The MENTOR Initiative
REDUCING DEATHS & SUFFERING FROM TROPICAL DISEASES

RAFT
RESILIENCE AGAINST FUTURE THREATS

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

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WHO-GMP

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LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

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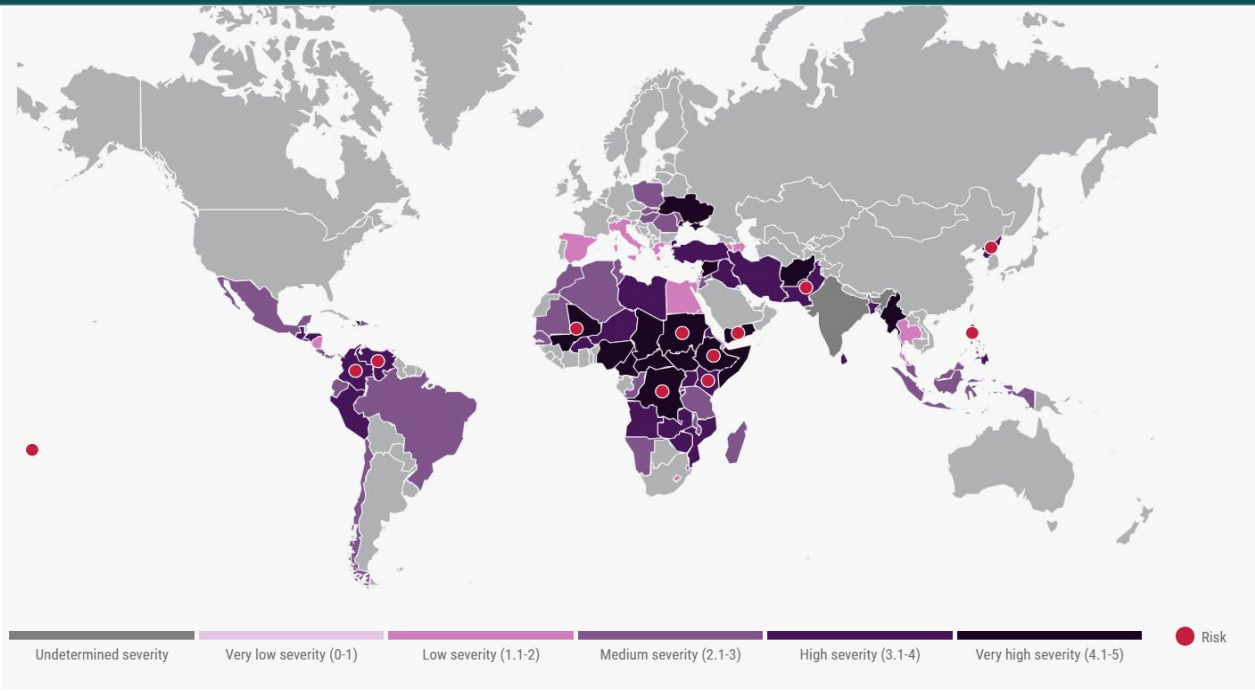
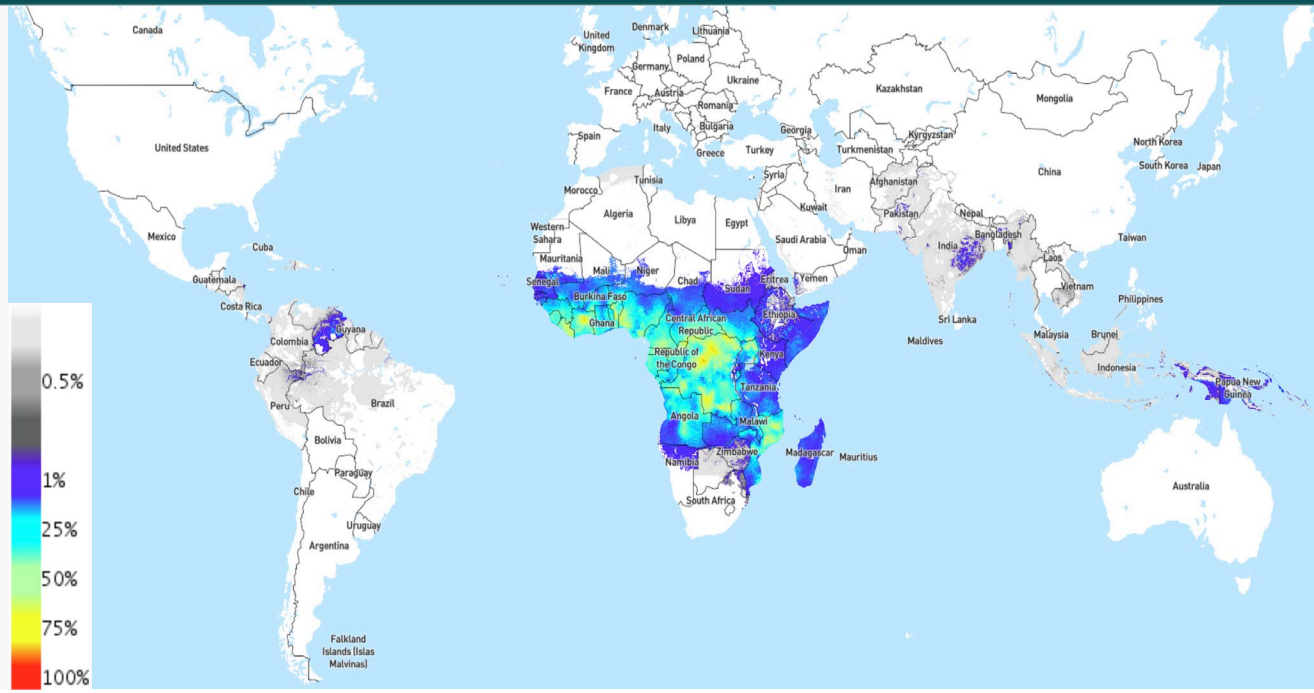
Humanitarian Emergencies and Malaria





