic (resting and inhabiting indoors), endophagic (indoor-biting), and night-biting. These characteristics mean that most malaria transmission occurs indoors (Huho 2013).

Indoor residual spraying (IRS) and insecticide-treated nets (ITNs) have been the most widely used malaria vector control tools to date (Bhatt 2015). However, some specialists have commented that these alone will be insufficient to eliminate the disease (Killeen 2014). The current core interventions can fail when few people use the nets, when insecticide spraying coverage is low, or when the vector itself is not amenable to control through these mechanisms (for example, when *Anopheles* spp bite outdoors (exophagy) or bite outside the times of bed net use). In addition, widespread

insecticide resistance observed across Africa may be contributing to decreased effectiveness of these interventions (Ranson 2016; WHO 2017b). These challenges have led researchers and policy specialists to explore other approaches to controlling malaria, especially options that are not reliant on the efficacy of the most frequently used class of insecticides, pyrethroids. In line with this, there is renewed interest in aspects of house design that may help prevent mosquitoes entering houses, biting people, and transmitting malaria. Although housing interventions have been widely used for malaria control in the past (Gachelin 2018), as the global malaria community promoted IRS in the 1940s as a simple solution, protecting people from malaria through housing was not widely considered. In light of the challenges associated with current vector control tools, specialists are now re-examining how housing may help protect people from malaria infection.

Housing and protection

Prior to our understanding of malaria transmission by mosquitoes, communities commonly used wire gauze to protect against flying insects (Gachelin 2018). At the end of the 19^{th} century, malaria transmission by female *Anopheles* mosquitoes was discovered. Simple houseproofing (screening) techniques were used in some of the early experiments contributing to the establishment of this link (Manson 1900; Celli 1901). Shortly after this discovery, many parts of the world began to use screening as an antimalarial measure (Lindsay 2002). Surveys conducted in America also suggested a link between house quality and malaria (Boyd 1926). In the late 1940s, large-scale IRS campaigns were implemented as dichlorodiphenyltrichloroethane (DDT) became available; this steered vector control programmes towards insecticidal tools.

As interest in housing interventions for malaria control has increased, researchers have collected data assessing housing as a risk factor for malaria in a range of geographical, epidemiological, and socioeconomic settings (Tusting 2015). These studies have investigated different features of houses that may influence malaria risk, including roof type, wall type, floor type, closed versus open eaves, the presence/absence of a ceiling, house elevation, and 'modern' housing versus traditional housing. Tusting 2015 summarized data from a variety of study designs: case-control, cohort, cross-sectional, randomized controlled trials; controlled before-and-after studies (when baseline measurements were comparable), cross-over studies, and interrupted time series (ITS) studies, with participants of any ages (excluding migrants, displaced people, or military) and conducted in real (not experimental) houses, comparing modern with traditional house features. Their analysis classified traditional houses as follows.

- Mud walls or stone walls; a thatched, wood, or mud roof; and earth floors in Africa
- Wood or bamboo walls, a thatched roof, and wooden (stilted) floors in Southeast Asia
- Mud or wood walls, a thatched roof, and earth or wooden (stilted) floors in South Asia
- Adobe or mud and wood walls, a thatched roof, and earth floors in South America

Primary outcomes included epidemiological and entomological indicators of malaria or malaria transmission. All studies included in the meta-analysis were observational. Risk of bias was assessed using the Effective Practice and Organization of Care (EPOC) tool for intervention studies, and the Newcastle-Ottawa Scale (NOS) tool for observational studies.

Overall, they found 53 studies that reported epidemiological outcomes. In three cohort studies evaluating mesh screening over windows, there was some evidence of an association between screening and the odds of clinical malaria was lower in screened houses, with an effect estimate (OR) of 0.56; but for malaria incidence, results from case-control, cross-sectional and cohort studies were inconsistent. One RCT showed reduced odds of anaemia in screened houses (OR 0.52). Studies comparing malaria rates in 'modern' houses compared to 'traditional' houses consistently showed lower odds of malaria infection and clinical malaria in modern houses. Modern wall materials were associated with a 0.27 reduced odds of malaria infection across 22 studies. Modern roof materials, such as corrugated iron, were associated with a lower incidence of clinical malaria. However, these were observational studies and likely to be confounded, which the authors note, along with other limitations. The authors evaluated risk of confounding as part of the Newcastle-Ottawa Score and showed that few studies attempted to control for household wealth. Although some did adjust for household wealth, there remains a risk of residual confounding from socioeconomic status.

