

Vector control for malaria prevention during humanitarian emergencies: a systematic review and meta-analysis



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Summary

Background Humanitarian emergencies can lead to population displacement, food insecurity, severe health system disruptions, and malaria epidemics among individuals who are immunologically naive. We aimed to assess the impact of different vector control interventions on malaria disease burden during humanitarian emergencies.

Methods In this systematic review and meta-analysis, we searched ten electronic databases and two clinical trial registries from database inception to Oct 19, 2020, with no restrictions on language or study design. We also searched grey literature from 59 stakeholders. Studies were eligible if the population was affected by a humanitarian emergency in a malaria endemic region. We included studies assessing any vector control intervention and in which the primary outcome of interest was malaria infection risk. Reviewers (LAM, JF-A, KC, BP, and LP) independently extracted information from eligible studies, without masking of author or publication, into a database. We did random-effects meta-analyses to calculate pooled risk ratios (RRs) for randomised controlled trials, odds ratios (ORs) for dichotomous outcomes, and incidence rate ratios (IRR) for clinical malaria in non-randomised studies. Certainty of evidence was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. This study is registered with PROSPERO, CRD42020214961.

Findings Of 12475 studies screened, 22 studies were eligible for inclusion in our meta-analysis. All studies were conducted between Sept 1, 1989, and Dec 31, 2018, in chronic emergencies, with 616611 participants from nine countries, evaluating seven different vector control interventions. Insecticide-treated nets significantly decreased *Plasmodium falciparum* incidence (RR 0.55 [95% CI 0.37–0.79]; high certainty) and *Plasmodium vivax* incidence (RR 0.69 [0.51–0.94]; high certainty). Evidence for an effect of indoor residual spraying on *P falciparum* (IRR 0.57 [95% CI 0.53–0.61]) and *P vivax* (IRR 0.51 [0.49–0.52]) incidence was of very low certainty. Topical repellents were associated with reductions in malaria infection (RR 0.58 [0.35–0.97]; moderate certainty). Moderate-to-high certainty evidence for an effect of insecticide-treated chaddars (equivalent to shawls or blankets) and insecticide-treated cattle on malaria outcomes was evident in some emergency settings. There was very low certainty evidence for the effect of insecticide-treated clothing.

Interpretation Study findings strengthen and support WHO policy recommendations to deploy insecticide-treated nets during chronic humanitarian emergencies. There is an urgent need to evaluate and adopt novel interventions for malaria control in the acute phase of humanitarian emergencies.

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Introduction

Humanitarian emergencies, of either natural or anthropogenic origins, can lead to large-scale population movement, food insecurity, and severe health system disruptions. As of 2022, the UN High Commissioner for Refugees estimates that there are 89.3 million people who have been forcibly displaced worldwide, including 53.2 million people who have been internally displaced, 21.3 million refugees, and 4.6 million asylum-seekers.¹ Humanitarian emergencies in Venezuela have led to a displacement of 4.4 million Venezuelan people and a 1200% increase in malaria cases between 2000 and 2020 in Venezuela, which is a stark reminder of how easily reversible malaria control gains are.² Venezuela now accounts for 73% of total malaria deaths on the continent.³ Globally, almost two-thirds of people affected by humanitarian emergencies

inhabit malaria endemic areas,⁴ particularly the WHO African region, which currently accounts for 94% of all malaria cases and deaths.³ Mass displacement can increase the risk of severe malaria epidemics, especially when populations with little or no previous disease exposure move into areas of more intense transmission or when individuals with subclinical infections transit into urban settings. Inadequate water, sanitation, and hygiene (WASH) facilities, drainage, and waste management systems all contribute to high levels of vector breeding and increased malaria transmission. Limited, disrupted, and overburdened national malaria control programmes and health services result in insufficient access to treatment and control measures, with poor health outcomes worsened by concomitant infectious diseases, malnutrition, security concerns,⁵ trauma, and anaemia.⁶

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Research in context

Evidence before this study

Humanitarian emergencies (natural, climate-related, or man-made) can increase risk of malaria epidemics and the incidence of severe disease, particularly when individuals with immunological naivety are displaced into high malaria transmission areas and when vector breeding increases due to flooding, loss of infrastructure, and inappropriate waste drainage and management systems. When reviewed previously by WHO, the evidence for vector control tools deployed during humanitarian emergencies was considered insufficient to develop formal policy. Few recommendations were given based on proven intervention effectiveness during non-emergency situations. We searched PubMed, without restriction on language or study design, using the terms “humanitarian emergency”, “malaria”, “vectors” or “mosquito” or “*Anopheles*”, “insecticide-treated net”, “indoor residual spraying”, “insecticide-treated plastic sheeting”, “insecticide-treated clothing”, “insecticide-treated blankets”, “topical repellents” for articles published between database inception and Oct 15, 2020. We found no published synthesis of the evidence base for malaria control interventions during emergency settings.

Added value of this study

We investigated the effect of different vector control interventions on malaria disease burden during humanitarian emergencies to provide a comprehensive global evidence summary and to highlight the complexities associated with generating robust evidence for vector control tools in such settings. Insecticide-treated nets (ITNs) were confirmed as effective for preventing both *Plasmodium falciparum* and *Plasmodium vivax* malaria infection in chronic emergencies with

adequate shelter. The evidence for an effect of indoor residual spraying (IRS) on preventing malaria infection during humanitarian emergencies was weaker. Other experimental vector control tools, including insecticide-treated chaddars or blankets and insecticide treatment of cattle, also showed promise in individual studies and might be transferable to acute emergencies or outdoor conditions. Key differences in vector and human behaviours might influence the effectiveness of these interventions between emergency settings and additional randomised studies are warranted.