- Humanitarian emergencies, of either natural or anthropogenic origins, are equivalent to **major disasters**, which lead to large-scale population movement, food insecurity and severe health system disruptions
- Humanitarian emergencies may increase risk of malaria epidemics and incidence of severe disease; when immunologically naïve individuals are displaced into high transmission areas

- UNHCR currently estimates 89.3M forcibly displaced people, incl. 53.2M IDP, 21.3M refugees, 4.6M asylum-seekers and 4.4M Venezuelans displaced abroad
- 2/3 inhabit malaria endemic regions, particularly WHO AFRO region
- Reversal of malaria gains during humanitarian emergency in Venezuela – 1200% increase in malaria between 2000-2020

Review Context, Objective & Methods

- Evidence for malaria vector control tools during humanitarian emergencies insufficient for WHO to develop policy recommendations; recommendations for ITNs and IRS based on proven efficacy in non-emergency situations

Primary review objective:

- To evaluate the impact of different vector control interventions on malaria disease burden during humanitarian emergencies

- Literature retrieved from 10 electronic databases and 2 clinical trial registries using ~200 search terms
- Grey literature from 29 technical groups/NGOs, 24 donors, stakeholders and policy makers and 6 industrial partners searched

PICO – Participants, Interventions, Comparisons

Setting	**An area with ongoing human malaria transmission or malariogenic potential**
Population	Refugees and IDP adults and children, affected by humanitarian emergencies
Intervention	Malaria-specific vector control intervention
Comparison	No malaria-specific vector control intervention

PICO – Outcomes & Data Analysis

Primary outcomes: Epidemiological

- Malaria case incidence (symptomatic infection)
- Malaria infection incidence
- Parasite prevalence (symptomatic and asymptomatic infection)

Secondary outcomes: Epidemiological

- All case mortality
- Severe malaria
- Anaemia prevalence

Secondary outcomes: Entomological

- Entomological inoculation rate (EIR)
- Adult mosquito density
- Sporozoite rate