The same research team subsequently examined data across several countries, drawing on the Demographic and Health Surveys (DHS) and Malaria Indicator Surveys (MIS) surveys across 21 sub-Saharan countries assessing the relationship between house quality and malaria (Tusting 2017). Wall, roof, and floor materials were classified as 'natural', 'rudimentary', or 'finished' by the DHS/MIS, and these definitions were used to create a binary housing quality variable comparing 'modern' with 'traditional' housing. DHS and MIS household wealth index scores were developed using principal component analysis (typically included variables describing durable asset ownership, access to utilities and infrastructure, and house construction materials were used as an indicator of socioeconomic status). They then adjusted effect estimates for household wealth based on this index score. The results suggested that modern housing was associated with a 9% to 14% reduction in the odds of malaria infection after adjusting for age, gender, ITN use, IRS coverage (where measured), household wealth, and cluster-level variables such as rural/urban status. The analysis was rigorous and covered data from a large population of 284,532 children. Again, a major limitation was that, despite controlling for household wealth, the wealth index used may not have been sufficient to account for socioeconomic differences associated with the house

features in question and there may as a result have been residual confounding by wealth. In addition, given the non-randomized nature of this study and the observational studies summarized in Tusting 2015, the observed effects may have occurred by chance. Given the risk of residual confounding by household wealth and the absence of dramatic differences, these summaries of observational data are suggestive of a relationship between housing and malaria, but not proof of an effect.

Several experimental entomological studies have also been conducted assessing the effect of full or partial screening of houses; alternative house typologies; and use of insecticidal eave tubes (Jatta 2018; Kampango 2013; Massebo 2013; Njie 2009; Ogoma 2010; Sternberg 2016; von Seidlein 2017). Preliminary studies have suggested that screening can reduce adult mosquito density: for example, Kampango 2013 showed a 61% to 84% reduction after covering gable ends with either four year old mosquito bed nets, untreated shade cloth, or deltamethrin-impregnated shade cloth. One household-randomized trial reported indoor mosquito density fell by 40% after screening doors and windows and closing wall openings and eave gaps with mud (Massebo 2013). A study assessing the effect of eave tubes, insecticide-treated netting fitted into tubes inserted into closed eaves, showed a 50% to 70% reduction in the number of mosquitoes recaptured compared to the control arm (Sternberg 2016). These studies provide some indication of the potential of these tools; however, experimental epidemiological studies are needed to provide stronger evidence of the effect of these interventions on malaria.

Description of the intervention

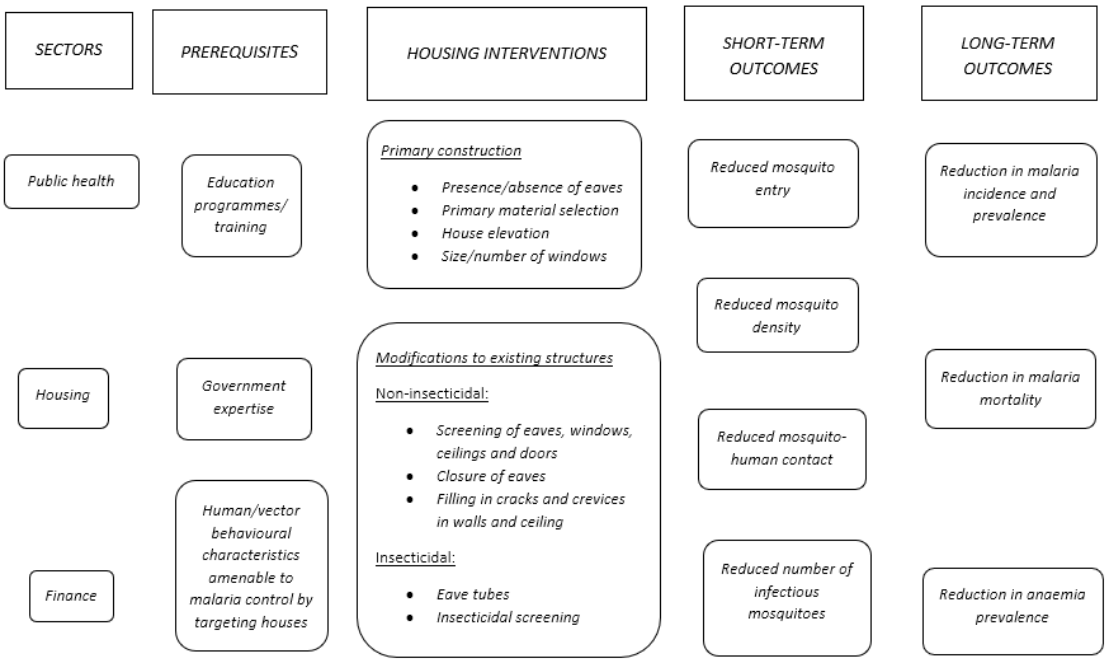
A broad range of actions related to housing can reduce mosquito density and human-mosquito contact, including selecting where houses are built (houses/villages can be strategically positioned away from known breeding sites to minimize malaria risk); clearing vegetation around the home to minimize resting sites; improving drainage and water supply to minimize breeding sites; better management of livestock and domesticated animals where zoophilic (those that are attracted to and feed on animals) vectors exist; and changes to the structure of the housing. All these actions put together may well help reduce the malaria burden and this is what the World Health Organization (WHO) terms an intersectoral action, where multiple sectors work collaboratively to engineer an environment that is less conducive to malaria transmission in combination with the householders and communities themselves. In this review, structural housing interventions to reduce indoor malaria transmission will be examined.