Implications of all the available evidence

No formal guidelines existed for malaria vector control in humanitarian emergencies. The results of this systematic review and meta-analysis support the use of ITNs in these settings, where shelter types and sleeping arrangements are appropriate for their use. We identified multiple barriers affecting the evaluation of vector control tools in humanitarian emergencies, including the rapid onset of these events, ethical design of appropriate control groups, inequitable access of study participants to concomitant improvements in malaria diagnosis and treatment, heterogeneities in refugee camp infrastructure, and recent requirements of two randomised controlled trials with epidemiological endpoints to provide evidence for approval of new classes of vector control tool. Most importantly, there is a clear and urgent need to evaluate novel, innovative, emergency-specific vector control interventions to complement ITN distributions, IRS campaigns, and parallel strategies to improve policy evaluation processes, expand market access, and stimulate the development of these niche vector control products. Study findings have now contributed directly to the latest WHO guidelines for malaria vector control.

During the initial phase of a humanitarian emergency, the priorities for malaria control are prompt and effective diagnosis and treatment.⁶ Selection of complementary vector control interventions in these situations depends on malaria infection risk, human and local vector population behaviours, available logistical support, and type of shelter.⁷ In some emergencies, effective case management can be supplemented with distribution of insecticide-treated nets (ITNs), first targeting the most susceptible populations, such as pregnant women and children younger than 5 years, with the end goal of achieving and maintaining universal coverage.^{8–10} Indoor residual spraying (IRS) is generally not feasible when dwellings are scattered widely, of a temporary nature, or constructed with surfaces that are unsuitable for spraying,¹¹ but it is more appropriate for protecting larger populations where housing is permanent and structurally sound, as are more often established when emergencies progress into the post-acute and recovery phases.^{6,12}

Other innovative community-level and personal vector control interventions have been designed specifically

for humanitarian emergencies, including shelter materials,^{13–15} bed sheets,^{16–18} blankets,¹⁹ and clothing that are treated with insecticides,²⁰ as well as topical repellents for individual use^{21,22} or to treat community livestock.²³ However, evidence for the effectiveness of vector control tools deployed during humanitarian emergencies has been considered insufficient by WHO to develop policy recommendations. Recommendations for ITNs and IRS during humanitarian emergencies are based on their proven efficacy in non-emergency situations, without consideration of the unique operational challenges associated with emergency settings.⁷ We did a systematic review and meta-analysis of the effect of different vector control interventions on malaria disease burden during humanitarian emergencies.

Methods

Search strategy and selection criteria

In this systematic review and meta-analysis, we adhered to the updated PRISMA 2020 guidelines.^{24,25} We searched Cochrane Infectious Disease Group Specialized Register,

Central Register of Controlled Trials, MEDLINE, Africa-Wide Information, the WHO Global Index Medicus, the Science Citation Index Expanded, the Conference Proceedings Citation Index—Science, Embase, Global Health, and LILACS to identify relevant studies from database inception to Oct 19, 2020. We did not impose any language or study design restrictions. Bibliographies of relevant articles retrieved from the searches were checked for additional publications. We also searched ClinicalTrials.gov and the ISRCTN registry to identify ongoing trials. Grey literature from 29 key non-governmental organisations, 24 donors, stakeholders, and policy makers, and six industrial partners were also searched. A full description of the search methods and terms is available online. Five reviewers (LAM, JF-A, BP, LP, and KC) used predetermined eligibility criteria to screen records and full texts, with adjudication by consensus in cases of disagreement. We ensured that multiple publications of the same study were included only once. We listed excluded studies, together with their reasons for exclusion, in the appendix (pp 3–20). References were managed using EndNote (X9.3.3) and screened using Rayyan.²⁶

Studies retrieved were eligible for inclusion in the systematic review and meta-analysis if they satisfied all criteria: the study population consisted of individuals of all age groups or children of specified age groups (ie ≤ 5 years or 6–15 years) who were affected by humanitarian emergencies (any phase) in malaria endemic regions; any malaria-specific vector control intervention was evaluated; and the primary outcome of interest was malaria infection risk, measured as case incidence, infection incidence, or parasite prevalence. An expanded definition of a humanitarian emergency can be found in the appendix (p 21). Studies retrieved were eligible for inclusion in secondary analyses if none of the primary malaria risk indicators were measured but at least one of the following secondary outcomes were reported: all-cause mortality, incidence of severe malaria, anaemia prevalence (<10 g/dL), entomological inoculation rate, adult mosquito density, sporozoite rate, intervention durability, occurrence of adverse events, and user acceptability and usage of interventions. The following study designs were eligible for inclusion in the primary meta-analysis: cluster-randomised, controlled before-and-after, cross-sectional, non-randomised crossover, case-control, and cohort studies, case series, interrupted time series, and programmatic evaluations. A detailed study design is available from the review protocol.²⁷

Data analysis

Two review authors (LAM and JF-A) independently extracted information from eligible studies, without masking to author or publication, into a database. Disagreements in data extraction were resolved by discussion and consensus between the two review

authors, with arbitration by a third (KC, BP, or LP) when necessary. Original study authors and research groups were contacted in cases of missing data or ambiguous reporting. Information on data extraction can be found in the appendix (pp 22).

Analyses were structured first by type of vector control intervention, second by outcome (separating *Plasmodium falciparum* and *Plasmodium vivax*), and third by study design. If a combination of vector control interventions were used (eg, IRS with ITNs), these were considered as separate interventions. Studies that reported sufficient data to calculate crude effects and studies that reported crude or adjusted effect measures with 95% CIs were included in the quantitative analysis.