Secondary outcome: Operational

- Intervention durability

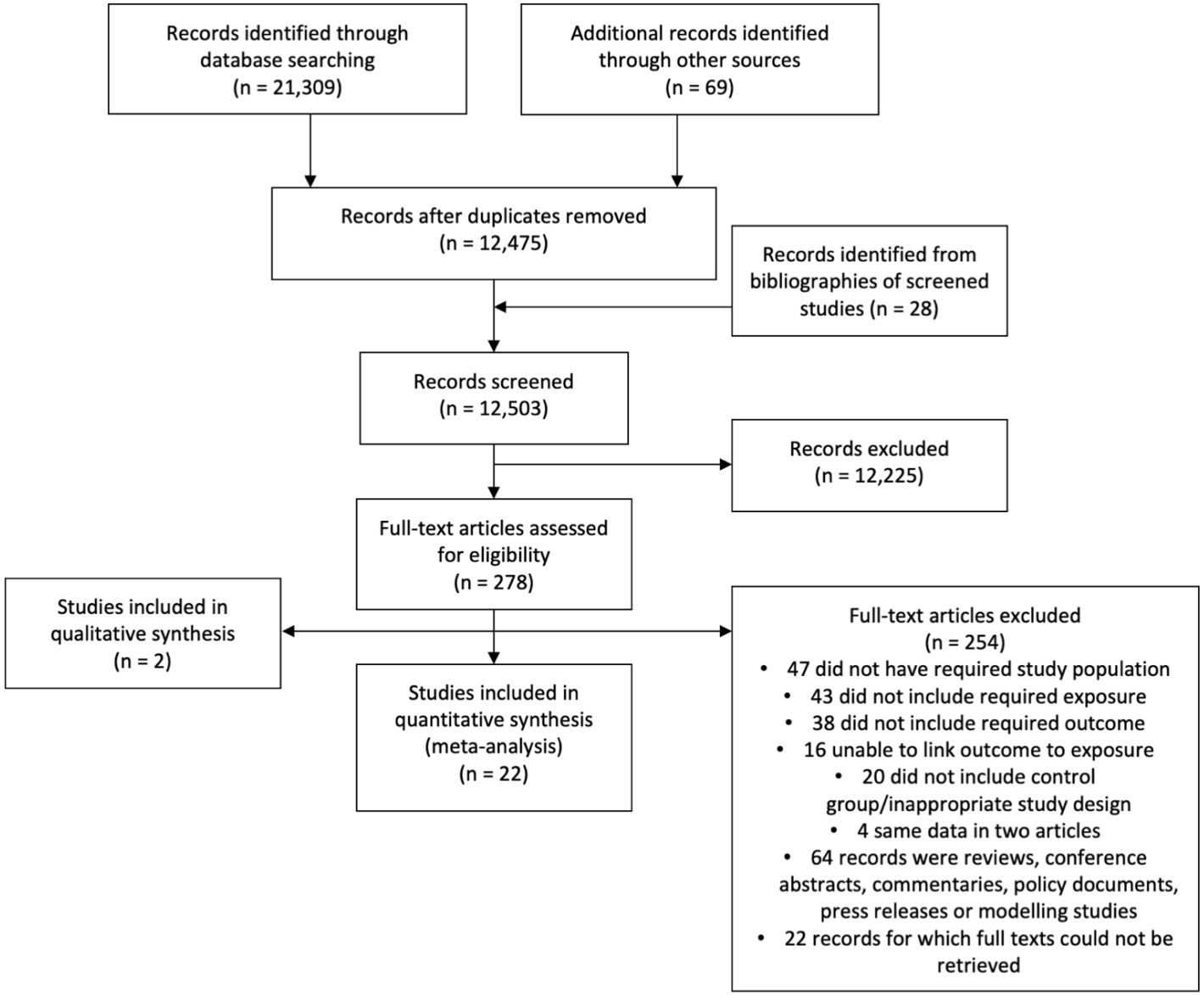
Secondary outcomes: Other Effects

- Adverse events
- Impact on human behaviour
- Impact on other vector-borne diseases

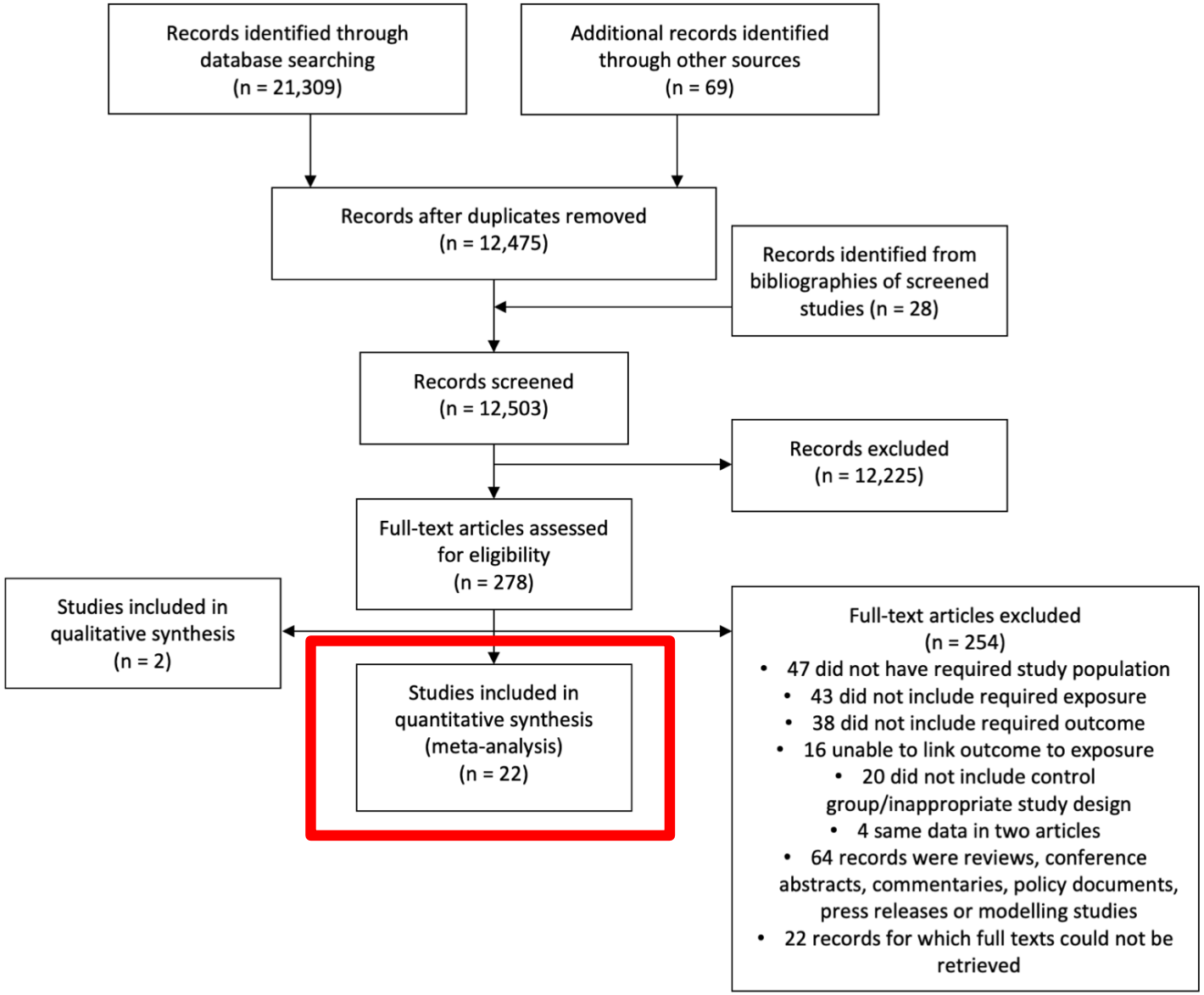
Data analysis:

- Random effects models for randomised controlled trials (risk ratios)
- Odds ratios for dichotomous outcomes in non-randomised studies
- Incidence rate ratios for clinical malaria incidence in non-randomised studies
- Risk of bias using Cochrane Risk of Bias tool (randomised) or Newcastle-Ottawa Scale (non-randomised)
- Certainty of evidence using Grading Recommendations, Assessment, Development and Evaluation (GRADE)