Structural housing interventions can be divided into three categories, described in more detail in Table 1:

- design and material specifications for primary construction;
- modifications or additions to the physical structure of existing houses;
- the incorporation of insecticide delivery systems into existing house structures.

There are a number of prerequisites for programmes incorporating housing interventions to both work and to be sustained longer term (Figure 1). Houses require a minimum level of structural integrity, where barriers such as screening can be applied and maintained. Those living in the houses also need to value change, see at the very least mosquitoes as a nuisance, and understand that malaria is a risk. Such community views will help people introduce some of the approaches themselves; help communities accept the provision of other aspects of such control; and are important to making the interventions work, such as closing doors/windows at night and blocking routes of entry for mosquitoes.

Figure 1. Logic model showing the sectors involved, prerequisites, and potential outcomes related to housing interventions.



Other benefits of housing interventions may help people value them, for example, the reduction in flies entering or other types of mosquito biting in houses. On the other hand, some externally imposed modifications may be inconvenient, disliked for other reasons (making the houses too hot, for example), and some structural changes may be strikingly different to traditional designs, and therefore may not be accepted culturally.

How the intervention might work

Some of the major *Anopheles* species in Africa have evolved with humans to be endophilic, endophagic, and they tend to bite during the night, when individuals are likely to be most vulnerable, at home sleeping (Gillies 1968). These behaviours make houses areas of high malaria risk and an important target for vector control interventions.

The goal of housing interventions for malaria vector control is to reduce the entry of mosquitoes into the home by blocking or covering entry routes into the house. Different strategies exist where all or combinations of doors, eaves, ceilings, and windows can be blocked using various materials. Which of these strategies is most effective will depend on different aspects of mosquito and human behaviour.

1. Primary house construction

The design of the house and the choice of materials used for house construction may be strategically designed to minimize malaria risk. Construction materials for various parts of the house may be more or less conducive to mosquito entry. This is likely related to how prone the material is to the development of holes, or changes in indoor temperature or humidity that reduce the survival of mosquitoes indoors, or both (Lindsay 2019).

Other considerations regarding primary construction include the following:

- Whether the house is elevated or left at ground level.

Previous studies have suggested that mosquitoes tend to bite at ground level, and that indoor vector density is significantly reduced in houses raised on stilts compared to houses at ground level (Charlwood 2003). It is also likely that the more windows per house, the higher the risk of mosquito entry will be, unless windows are properly screened.

- The presence/absence of eaves or gables, or both. In areas where eaves and gables are a common feature of the house, open eaves are the main port of entry for anopheline mosquitoes (Lindsay 1988). Closing eaves has been shown to greatly reduce malaria risk and may be an important consideration in primary house construction.

2. Modifications or additions to existing houses

The need for ventilation and light means that the presence of openings in house structures is inevitable. Many of the interven-

tions under consideration involve partial or full screening of these openings in the house structure, usually with PVC-coated fibreglass or metal mesh, or filling in gaps in wall structures with cement, mortar and rubble. Eave gaps can be screened in houses where they exist. Doors (and windows, when present) are also important routes of entry; how effective the screening of doors and windows is will depend on their size, and how often they are left open (Jawara 2018).

Incorporating insecticidal delivery systems

Although the non-insecticidal nature of many housing interventions is appealing, there are ways in which insecticides can be incorporated into house structures. Eave tubes, for example, have been designed whereby tubes are inserted into the wall under the roof of the house and electrostatic netting within each eave tube is coated with insecticide (Andriessen 2015). Screening of houses using insecticidal netting is also possible, although challenges exist concerning the photodegradation of insecticide in treated netting, with potentially increased exposure to UV light compared to insecticides in ITNs or IRS (Kayedi 2008).