Epidemiological data were combined in meta-analyses. Meta-analyses of both crude and adjusted results were reported. Random-effects models were used to calculate pooled effect measures (risk ratios [RRs] for randomised controlled trials, odds ratios [ORs] for dichotomous outcomes in non-randomised studies, and incidence rate ratios [IRRs] for clinical malaria incidence in non-randomised studies). Study effects were combined in the meta-analysis using the generic inverse method for non-randomised studies with adjusted results.²⁸ For cluster-randomised controlled trials or non-randomised cluster trials, adjusted measures of effect were extracted. If study authors did not perform any adjustment for clustering, raw data were adjusted using an intraclass correlation coefficient (ICC). If no ICC was reported, this was estimated with reference to similar studies. If the ICC was estimated, sensitivity analyses were done to investigate the robustness of our analyses.

Risk of bias for randomised controlled trials was assessed using the Cochrane risk of bias tool.²⁹ Risk of bias for non-randomised studies was assessed using the Newcastle-Ottawa scale.³⁰ There were insufficient studies identified to assess publication bias; however, we had planned to assess this by visual inspection of funnel plots and Egger test for funnel plot asymmetry.³¹ Certainty of the evidence was evaluated for all comparisons using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.³²

We did analyses in Review Manager (version 54.1). This study is registered with PROSPERO, CRD42020214961.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Our initial search yielded 21 309 records, of which 12 475 remained after removing duplicates (figure 1). An additional 28 records were identified from the bibliographies of screened studies. After exclusions, 278 full-text articles were assessed for eligibility, of which 24 records were considered for inclusion in the systematic

For more on the **search methods and terms** see https://osf.io/r6n7k/?view_only=38d7a705d743435097f170bbebaa0623

See Online for appendix

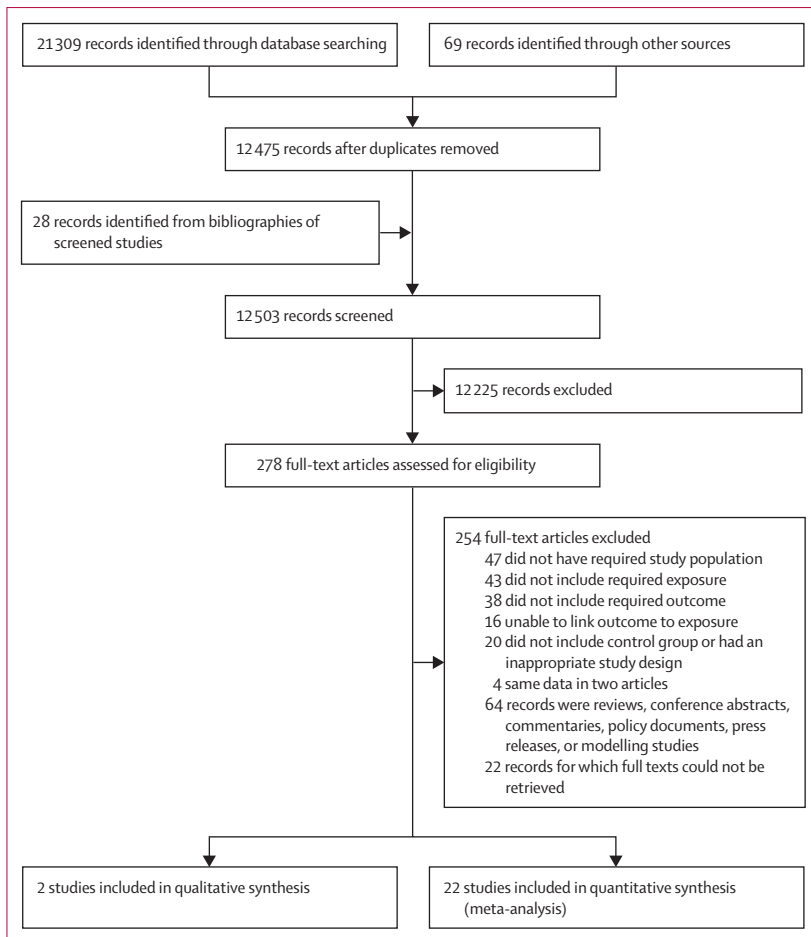


Figure 1: Study selection

review (qualitative synthesis^{8,10–14,16,20,21,23,33–46}, table); 22 of these studies contained the necessary data for inclusion in the quantitative analysis (appendix pp 23–35). One record was excluded from the quantitative analysis because it was a study with no events,³³ and another was excluded because it did not have a true control group.¹³ All studies included in the meta-analysis were conducted between Sept 1, 1989 and Dec 31, 2018 during chronic or protracted humanitarian emergencies in nine countries in WHO regions: five in sub-Saharan Africa (four in Democratic Republic of the Congo, one in Kenya, one in Sierra Leone, two in Sudan, one in Uganda), two in the Eastern Mediterranean (eight in Pakistan and one in Afghanistan) and two in South-East Asia (one in Myanmar, one in Thailand, and two in the Thai–Myanmar border; appendix p 36). Sources of all humanitarian emergencies were violent conflict, usually due to political, religious, or ethnic persecution and all studies included in the quantitative analysis were in refugee camps and settlements that had been established for several years or more. 11 of the included studies involved internally displaced people (fleeing from conflict in Myanmar or Thailand,^{10,34–36} Democratic Republic of

the Congo,^{37–40} Sierra Leone,¹⁴ Sudan,⁴¹ or Uganda⁸). The remaining 11 studies were in refugee populations (either Afghan refugees in Pakistan,^{12,16,21,23,42–45} or people resettled back in Afghanistan after time spent in Pakistan,⁴⁶ Somalian refugees in Kenya²⁰ or Ethiopian refugees in Sudan¹¹).