PRISMA Diagram



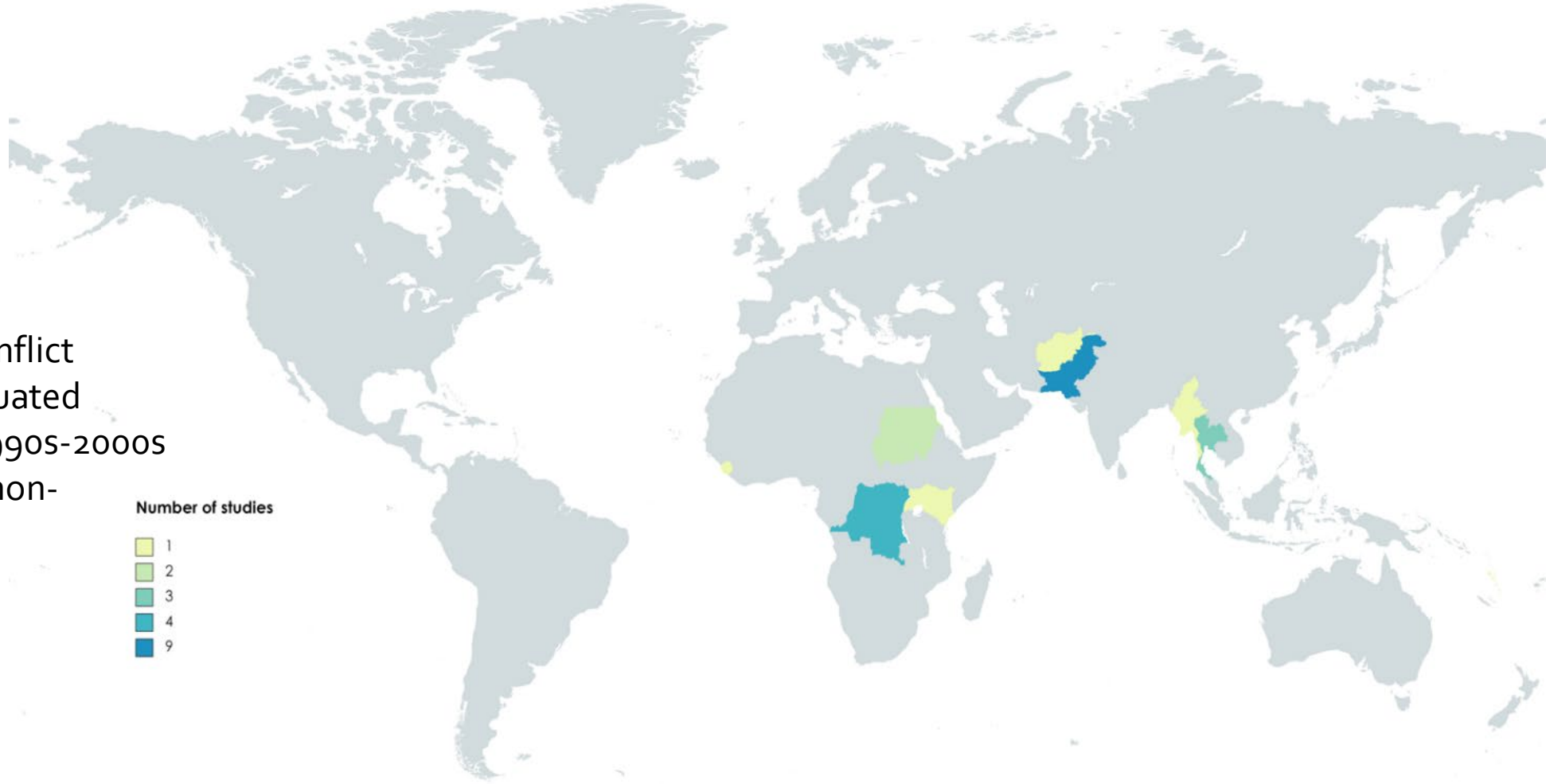
PRISMA Diagram



Eligible Studies

- Studies from 9 countries:
- 5 sub-Saharan Africa
- 2 Eastern Mediterranean
- 2 South-East Asia
- 616,611 participants

- All emergencies due to conflict
- 7 vector control tools evaluated
- Most studies from early 1990s-2000s
- 9 randomized studies; 13 non-randomized