Acceptability and implementation

Housing interventions for vector control have several appealing characteristics: there is likely a reduced risk of human toxicity compared to ITNs or IRS (non-insecticidal interventions are at low risk of being toxic to humans and for insecticidal interventions, the positioning of the treated material means that they do not come into close contact with householders); there may be little or no maintenance required; they offer household-level protection; and the efficacy of non-insecticidal interventions is not threatened by insecticide resistance. It is likely that effective housing interventions will also reduce entry of nuisance insects and other disease vectors such as day-biting mosquitoes and flies carrying diarrhoeal agents (Ogoma 2010). This would provide additional health benefits, and may also increase the attractiveness of the intervention to householders.

On the other hand, there may be unintended effects that reduce the acceptability and feasibility of these interventions. For example, adequate ventilation is important in these tropical and subtropical climates, where respiratory diseases are a major cause of death (FIRS 2017). In many parts of Africa, traditional huts tend not to have windows, and open eaves are therefore an important source of light and ventilation. The closure of eaves, for example, may therefore be uncomfortable and may increase risk of respiratory diseases (Bruce 2000).

If shown to be effective, there are uncertainties regarding how best to implement these interventions. In trials, housing interventions are likely to mimic a 'top down' approach, with the intervention applied and paid for by the researchers. However, long term sustainability of housing improvements to reduce malaria will depend on changes in construction practices and on the willingness and capacity for householders to implement the modifications themselves. Improving community knowledge, perception, and practices may therefore be an important aspect of the implementation strategy (Kaindoa 2018). Policymakers and public health specialists will also need to consider how implementation strategies can ensure equitability. Considering houses need to have certain basic features for many of these interventions to be successful, housing interventions may disproportionately benefit those of a higher socioeconomic status unless programmes are specifically targeted. With this in mind, our review will also examine aspects of the delivery of housing modifications to help us discuss implementation and sustainability, including the level of community involvement in the implementation of the modifications and their maintenance.

Why it is important to do this review

Increasing levels of insecticide resistance and concerns regarding mosquitoes that are not well targeted by current interventions is leading to increased interest in alternative vector control tools. A recent review on housing and malaria, Tusting 2015, summarized a variety of studies and concluded that housing is an important risk factor for malaria. However, most of the included studies were limited in terms of study design and at risk of residual confounding by household wealth. Although entomological and observational studies show potential for house modifications as a malaria control tool, experimental studies using epidemiological outcomes are needed to establish a causal relationship between structural housing interventions and malaria. In this review, we summarize data from experimental and quasi-experimental studies, covering non-insecticidal and insecticidal interventions related to both primary construction and modifications to existing houses. This is an active field, so this review will provide a good global evidence summary that can be updated as new evidence emerges.

OBJECTIVES

Primary

To assess the effects of different structural house modifications on malaria disease burden.

Secondary

To explore whether effects vary with level of transmission.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials

- Cluster-randomized controlled trials (cluster-RCTs) with at least two clusters per arm
- Cluster-randomized cross-over studies with at least three data points both before and after the intervention is introduced
- Cluster-randomized studies using a stepped-wedge approach

Quasi-experimental trials

- Controlled before-and-after studies with baseline data, a contemporaneous control group, and at least two sites per arm
- Controlled ITS with at least three data points before and after the intervention is introduced
- Non-randomized cross-over studies with a clearly defined point in time when the cross-over occurred, and monitoring of at least two transmission seasons before and after the cross-over
- For consumer views, we will seek qualitative studies (observations, interviews, focus groups) that have been conducted alongside studies

Types of participants

Any individuals living in an area where malaria transmission is known to exist, excluding migrant populations or displaced individuals.

Types of interventions

We will group the interventions that we will assess as shown in Table 2.

There should be no major structural differences between the intervention and control arm other than the intervention itself that are likely to influence mosquito entry.

We will exclude the following.

- Interventions to mobile homes
- Insecticide delivery systems, such as wall linings or curtains

Any co-interventions should be balanced across the control and intervention arms.

Types of outcome measures

Primary outcomes

Studies must include one of the primary outcomes.