Seven different vector control interventions were deployed alone (21 of 22 studies) or in combination (one of 22 studies): ITNs (12 studies),^{8,10,33–35,37–41,43–46} IRS (three),^{11,12,42} ITNs and IRS (one),⁴⁴ insecticide-treated plastic sheeting (one),¹⁴ insecticide-treated chaddars (equivalent to shawls or blankets; one),¹⁶ insecticide-treated clothing (one),²⁰ topical repellents (two),^{21,36} and insecticidal treatment of livestock (one;²³ table and appendix pp 23–35). Nine studies were either cluster-randomised controlled trials (cRCTs; six; either household-randomised or village-randomised) or randomised trials at the individual level (three). 13 studies were non-randomised, including a before-and-after study (one), a controlled before-and-after study (one), cross-sectional surveys (seven), cross-sectional surveys with nested case-control studies (two), a cohort trial (one), and a non-randomised trial (one). Where appropriate, for cRCTs the data were adjusted for clustering and sensitivity analyses were done for outcomes in which the ICC was estimated. For all outcomes, the sensitivity analyses showed that using an estimated ICC did not greatly influence the effect size (appendix pp 36–42).

The majority of studies included in the meta-analysis (13 of 22) evaluated ITNs,^{8,10,33–35,37–41,43–46} and demonstrated a significant reduction in *P. falciparum* case incidence (RR 0.55 [95% CI 0.37–0.79]; four cRCTs; high certainty),^{10,34,35,45} *P. vivax* case incidence (RR 0.69 [0.51–0.94]; three cRCTs; moderate certainty; figure 2),^{10,35,45} and *P. falciparum* prevalence (RR 0.60 [0.40–0.88]; two cRCTs; high certainty; appendix pp 43–44) over 10 months. These studies took place during chronic humanitarian emergencies on the Thai–Myanmar border,^{34,35} within Myanmar,¹⁰ and within Pakistan⁴⁵ (appendix p 43).

Four studies deployed IRS, with evidence from observational studies in Pakistan supporting a reduction in *P. falciparum* incidence (IRR 0.57 [95% CI 0.53–0.61]; one before-and-after study; very low certainty)¹² and *P. vivax* incidence (IRR 0.51 [0.49–0.52]; one before-and-after study; very low certainty).¹² *P. vivax* prevalence was not significantly affected by IRS (OR 0.74 [95% CI 0.25–2.14]; one cross-sectional study and one controlled before-and-after study; very low certainty;^{42,44} figure 3; appendix pp 44–45). However, the only cRCT to evaluate IRS in eastern Sudan did not observe an effect on *P. falciparum* prevalence (RR 1.31 [95% CI 0.91–1.88]; low certainty;¹¹ appendix pp 44–45). Furthermore, a single cross-sectional study in Pakistan showed a combined effect of ITNs and IRS on *P. vivax* prevalence (OR 0.26 [95% CI 0.10–0.67]; very low certainty;⁴⁴ appendix p 45).

Country	Plasmodium species	Vector species	Population		Age	Sex	Ethnicity	Intervention	Comparison	Outcomes included (epidemiological)				
			Intervention, n	Control, n						Malaria incidence	Malaria prevalence	All-cause mortality	Severe malaria	Anaemia prevalence
Randomised controlled trials														
Smithuis et al, 2013 ¹⁰	Myanmar	Plasmodium falciparum and Plasmodium vivax	..	3989 (prevalence) and 3859 (incidence)	4053 (prevalence) and 3969 (incidence)	<10 years	Male and female	Rakhine	ITNs	No ITNs	Yes	Yes	Yes	Yes
Rowland et al, 2001 ²³	Pakistan	P falciparum and P vivax	Anopheles stephensi; Anopheles culicifacies; Anopheles subpictus; Anopheles fluviatilis; Anopheles annularis	37206 (total community size)	56329 (total community size)	All	Male and female	Afghan	Insecticidal livestock treatment	No cattle treatment	Yes	No	No	No
Rowland et al, 1999 ¹⁶	Pakistan	P falciparum and P vivax	A stephensi; A subpictus; Anopheles nigerrimus	765 (prevalence) and 15120 (incidence)	845 (prevalence) and 15903 (incidence)	All	Male and female	Afghan	Insecticide treatment of chaddars	Placebo treatment	Yes	No	No	No
Rowland et al, 1996 ⁴⁵	Pakistan	P falciparum and P vivax	A stephensi; A culicifacies; A subpictus; A nigerrimus	1398	1394	All	Male and female	Afghan	ITNs	No ITNs	Yes	No	No	No
Rowland et al, 2004 ²¹	Pakistan	P falciparum and P vivax	A stephensi; A culicifacies	618	530	All	Male and female	Afghan	DEET (repellent)	Placebo moisturising lotion with no repellent effect	No	Yes	No	No
Charlwood et al, 2001 ¹¹	Sudan	P falciparum and P vivax	Anopheles arabiensis; Anopheles pharoensis	134	144	All	Male and female	Eritrean or Tigrean	IRS	No IRS	Yes	No	Yes	No
Dolan et al, 1993 ²⁴	Thailand	P falciparum and P vivax	..	103 (ITN) and 100 (untreated net)	77 (untreated net) and 27 (no net)	26 years (mean)	Female	Karen	ITNs and untreated nets	No study net; use of untreated net that was already owned	Yes	No	No	Yes
Luxemburger et al, 1994 ²⁵	Thailand	P falciparum and P vivax	..	155	163	4 to 15 years	Male and female	Karen	ITNs and untreated nets	Untreated net	Yes	Yes	No	No
McGready et al, 2001 ²⁶	Thailand	P falciparum and P vivax	..	449	448	24 years (mean)	Female	Karen	Repellent	Thanaka	No	Yes	No	Yes