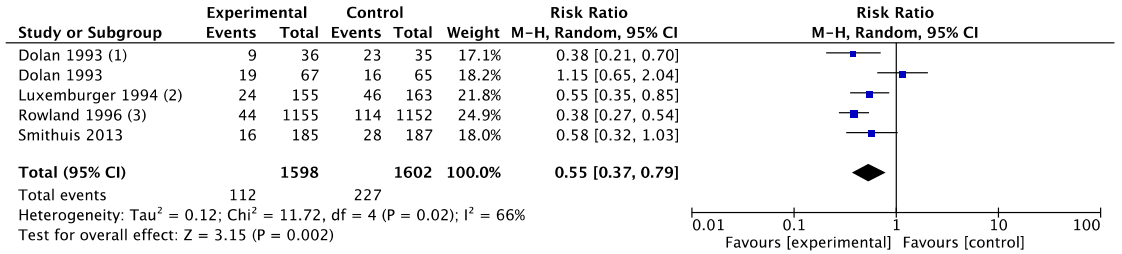
Summary of Findings - ITNs

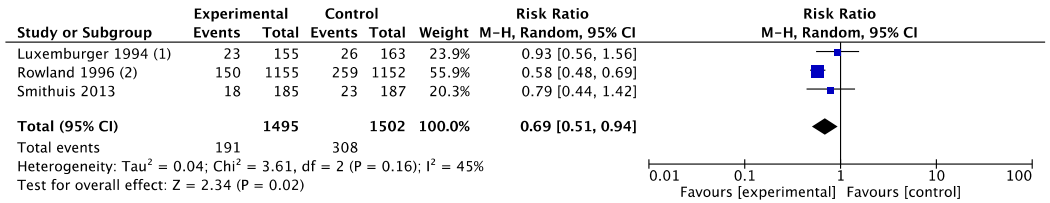
ITNs compared to no ITNs for preventing malaria

Patient or population: refugees/IDPs affected by humanitarian emergencies
Setting: humanitarian emergencies
Intervention: ITNs
Comparison: no ITNs

Outcomes	Anticipated absolute effects (95% CI)		Relative effect (95% CI)	Number of participants/person-years (studies)	Certainty of the Evidence (GRADE)	Comments
	No ITNs	Risk difference with ITNs				
P. falciparum case incidence	70 per 1000	**32 fewer per 1000** (44 fewer to 15 fewer)	**RR 0.55** (0.37 to 0.79)	3200 (4 RCTs)	⨁⨁⨁⨁ HIGH [a]	ITNs result in large reduction in *P. falciparum* case incidence.
P. falciparum prevalence	37 per 1000	**15 fewer per 1000** (22 fewer to 4 fewer)	**RR 0.60** (0.40 to 0.88)	2079 (2 RCTs)	⨁⨁⨁⨁ HIGH [a]	ITNs result in large reduction in *P. falciparum* prevalence.
P. vivax case incidence	132 per 1000	**41 fewer per 1000** (65 fewer to 8 fewer)	**RR 0.69** (0.51 to 0.94)	2812 (3 RCTs)	⨁⨁⨁◯ MODERATE [a]	ITNs likely reduces *P. vivax* case incidence.
P. vivax prevalence	99 per 1000	**0 fewer per 1000** (25 fewer to 34 more)	**RR 1.00** (0.75 to 1.34)	2079 (2 RCTs)	⨁⨁◯◯ LOW [a,b]	ITNs may result in little to no difference in *P. vivax* prevalence.

a. Wide confidence intervals
b. There is uncertainty about the magnitude of effect of the intervention, as it fails to exclude benefit or harm.





Footnotes
(1) individually randomised
(2) household randomised

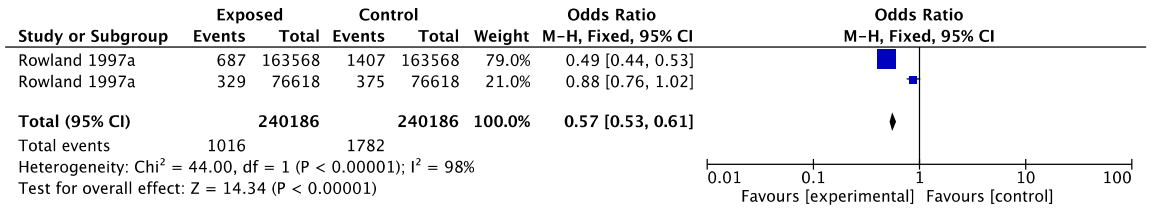
Summary of Findings - IRS

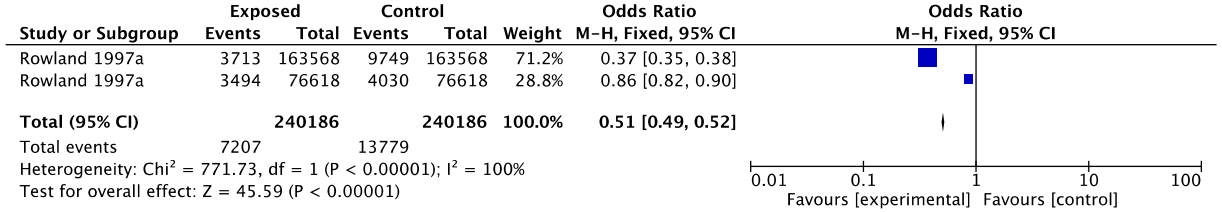
IRS compared to no IRS for preventing malaria

Patient or population: refugees/IDPs affected by humanitarian emergencies
Setting: humanitarian emergencies
Intervention: IRS
Comparison: no IRS