- Malaria case incidence: measured as a count per person unit time or the number of new uncomplicated malaria cases. We will use site-specific definitions as long as they have demonstrated (a) a fever or history of fever, and (b) confirmed parasitaemia (by blood smear microscopy, rapid diagnostic test (RDT), or polymerase chain reaction (PCR))
- Malaria infection incidence: measured as count per person unit time or the number of new infections (individuals must have confirmed parasitaemia by blood smear, RDT, or PCR)
- Parasite prevalence (clinical and subclinical malaria): the proportion of surveyed individuals with confirmed parasitaemia at a community household survey

Secondary outcomes

Epidemiological

- All-cause mortality
- Anaemia prevalence as per WHO cut-offs based on haemoglobin measurements taken in community household surveys (Table 3; WHO 2011)
- Other disease case incidence including other vector-borne diseases, diarrhoeal diseases

Entomological

- Transmission intensity (measured using EIR): the estimated number of bites by infectious mosquitoes per person per unit time. This is measured using the human biting rate (the number of mosquitoes biting an individual over a stated period measured directly using human baits or indirectly using light traps, knock-down catches, baited huts, or other methods of biting rate determination) multiplied by the sporozoite rate.
- Adult mosquito density: measured by a technique previously shown to be appropriate for the vector (for example, using human baits, light traps, knock-down catches, baited huts, or other methods)
- Sporozoite rate: measured as the number of caught adult mosquitoes positive for malaria sporozoites. Sporozoites can be detected through molecular or immunological methods.

Any adverse effects

We will also seek any data within the trials as to whether the housing interventions influence the proportion of time spent inside or outside the house; whether the interventions influence respiratory disease or diarrhoeal illness; whether they influence other insects or pests in the house; whether the interventions are associated with declines in bed net usage; and any indications of the influence of interventions on malaria incidence in neighbouring huts or houses.

User acceptability

Any measure of user acceptability collected during the conduct of the trial and reported by treatment arm. This includes cross-sectional survey data of reported acceptability and qualitative data on views about the intervention.

Search methods for identification of studies

Electronic searches

We will search the following databases using the search terms and strategy described in Appendix 1: the Cochrane Infectious Diseases Group Specialized Register; Central Register of Controlled Trials (CENTRAL), published in the Cochrane Library; MEDLINE (PubMed); Embase (OVID); CAB Abstracts (Web of Science); and LILACS. We will also search the WHO International Clinical Trials Registry Platform (www.who.int/ictrp/search/en/), ClinicalTrials.gov (www.clinicaltrials.gov), and the ISRCTN registry (www.isrctn.com/) to identify ongoing trials, using the search terms outlined in Appendix 1.

We will identify qualitative research associated with the studies by:

- Examining the trial reports for concomitant qualitative data collection in the methods
- Searching MEDLINE using key terms to identify the trial such as the location or year for qualitative studies
- Contacting the authors to determine if qualitative studies had been conducted

Searching other resources

We will contact researchers working in the field for unpublished data. We will also check the citations of all studies identified by the above methods.

Data collection and analysis

Selection of studies

Two review authors (JFA and EAO) will independently assess the titles and abstracts of studies identified by the literature searches. These two review authors will assess full-text copies of potentially relevant studies for inclusion using an eligibility form based on the inclusion criteria. We will include studies irrespective of whether data were reported in a 'usable' way. We will compare the results of our assessments and will resolve any disagreements by discussion and consensus, with arbitration by a third review author if necessary. We will ensure that multiple publications of the same study are included once. We will list excluded studies, together with their reasons for exclusion, in a 'Characteristics of excluded studies' table. We will illustrate the study selection process in a PRISMA diagram.

Data extraction and management

Two review authors (JFA and EAO) will independently extract information from the included studies using prepiloted electronic data extraction forms. In case of differences in extracted data, the two review authors will discuss these differences to reach consensus. If unresolved, we will consult a third review author. In case of missing data, we will contact the original study author(s) for clarification.

We will extract data on the following:

- Study design: type of study; method of participant selection; adjustment for clustering (for cluster-RCTs (cRCTs)); sample size
- Participants: study settings; population characteristics including age, gender, ethnicity, recruitment rates; withdrawal, and loss to follow-up. We will also describe participants in terms of the socioeconomic status of households or the community they live in. We anticipate this will be estimated in studies through calculating an index based on asset ownership (such as ownership of a radio, bicycle, car, or motorbike). The indicators used to create this index are likely to vary between studies, but we will attempt to compare indicators and categorize participants into socioeconomic groups
- Interventions: full details of intervention and any co-interventions and any theory informing it; coverage of intervention and any co-interventions; compliance of any co-interventions; typology of the house
- All outcomes: definition of outcome; diagnostic method or surveillance method; passive or active case detection; duration of follow-up; time points at which outcomes were assessed; number of events; number of participants or unit time; statistical power; unit of analysis; incomplete outcomes/missing data; Plasmodium species; mosquito net usage
- Entomological outcomes: primary and secondary vector(s) species; vector(s) behaviour (adult habitat, peak biting times, exophilic/endophilic, exophagic/endophagic, anthropophilic/zoophilic); method of mosquito collection(s); malaria endemicity; eco-epidemiological setting; population proximity and density; insecticide resistance status (where an insecticidal house improvement tool was investigated)
- Other: primary construction materials; topology of study site; cost of the intervention; who was responsible for implementing the intervention

We will examine how the intervention was delivered, who delivered it, and we will describe the contribution and engagement of the householders to the process.