(Table continues on next page)

Country	Plasmodium species	Vector species		Population		Age	Sex	Ethnicity	Intervention		Outcomes included (epidemiological)			
		Intervention, n	Control, n	Intervention, n	Control, n				Malaria incidence	Malaria prevalence	All-cause mortality	Severe malaria	Anaemia prevalence	
Non-randomised controlled studies														
Rowland et al, 2002 ⁴⁶	P falciparum and P vivax	A stephensi; A fluviatilis; A culicifacies; Anopheles pulcherrimus	2319	1343	All	Male and female	Afghans	ITNs and untreated nets	No ITN	No	Yes	No	No	No
Brooks et al, 2017a ³⁷	P falciparum	..	85	326	All	Male and female	Congolese	ITNs	No ITN	No	Yes	No	No	No
Brooks et al, 2017b ³⁸	P falciparum	..	269	482	All	Male and female	Congolese	ITNs	No ITN	No	Yes	No	Yes	No
Charchuk et al, 2016 ³⁹	P falciparum	..	200 (cross-sectional study) and 100 (case-control study)	200 (cross-sectional study) and 100 (case-control study)	<5 years	Male and female	Congolese or Nande	ITNs	No ITN	No	Yes	No	No	No
Ma et al, 2017 ⁴⁰	P falciparum	..	169	473	2 months to 5 years	Male and female	Congolese or Nande	ITNs	No ITN	No	Yes	No	No	No
Kimani et al, 2006 ²⁰	198	101	All	Male and female	Somalian	ITCs	Untreated clothing (dipped in water)	No	Yes	No	No	No
Bourma et al, 1996 ³	P falciparum and P vivax	A stephensi; A culicifacies	27 300	98 000	All	Male and female	Afghan and Pakistani	Insecticide treatment of tents	IRS (malathion; 50% water soluble powder at 2 g/m ²) on house walls	No	Yes	No	No	No
Rowland et al, 1994 ⁴²	P falciparum and P vivax	A stephensi; A culicifacies; A subpictus; Anopheles superpictus; A annularis; A fluviatilis	2600	221	5-15 years	Male and female	Afghan	IRS	No IRS	No	Yes	No	No	No
Rowland et al, 1997a ⁴³	P falciparum and P vivax	..	173	186	All	Male and female	Afghan	ITNs	No ITN	No	Yes	No	No	No
Rowland et al, 1997b ²⁷	P falciparum and P vivax	Anopheles maculatus; A pulcherrimus; A nigerrimus; A stephensi; A culicifacies; A subpictus; A superpictus; A annularis; A fluviatilis	2683	225	All	Male and female	Afghan	IRS	No IRS	No	Yes	No	No	No

(Table continues on next page)

The use of topical repellents was also associated with a significant decrease in *P falciparum* infection incidence (RR 0.58 [95% CI 0.35–0.97]; moderate certainty) but not *P vivax* infection incidence (RR 1.06 [0.60–1.85]; low certainty), in two cRCTs in Pakistan and Thailand^{21,36} (figure 4, appendix p 46).

Four of six remaining studies evaluated vector control interventions specifically designed for use during humanitarian emergencies. Individual studies showed that insecticide-treated plastic sheeting led to a reduction of *P falciparum* case incidence over 4 months (RR 0.68 [95% CI 0.62–0.74]; one cohort study; very low certainty) in Sierra Leone⁴⁴ (appendix p 47), and of insecticide-treated clothing on *P falciparum* prevalence (OR 0.29 [95% CI 0.14–0.60]; one non-randomised study; very low certainty) in Kenya²⁰ (appendix p 48). In addition, insecticide-treated chaddars or blankets reduced *P falciparum* case incidence (RR 0.56 [95% CI 0.39–0.80]; moderate certainty) but not *P vivax* case incidence (RR 0.74 [95% CI 0.54–1.02]; low certainty; one study) and insecticide-treated cattle significantly reduced both *P falciparum* incidence and prevalence (incidence: IRR 0.44 [95% CI 0.22–0.86]; moderate certainty; prevalence: RR 0.46 [95% CI 0.31–0.70]; high certainty; one study) and *P vivax* incidence but not prevalence (incidence: IRR 0.69 [95% CI 0.50–0.95]; moderate certainty; prevalence: RR 0.60 [95% CI 0.33–1.08]; moderate certainty) in Pakistan in two cRCTs (appendix pp 49–50).^{16,23}

Regarding secondary outcomes, anaemia was measured in five studies, with ITNs having no significant change on haemoglobin levels (RR 0.95 [95% CI 0.81 to 1.11]; moderate certainty; two cRCTs in interior Myanmar¹⁰ and the Thai–Myanmar border;³⁴ and mean difference –0.10 [–0.34 to 0.14]; very low certainty; a cross-sectional survey in Uganda⁸); insecticide-treated plastic sheeting decreased anaemia prevalence (mean difference 0.71 [95% CI 0.48 to 0.94]; very low certainty; one cohort study in Sierra Leone¹⁴). By comparison topical repellents had no impact on anaemia prevalence (RR 1.06 [95% CI 0.91 to 1.23]; low certainty; one cRCT in Thailand³⁶). There was insufficient published data for all other secondary outcomes to perform quantitative analyses.