Outcomes	Anticipated absolute effects (95% CI)		Relative effect (95% CI)	Number of participants/person-years (studies)	Certainty of the Evidence (GRADE)	Comments
	No IRS	Risk difference with IRS				
P. falciparum incidence (crude IRRs)	7 per 1000 person-years	**3 fewer per 1000** (3 fewer to 3 fewer)	**Rate ratio 0.57** (0.53-0.61)	48,0377 (1 observational study)	⨁◯◯◯ VERY LOW[c,f]	The evidence is very uncertain about the effect of IRS on *P. falciparum* incidence: crude IRRs.
P. falciparum prevalence	257 per 1000	**80 more per 1000** (23 fewer to 226 more)	**RR 1.31** (0.91-1.88)	278 (1 RCT)	⨁⨁◯◯ LOW[a,b]	IRS may result in little to no difference in *P. falciparum* prevalence.
P. vivax incidence (crude IRRs)	57 per 1000 person-years	**28 fewer per 1000** (29 fewer to 28 fewer)	**Rate ratio 0.51** (0.49-0.52)	48,0372 (1 observational study)	⨁◯◯◯ VERY LOW[c,f]	The evidence is very uncertain about the effect of IRS on *P. vivax* incidence: crude IRRs.
P. vivax prevalence (crude ORs)	78 per 1000	**19 fewer per 1000** (57 fewer to 75 more)	**OR 0.74** (0.25-2.14)	4,708 (2 observational studies)	⨁◯◯◯ VERY LOW[a,b,c,d,e]	The evidence is very uncertain about the effect of IRS on *P. vivax* prevalence: crude ORs.

a. Very wide confidence intervals.
b. There is uncertainty about the magnitude of effect of the intervention, as it fails to exclude benefit or harm.
c. All studies were non-randomised and observational.
d. Only two studies were included, and both were conducted in Pakistan. The results may not be generalisable to other settings.
e. Minimal overlap of confidence intervals and considerable heterogeneity (I2 = 81%, p = 0.02).
f. Only one study was included, and was conducted in Pakistan. The results may not be generalisable to other settings.





Summary of Findings – ITCs & ITPS

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Insecticide-treated clothing compared to no insecticide-treated clothing for preventing malaria

Patient or population: refugees/IDPs affected by humanitarian emergencies
Setting: humanitarian emergencies
Intervention: insecticide-treated clothing
Comparison: untreated clothing

Outcomes	Anticipated absolute effects (95% CI)		Relative effect (95% CI)	Number of participants/person-years (studies)	Certainty of the Evidence (GRADE)	Comments
	No insecticide-treated clothing	Risk difference with insecticide-treated clothing				
P. falciparum prevalence: adjusted ORs	659 per 1000	**284 fewer per 1000** (412 fewer to 130 fewer)	**OR 0.29** (0.14-0.60)	181 (1 observational study)	⊕◯◯◯ VERY LOW[a,b]	The evidence is very uncertain about the effect of insecticide-treated clothing on *P. falciparum*: adjusted ORs.

a. All studies were non-randomised and observational.
b. Only one study was included, which was conducted in Kenya. The results may not be generalisable to other settings.

Insecticide-treated plastic sheeting compared to no insecticide-treated plastic sheeting for preventing malaria

Patient or population: refugees/IDPs affected by humanitarian emergencies
Setting: humanitarian emergencies
Intervention: insecticide-treated plastic sheeting
Comparison: untreated plastic sheeting

Outcomes	Anticipated absolute effects (95% CI)		Relative effect (95% CI)	Number of participants/person-years (studies)	Certainty of the Evidence (GRADE)	Comments
	No insecticide-treated plastic sheeting	Risk difference with insecticide-treated plastic sheeting				
P. falciparum incidence: adjusted IRRs	4 per 1000 person-years	**1 fewer per 1000** (2 fewer to 1 fewer)	**Rate ratio 0.68** (0.62-0.74)	31,023 (1 observational study)	⊕◯◯◯ VERY LOW[a,b]	The evidence is very uncertain about the effect of insecticide-treated plastic sheeting on *P. falciparum* incidence: adjusted IRRs.
P. falciparum prevalence (adjusted ORs)	514 per 1000	**56 fewer per 1000** (110 fewer to 0 fewer)	**OR 0.80** (0.64-1.00)	1,610 (1 observational study)	⊕◯◯◯ VERY LOW[a,b,c]	The evidence is very uncertain about the effect of insecticide-treated plastic sheeting on *P. falciparum* prevalence: adjusted ORs.

a. All studies were non-randomised and observational.
b. Only one study was included, which was conducted in Sierra Leone. The results may not be generalisable to other settings.
c. There is uncertainty about the magnitude of effect of the intervention, as it fails to exclude benefit or harm.

Summary of Findings – Insecticide-Treated Cattle

Insecticide-treated cattle compared to no insecticide-treated cattle for preventing malaria Patient or population: refugees/IDPs affected by humanitarian emergencies Setting: humanitarian emergencies Intervention: insecticide-treated cattle Comparison: no insecticide-treated cattle						
Outcomes	**Anticipated absolute effects (95% CI)**		**Relative effect (95% CI)**	**Number of participants/person-years (studies)**	**Certainty of the Evidence (GRADE)**	**Comments**
	No insecticide-treated cattle	**Risk difference with insecticide-treated cattle**				
***P. falciparum* incidence**	11 per 1000 person-years	**6 fewer per 1000** (9 fewer per 2 fewer)	**Rate ratio 0.44** (0.22-0.86)	93,535 (1 RCT)	⊕⊕⊕◯ MODERATE[a]	Insecticide-treated cattle likely results in a large reduction in *P. falciparum* incidence.
***P. falciparum* prevalence**	19 per 1000	**10 fewer per 1000** (13 fewer to 6 fewer)	**RR 0.46** (0.31-0.70)	19,152 (1 RCT)	⊕⊕⊕⊕ HIGH	Insecticide-treated cattle results in large reduction in *P. falciparum* prevalence.
***P. vivax* incidence**	72 per 1000 person-years	**22 fewer per 1000** (36 fewer to 4 fewer)	**Rate ratio 0.69** (0.50 to 0.95)	93,535 (1 RCT)	⊕⊕⊕◯ MODERATE[a]	Insecticide-treated cattle likely results in a large reduction in *P. vivax* incidence.
***P. vivax* prevalence**	82 per 1000	**33 fewer per 1000** (55 fewer to 7 more)	**RR 0.60** (0.33-1.08)	19,152 (1 RCT)	⊕⊕⊕◯ MODERATE[b]	Insecticide-treated cattle may result in a large reduction in *P. vivax* prevalence.

a. Downgraded by 1 for imprecision: CIs span from a small effect to a large effect.
b. Downgraded by 1 for imprecision: CIs include both a large effect and no effect.