If studies have examined single interventions, we will group these together with other studies examining the same intervention to obtain the size of effect that might be achieved.

If studies have examined multiple interventions, we will group these in the following way:

- Non-insecticidal strategies combining at least two interventions
- Strategies combining at least two interventions, where one or more of these interventions is insecticidal

Assessment of risk of bias in included studies

Two review authors (JFA and EAO) will independently assess the risk of bias using the Cochrane 'Risk of bias' tool (Higgins 2011). We will justify judgements made in the 'Risk of bias' tables. For trials that randomize clusters, we will assess additional components, namely recruitment bias, baseline imbalances, loss of clusters, incorrect analysis, and comparability with trials that randomize individuals. For randomized cross-over trials, we will also assess: whether the cross-over design is suitable; whether there is a carry-over effect; whether only first period data are available; incorrect analysis; and comparability of results with those from parallel-group trials.

For observational and quasi-experimental studies, we will use the Cochrane Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I) (Sterne 2016). We will use ROBINS-I to assess the risk of bias for all included observational studies. We will assess risk of bias through a hierarchy of domains, starting with critical then serious, moderate, and low. If any domain reaches critical risk of bias, we will not continue with the assessment, as further evaluation will not influence how we assess the certainty of the evidence. As the risk of bias in the effect of an intervention may be different for different outcomes, we will make a 'Risk of bias' assessment for each outcome. The confounding domains have been outlined in Appendix 2.

The quality of included qualitative studies will be assessed using a modified version of the tool developed by the EPPI-centre, outlined in (Eshun-Wilson 2019).

Measures of treatment effect

We will use risk ratios to compare the effect of the intervention with the control for dichotomous data. For continuous data, we will present the mean difference; and for count/rate data, we will use rate ratios. We will use adjusted measures of effect to summarize treatment effects from non-randomized studies. We will present all results with 95% confidence intervals (CIs).

Unit of analysis issues

We will take into account the level at which randomization occurred, such as cross-over trials, cluster-RCTs, and multiple observations for the same outcome.

For cluster-RCTs, or cluster non-randomized trials, we will extract adjusted measures of effect, where possible. If the study authors did not perform any adjustment for clustering, we will adjust the raw data using an ICC value. If an ICC is not reported in the paper, we will obtain this from similar studies, or estimate the ICC value. If we estimate the ICC value, we will perform sensitivity analyses to investigate the robustness of our analyses.

If we identify studies for inclusion that have multiple intervention arms, we will include data from these studies by either combining treatment arms, or by splitting the control group so that we only include these participants in the meta-analysis once.

For randomized cross-over trials, where neither carry-over nor period effects are thought to be a problem, we will use a paired t-test for the analysis of continuous data from two-period, two-armed cross-over trials.

Dealing with missing data

In case of missing data, we will apply available-case analysis, only including data on the known results. The denominator will be the total number of participants who had data recorded for the specific outcome. For outcomes with no missing data, we plan to perform analyses on an intention-to-treat basis. We will include all participants randomized to each group in the analyses and will analyse participants in the group to which they were randomized.

Assessment of heterogeneity

We will inspect forest plots for overlapping CIs and will assess statistical heterogeneity in each meta-analysis using the I^2 statistic values and Chi^2 statistics. We will regard heterogeneity as moderate if I^2 statistic values are between 30% to 60%; substantial if they are between 50% to 90%; and considerable if they are between 75% to 100% (Higgins 2011). We will regard a Chi^2 test statistic with a P value ≤ 0.10 indicative of statistically significant heterogeneity. We will explore clinical and methodological heterogeneity through consideration of the trial populations, methods, and interventions, and by visualization of trial results.

Assessment of reporting biases

If there are 10 or more trials included in each meta-analysis, we will investigate reporting biases (such as publication bias) using funnel plots. We will assess funnel plot asymmetry visually, and use formal tests for funnel plot asymmetry (Harbord 2006). If we detect asymmetry in any of these tests or by a visual assessment, we will explore the reasons for asymmetry.

Data synthesis

We will group the interventions as either insecticidal or non-insecticidal.