Due to the absence of a published protocol for all studies, there were some concerns regarding the risk of bias in the selection of the reported result for cRCTs. However, in all other domains, the risk of bias was low for all studies apart from the study by Rowland and colleagues (1999),¹⁶ in which there were concerns related to bias due to deviations from the intended intervention (appendix p 51). There was a high risk of bias in two case–control studies,^{39,46} which were scored low on the Newcastle-Ottawa scale in the representativeness of cases, selection of controls, and ascertainment of exposure (appendix p 52). There was a moderate risk of bias for the 11 cross-sectional, controlled before-and-after,

Country	Plasmodium species	Vector species		Population		Control, n	Age	Sex	Ethnicity	Intervention	Comparison	Outcomes included (epidemiological)			
		Intervention, n	Control, n	Malaria incidence	Malaria prevalence							All-cause mortality	Severe malaria	Anaemia prevalence	
(Continued from previous page)															
Wahid et al, 2016 ⁴⁴	P falciparum and P vivax	A stephensi; A culicifacies	695	110	All	Male and female	Afghan	ITNs and IRS	No ITN or IRS	No	No	No	No	No	
Burns et al, 2012 ¹⁴	P falciparum	A gambiae sensu lato; Anopheles funestus sensu lato	106	116	4 to 36 months	Male and female	Liberian	ITPS	UPS	Yes	Yes	No	No	Yes	
Eshag et al, 2020 ⁴¹	P falciparum and P vivax	..	372	8	All	Male and female	Sudanese	ITNs	No ITN	No	Yes	No	No	No	
Spencer et al, 2004 ⁸	P falciparum	..	1169	..	All	Male and female	Ugandan	ITNs	No ITN	No	Yes	No	No	Yes	
Chan et al, 2017 ²³	P falciparum and P vivax	..	3009	..	All	Male and female	Melanesian or Polynesian	ITNs	No ITN	No	Yes	No	No	No	

IRS=indoor residual spraying; ITC=insecticide-treated clothing; ITN=insecticide-treated net; ITPS=insecticide-treated plastic sheeting; UPS=untreated plastic sheeting.

Table: Characteristics of included studies

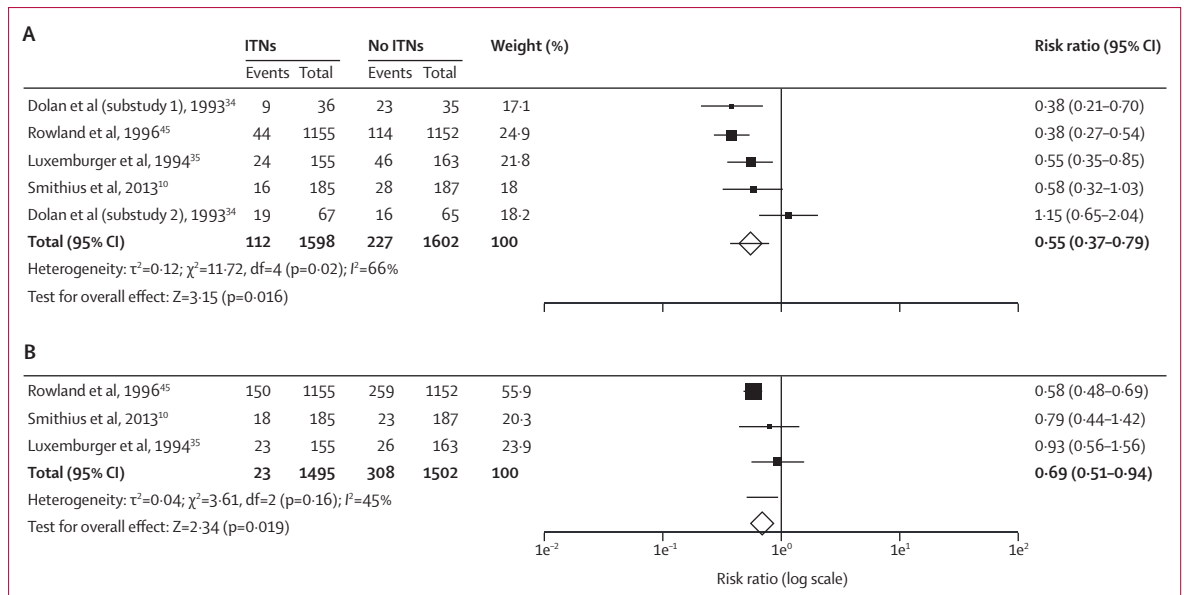


Figure 2: The effect of ITNs on malaria case incidence
 (A) *Plasmodium falciparum* case incidence. (B) *Plasmodium vivax* case incidence. Error bars show 95% CIs. ITN=insecticide-treated nets.