Summary of Findings – Insecticide-Treated *Chaddars* & Topical Repellents

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Insecticide-treated chaddars compared to no insecticide-treated chaddars for preventing malaria

Patient or population: refugees/IDPs affected by humanitarian emergencies
Setting: humanitarian emergencies
Intervention: insecticide-treated chaddars
Comparison: untreated chaddars

Outcomes	Anticipated absolute effects (95% CI)		Relative effect (95% CI)	Number of participants/person-years (studies)	Certainty of the Evidence (GRADE)	Comments
	No insecticide-treated chaddars	Risk difference with insecticide-treated chaddars				
P. falciparum **case incidence**	116 per 1000	**51 fewer per 1000** (71 fewer to 23 fewer)	**RR 0.56** (0.39-0.80)	682 (1 RCT)	⊕⊕⊕◯ MODERATE[a]	Insecticide-treated chaddars/top-sheets likely results in a large reduction in *P. falciparum* case incidence.
P. vivax **case incidence**	222 per 1000	**58 fewer per 1000** (102 fewer to 4 more)	**RR 0.74** (0.54-1.02)	682 (1 RCT)	⊕⊕◯◯ LOW[b]	Insecticide-treated chaddars/top-sheets may reduce *P. vivax* case incidence.

a. Wide confidence intervals.
b. Downgraded by 2: very wide confidence intervals indicating that the true effect could be large or there could be no effect.

Topical repellents compared to no topical repellents for preventing malaria

Patient or population: refugees/IDPs affected by humanitarian emergencies
Setting: humanitarian emergencies
Intervention: topical repellents
Comparison: no topical repellents

Outcomes	Anticipated absolute effects (95% CI)		Relative effect (95% CI)	Number of participants/person-years (studies)	Certainty of the Evidence (GRADE)	Comments
	No topical repellents	Risk difference with topical repellents				
P. falciparum **infection incidence**	71 per 1000	**30 fewer per 1000** (46 fewer to 2 fewer)	**RR 0.58** (0.35-0.97)	1822 (2 RCTs)	⊕⊕⊕◯ MODERATE[a]	Topical repellents likely reduce *P. falciparum* infection incidence.
P. vivax **infection incidence**	188 per 1000	**11 more per 1000** (75 fewer to 160 more)	**RR 1.06** (0.60-1.85)	1822 (2 RCTs)	⊕⊕◯◯ LOW[a,b]	Topical repellents may result in little to no difference in *P. vivax* infection incidence.

a. Very large confidence intervals
b. There is uncertainty about the magnitude of effect of the intervention, as it fails to exclude benefit or harm.

Key Discussion Points

- High certainty evidence for ITN deployment in chronic humanitarian emergencies – reduced *P. falciparum* and *P. vivax* by 45% and 31%, respectively
- Similar effect sizes reported from meta-analyses of ITNs during non-emergencies
- Significant pragmatic barriers to ITN use during emergencies:
  - Inadequate sleeping arrangements/over-crowding
  - ITN mis-use/illegal trade of donated goods
  - Poor durability due to harsh conditions
  - Inadequate IEC/BCC about net care

- Lower certainty evidence for IRS - similar to non-emergency settings
- IRS has some advantages over ITNs during emergencies (when shelter structures are appropriate):
  - Less behavior change
  - More choice of insecticides for resistance management
  - Community-level protection
  - Reduces other vector species (e.g. sandflies) and nuisance pests

- Low certainty evidence for ITCs/ITPS, topical repellents and *chaddars*
- Greater investment from the private sector needed for 'niche' vector control tools