We will analyse data using Review Manager 5 (RevMan 5) (RevMan 2014). We will use fixed-effect meta-analysis to combine data if heterogeneity is absent. If considerable heterogeneity is present, we will combine data using random-effects meta-analysis

and report an average treatment effect. We will decide whether to use fixed-effect or random-effects models based on the consideration of clinical and methodological heterogeneity between trials. We will stratify the analysis by study design, and will place any studies conducted in epidemic settings in a separate analysis.

Certainty of the evidence

We will assess the certainty of the evidence using the GRADE approach (Guyatt 2011). For RCTs, we will rate each primary outcome as described by Balshem 2011. For non-randomized studies, we will use the GRADE approach to rate primary outcomes where there is a low risk of bias from the ROBINS-I tool. The studies will start as high-certainty evidence. Where the following outcome domains are marked at moderate, high, or unclear risk of bias, the study will start as low-certainty evidence.

- Bias due to confounding
- Bias due to missing data
- Bias in selection of the reported result

We will use the following evidence grades:

- High: we are very confident that the true effect lies close to that of the estimate of the effect
- Moderate: we are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect
- Low: our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect
- Very low: we have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect

RCTs start as high-certainty evidence, but can be downgraded if there are valid reasons within the following five categories: risk of bias, imprecision, inconsistency, indirectness, and publication bias.

Non-randomized studies can be upgraded (provided they are not downgraded for any reason) if there is a large effect, a dose-response effect, and if all plausible residual confounding would reduce a demonstrated effect or would suggest a spurious effect if no effect was observed (Balshem 2011).

We will summarize qualitative findings on consumer views narratively. If there are a sufficient number of included studies, two review authors will independently code the studies, and use thematic synthesis to identify themes and subthemes.

We will summarize our quantitative findings in a 'Summary of findings' table.

Subgroup analysis and investigation of heterogeneity

We intend to investigate heterogeneity by subgrouping data based on malaria endemicity (low, < 50% parasite rate in children; and high, > 50% parasite rate in children).

Sensitivity analysis

We will perform sensitivity analysis on the primary outcome to see the effect of exclusion of trials at high risk of bias (for incomplete outcome data) on the overall results. If the ICC value is estimated, we will undertake sensitivity analyses to investigate the impact of varying the ICC value on meta-analysis results.

ACKNOWLEDGEMENTS

The Academic Editor is Dr Joseph Okebe.

We are grateful to Vittoria Lutje, Information Specialist with the Cochrane Infectious Diseases Group (CIDG), for help with the literature search strategy.

JFA is supported by the Research, Evidence and Development Initiative (READ-It) project. The CIDG editorial base and READ-It are funded by UK aid from the UK government for the benefit of low- and middle-income countries (project number 300342-104). The views expressed do not necessarily reflect the UK government's official policies.

EAO is supported by PIIVeC, the Partnership for Increasing the Impact of Vector Control. PIIVeC is funded by the Medical Research Council of the UK (grant number MR/P027873/1) through the Global Challenges Research Fund.

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* *Indicates the major publication for the study*

ADDITIONAL TABLES

Table 1. Types of intervention

Intervention		Modification
Primary construction		
Construction materials	Wall	Mud or thatch replaced with wood, cement, or brick
	Roof	Thatch replaced with corrugated iron or tiles
	Door	Different designs for doors and door frames exist, with varying levels of some doors with mechanisms to assure self-closing
	Eave	Closure of eaves
Design	Elevation	House built above ground level on stilts
	Windows	Fewer or smaller windows
Modifications to existing houses		
Non-insecticidal		
Screening		Covering of potential entry points (ceilings, eaves, doors, windows gable ends) with: commonly PVC-coated fibreglass or metal mesh, or with alternative materials found around the home
Eaves		Eaves commonly filled in with either mud or with a sand/rubble/cement mixture
Wall maintenance		Filling in of cracks and crevices with mud or sand/rubble/cement mixture
Insecticidal		
Eave tubes		Eaves are closed and tubes with insecticide-coated electrostatic netting are inserted
Insecticidal screening		Screening potential entry points with insecticidal materials such as treated mosquito netting

Table 2. Types of interventions included in review

Intervention	Comparison
Primary construction	
Alternative wall, roof, door type, or eave closure	Traditional/standard wall, roof, door type, eave open
Elevated house	House at ground level
Reduced number of windows per household	An increased number or size of windows

Table 2. Types of interventions included in review (*Continued*)

Modifications to existing houses	
Non-insecticidal	
Screening of ceilings, doors, eaves, windows, or any combination of these	No screening or a quantifiable reduction in the extent of screening
Closure of eaves	Open eaves
Filling in of cracks and crevices in walls or ceilings	No filling in of cracks and crevices
Insecticidal	
Any structural house modification that incorporates an insecticide	No incorporation of insecticidal delivery system to house structure