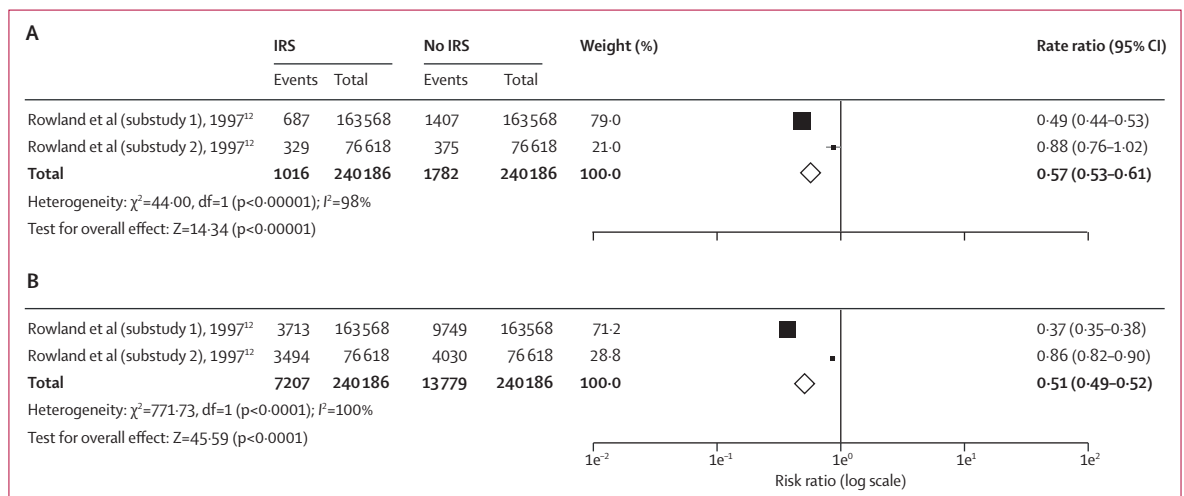


Figure 3: The effect of IRS on malaria case incidence
 (A) *Plasmodium falciparum* case incidence. (B) *Plasmodium vivax* case incidence. Error bars show 95% CIs. IRS=indoor residual spraying.

and before-and-after studies.^{8,12,20,37-42,44,46} Bias was attributed to the absence of information on non-responding participants, exposures not being formally validated through a measurement tool, and because some studies did not control for any potential confounders (appendix p 53). There was a low risk of bias in the one cohort study¹⁴ (appendix p 54). There were insufficient studies to test for asymmetry in the meta-analysis for any outcome measurement per intervention. The GRADE assessments indicated moderate-to-high certainty evidence for the effect of ITNs, insecticide-treated chaddars and blankets, topical repellents, and insecticide-treated cattle on malaria outcomes during humanitarian emergencies.

The GRADE approach indicated very low or low certainty evidence for the effect of IRS, IRS and ITNs, insecticide-treated clothing, and insecticide-treated plastic sheeting on malaria outcomes during humanitarian emergencies.

Discussion

Study findings showed high certainty evidence that ITN deployment in chronic humanitarian emergencies can reduce *P falciparum* incidence by 45% and *P vivax* by 31%. Similar effect sizes have been reported from recent meta-analyses of ITNs used in non-emergency malaria-endemic settings.⁴⁷ The contemporary effectiveness of ITNs is predicated on several factors, including

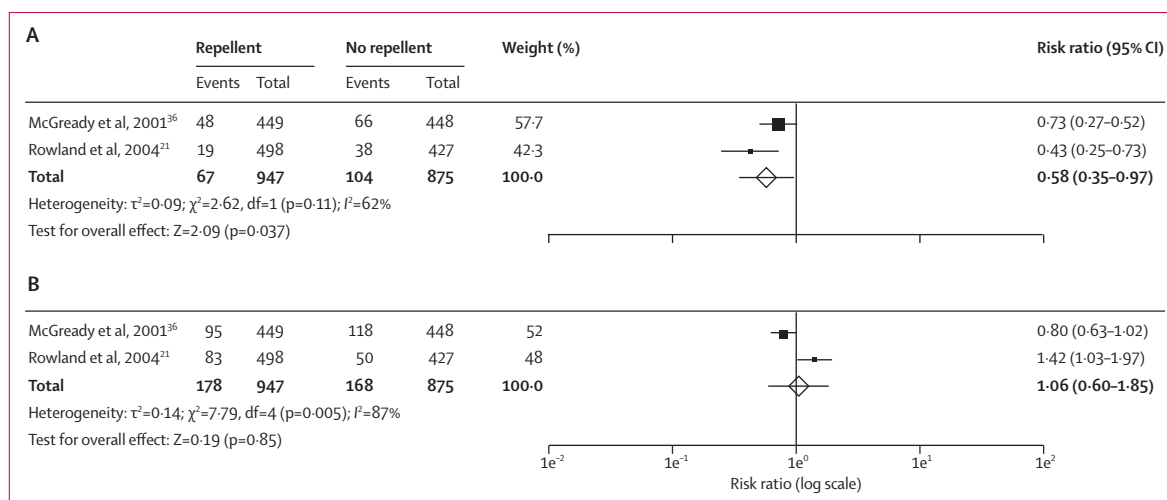


Figure 4: The effect of topical repellents on malaria infection incidence

(A) *Plasmodium falciparum* infection incidence. (B) *Plasmodium vivax* infection incidence. Error bars show 95% CIs.

net access, use, and durability, insecticide retention and bioefficacy, and vector susceptibility.⁴⁸ Several operational studies have highlighted substantial pragmatic barriers to ITN use in mobile populations of internally displaced people, including inadequate sleeping arrangements, overcrowding, violence, misuse of ITNs, rapid development of net holes from harsh living conditions, and inadequate information education communication and behaviour change communication (IEC/BCC) about net care in populations that are unreceptive, have low levels of literacy, or have high levels of trauma.^{8,37,49,50} Another complication of deploying personal protective vector control interventions is the economic vulnerability of internally displaced people relative to neighbouring or host communities, which can encourage trade in donated goods, theft, heightened tensions, and even violence against internally displaced people by those who were not beneficiaries of charitable commodities.^{37,49} Adapted ITN delivery mechanisms and coordinated monitoring and evaluation programmes, in particular accurate population mapping, continuous community-based distribution systems, hang-up campaigns reinforcing key IEC/BCC messages, and strengthened intersectoral partnerships, are crucial to achieve and maintain high ITN coverage and use during humanitarian emergencies.⁴⁹