Key Limitations

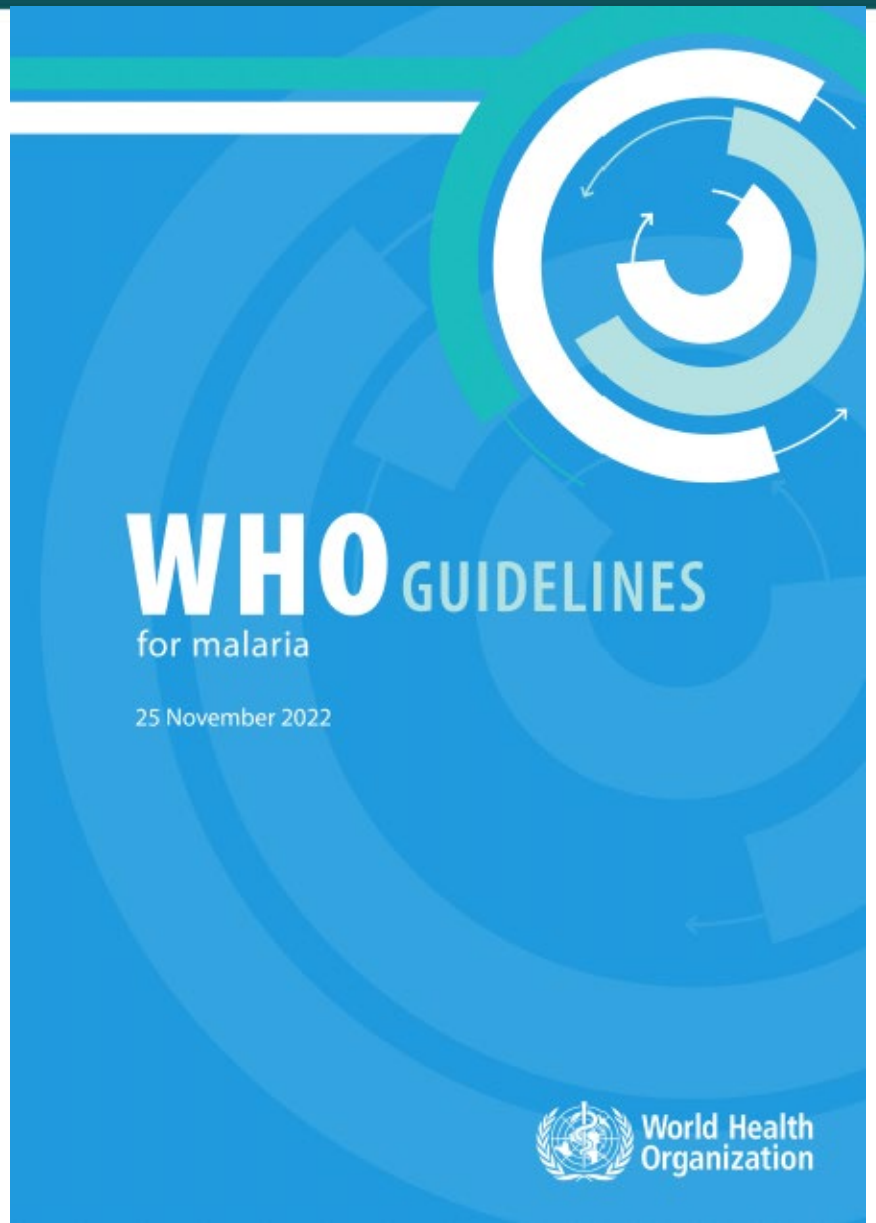
Study design/data collection limitations

- Studies may lack a true control group – unethical during emergencies not to distribute vector control interventions equitably; comparisons to adjacent villages/communities instead
- Vector control tool deployment in emergencies often accompanied by improvements to malaria diagnosis/treatment and health facility access; resource allocation assumed to be equal; overestimation of vector control intervention effect size
- Refugee settlement infrastructure, road access assumed to be uniform; data not captured systematically
- Challenging to design prospective studies in emergencies (especially acute); cannot collect baseline data, design protocols, obtain ethical approval, map study areas, stratify intervention deployment

Limitations of available literature

- Studies conducted in chronic/protracted emergencies of 10+ years
- Majority of randomized data from Asia (13/22), with less from sub-Saharan Africa (9/22); key differences in vector behaviour, particularly exophilic/exophagic, anthropophilic/zoophilic tendencies
- Most studies used pyrethroid insecticides before widespread insecticide resistance

World Health Organization Policy Recommendations



Strong recommendation for , High certainty evidence

Insecticide-treated nets: Humanitarian emergency setting (2022)

Insecticide-treated nets (ITNs) should be deployed for the prevention and control of malaria in children and adults in areas with ongoing malaria transmission affected by a humanitarian emergency.

Remark:
This recommendation is limited to classes of ITNs currently recommended by WHO. As with ITNs deployed in more stable settings, WHO recommends that ITNs that are prequalified by WHO be selected for use in humanitarian emergencies.

When considering deployment of ITNs in humanitarian emergencies, the infrastructure, access, logistical capacity and resources available must be taken into account, as these may influence the feasibility and cost of procuring and deploying nets.

Conditional recommendation for , Very low certainty evidence

Indoor residual spraying: Humanitarian emergency setting (2022)

IRS can be deployed for the prevention and control of malaria in children and adults in areas with ongoing malaria transmission affected by a humanitarian emergency.

Remark:
The conditionality of this recommendation is largely driven by the very low certainty of the evidence that IRS reduces malaria in such settings and due to concerns around feasibility and cost.

When deciding whether IRS may be appropriate for prevention and control of malaria in humanitarian emergency settings, programmes should consider:

- whether the structures are suitable for spraying. Some shelters provided in emergency settings may not be suitable for application of insecticides, such as open-sided structures and those built from materials that affect the residual nature of the insecticides;
- whether the target coverage of IRS can be feasibly achieved in the setting;
- whether there are sufficient resources to cover the relatively high costs associated with an IRS programme. In such settings, transport of commodities to hard-to-reach areas, coupled with the need to quickly procure items and establish human capacity to deliver the intervention, is likely to incur higher costs than when deploying IRS in more stable settings.

As with the deployment of IRS in more stable settings, WHO recommends that WHO-prequalified insecticides be selected for IRS use in humanitarian emergencies. It is important to ensure that the vector population is susceptible to the insecticide selected for spraying.

THANK YOU!

ANY QUESTIONS?