Table 3. Haemoglobin levels used to diagnose anaemia[a]

Population	Non-anaemic[b]	Anaemia[b]		
		Mild	Moderate	Severe
Children 6 to 59 months of age	≥ 110	100 to 109	70 to 99	< 70
Children 5 to 11 years of age	≥ 115	110 to 114	80 to 109	< 80
Children 12 to 14 years of age	≥ 120	110 to 119	80 to 109	< 80
Non-pregnant women (15 years of age and above)	≥ 120	110 to 119	80 to 109	< 80
Pregnant women	≥ 110	100 to 109	70 to 99	< 70
Men (15 years of age and above)	≥ 130	110 to 129	80 to 109	< 80

[a] WHO 2011.
[b] Haemoglobin (g/L).

APPENDICES

Appendix 1. Draft search strategy

Search set	Search terms
1	Malaria* ti, ab, [Mesh]
2	Plasmodium ti, ab, [Mesh]
3	Anopheles ti, ab, [Mesh]
4	"Mosquito Control"[Mesh]
5	1 or 2 or 3 or 4
6	House or houses or housing or hut or huts or building* or dwelling* or shelter or shelters [ti, ab]
7	roof* or eave* or wall* or window* or door* or ceiling* or floor or floors or gable or gables or stilts or elevation or elevated or "netting barrier*" [ti, ab]
8	"living environment" or construction* [ti, ab]
9	"Housing "[Mesh]
10	"Architecture"[Mesh] or architect* [ti, ab]
11	6 or 7 or 8 or 9 or 10
12	5 and 11

This is the preliminary search strategy for MEDLINE (PubMed). It will be adapted for other electronic databases. We will report all search strategies in full in the final review version.

Appendix 2. ROBINS-I tool

Specify the review question

Participants	All age groups living in an area with malaria
Experimental intervention	Modifications to primary construction design and specifications, including: choice of material used for walls, roofs, or doors; house elevation; closed eaves versus open eaves Modifications or additions to existing houses including: screening of ceilings, doors, eaves, windows, or any combination of these; changes to size or number of windows or doors per household; filling in of cracks and crevices in walls or ceilings

(*Continued*)

	Any structural house modification incorporating insecticide
Comparator	For modifications to primary construction design and specification: wall, roof, or door types traditionally/most commonly used in the local area; house at ground level or open eaves For modifications or additions to existing houses: no screening or a quantifiable reduction in screening; a quantifiable difference in the number of or size of windows or doors; no filling in of cracks and crevices For incorporation of insecticidal delivery systems: no incorporation of insecticidal delivery system to house structure For all of these comparators, there should be no major structural differences between the intervention and control arm other than the intervention itself that are likely to influence mosquito entry
Outcomes	Malaria case incidence, incidence of new malaria infections, malaria parasite prevalence

List the confounding domains relevant to all or most studies

Socioeconomic status: people of lower socioeconomic status may be less likely to live in houses with walls appropriate for house modifications and therefore less likely to be selected for the intervention group. Socioeconomic status is considered a prognostic factor for malaria (Somi 2007).

Geographical location: people living in certain geographical regions may live in houses that are more appropriate or more convenient for implementation of house interventions and therefore may be more likely to be selected for the intervention group. Malaria transmission is also heterogenous across different geographical regions and can therefore be a predictor of malaria risk (Bousema 2012).

List co-interventions that could be different between intervention groups and that could impact on outcomes

Use of other (non-insecticidal) vector control tools: individuals receiving the intervention may be less inclined to use other vector control interventions such as bed nets.

WHAT'S NEW

Date	Event	Description
15 August 2019	Amended	PIIVeC funding acknowledgement added for EAO

CONTRIBUTIONS OF AUTHORS

All protocol authors contributed to the protocol design and approved the final version. JFA wrote the full text of the protocol. All review authors read and approved the final protocol draft.

DECLARATIONS OF INTEREST

JFA has no known conflicts of interest to declare.

EAO has no known conflicts of interest to declare.

MN has no known conflicts of interest to declare.

PG is the Director of the Research, Evidence and Development Initiative (READ-It) project (project number 300342-104) and CIDG Co-ordinating Editor.

SOURCES OF SUPPORT

Internal sources

- Liverpool School of Tropical Medicine, UK.

External sources

- Department for International Development (DFID), UK.

Project number 300342-104

- Partnership for Increasing the Impact of Vector Control (PIIVeC), UK.

Provided support to EAO. PIIVeC is funded by the Medical Research Council of the UK (grant number MR/P027873/1) through the Global Challenges Research Fund.