There were some indications that IRS can prevent *P falciparum* and *P vivax* infection during humanitarian emergencies. However, the certainty of evidence was very low, aligning with previous results from non-emergency settings, which highlighted the need for additional trials to quantify the effect size of IRS in different transmission settings.⁵¹ Based on ITN and IRS efficacy during non-emergency situations, WHO has suggested these two tools for use in emergencies, and our study findings strengthen and support this policy for ITNs where sleeping arrangements are appropriate

(ie, where there is somewhere to hang a bed net). Compared with ITNs, IRS requires fewer behavioural changes, which can impede intervention use during humanitarian emergencies, and the arsenal of available insecticides is greater, an asset with regards to the pervasive problem of insecticide resistance among major malaria vector populations.⁵² However, IRS does require planning, timely application, specialist experience, greater logistical resources for implementation, and sustained donor initiatives.⁵³ One strategy to circumvent some of these limitations has been to exploit utilitarian emergency materials, such as plastic sheeting, tarpaulins, and tents, as longer-term mechanisms of insecticide delivery.^{13,15,54-59} In this systematic review, we only identified one study that reported very low certainty evidence of the effect of insecticide-treated plastic sheeting on *P falciparum* case incidence in west Africa during a chronic emergency.¹⁴ This concept has also been extended to treating personal material items during emergencies, including clothing, blankets, and bedsheets, with pyrethroid insecticides,^{16,18,20,60} with moderate evidence for a reduction in *P falciparum* case incidence from a household-randomised trial of permethrin-treated chaddars in Pakistan¹⁶ and lower certainty evidence for insecticide-treated clothing to prevent malaria infection in Kenya.²⁰ As none of these products are currently commercially available, there is an urgent need to design and further evaluate novel, innovative, and emergency-specific vector control tools to complement ITN distributions and IRS campaigns. The simultaneous deployment of several malaria control tools has been identified as a priority in humanitarian emergencies among experts, with insecticide-treated covers and blankets considered favourable because of their transportability and flexibility for use in mobile populations.⁵³ The private sector has largely failed to

develop these niche vector control tools, particularly those that might not have a market share for routine use in stable malaria endemic settings.⁶¹

Topical repellents and insecticide-treated cattle were also associated with significant reductions in malaria incidence in the Eastern Mediterranean and South-East Asia with moderate-to-high certainty evidence.^{21,23,36} However, by comparison with sub-Saharan Africa, there are key differences in malaria vector populations between these areas, particularly exophilic or exophagic and anthropophilic or zoophilic tendencies, which might influence the efficacy of these vector control interventions. Insecticide-treated cattle was an effective intervention in Pakistan,^{23,62} where vector populations are highly zoophilic and the study population lived in established housing settlements. It could be assumed that this strategy would also show promise in areas where *Anopheles arabiensis* is a major vector species in sub-Saharan Africa.^{63–65} Topical repellents have not always performed well in malaria-endemic parts of Africa, largely due to issues of IEC/BCC, standardised repellent formulation, user compliance, and duration of protection, which can all contribute to participants being unprotected at peak vector biting times.^{66,67} Differences in vector behaviour were also apparent in some of the eligible ITN studies from South-East Asia, where the evidence for an effect of ITNs on malaria transmission was weak in rural, non-conflict areas due to early biting and exophilic or exophagic behaviours of most primary vectors.^{68,69} A similar absence of protection from malaria was observed in populations of internally displaced people in the same region.¹⁰

In several cases, published data were limited to observational studies or retrospective programmatic evaluations,^{8,12,37–39,42–44,46} or from randomised studies, which were done in much more stable internally displaced people and refugee settlements, established for a number of years.^{10,11,16,22,23,34–36,45} We were only able to identify one study done in acute settings, which was done during a tropical cyclone in Vanuatu and was excluded because it had no malaria events.³³ Most eligible randomised studies were done in chronic humanitarian emergencies in the Eastern Mediterranean and in South-East Asia, with comparatively fewer done in sub-Saharan Africa, where most of the malaria disease burden is now concentrated³ and substantial numbers of humanitarian emergencies are ongoing.¹ In addition, most eligible studies were done between 1990 and mid-2000s. Due to the age of these studies, some key details, such as reporting methods of cluster randomisation, were not always described adequately because of the available reporting guidelines at the time, thereby downgrading their overall GRADE assessment.⁷⁰ Furthermore, all eligible studies evaluated interventions using insecticides (primarily pyrethroids), which might not be used for malaria vector control due to widespread insecticide resistance.^{71–73} New dual-active ingredient ITNs, piperonyl butoxide ITNs, novel IRS compounds, attractive toxic sugar baits,⁷⁴ and spatial

repellents⁷⁵ are undergoing phase 3 trials in non-emergency settings to determine their efficacy against pyrethroid-resistant malaria vector populations.^{76–80} Additional randomised trials evaluating the efficacy of these new tools, and other existing ones, are warranted in emergency settings, spanning a range of geographical areas, malaria vector species, and insecticide resistance intensities, to strengthen the evidence basis for use of vector control tools to prevent malaria infection among internally displaced people and refugees.

Contributors

LAM and MR conceived of the study concept. LAM, JF-A, BP, and MR developed the study design. LAM, JF-A, KC, BP, and LP screened the literature and extracted data from the articles. JF-A and KC led the data analysis, with support from LAM, BP, LP, and MR. LAM wrote the first draft of the manuscript, which was revised by all authors. All authors reviewed and agreed with the final version of the report. All authors had access to all the data in the study and had final responsibility for the decision to submit for publication. LAM, JF-A, and KC accessed and verified the data.

Declaration of interests

We declare no competing interests.

Data sharing

As this study is a systematic review and meta-analysis, there is no primary data to be shared. Raw extracted data are available from the corresponding author on reasonable request.

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