4.1.1. Interventions recommended for large-scale deployment

Clinical Question/ PICO

Population:	Adults and children living in areas with ongoing malaria transmission
Intervention:	Insecticide-treated nets or curtains
Comparator:	No nets

Summary

Summary of evidence from systematic review

Of the 23 included studies, 21 were cluster RCTs (six with households as the cluster and 15 with villages as the cluster) and two were individual RCTs; 12 studies compared ITNs with untreated nets, and 11 studies compared ITNs with no nets. Based on WHO regions, 12 studies were conducted in Africa (Burkina Faso, Cote d'Ivoire, Cameroon, Gambia (two studies), Ghana, Kenya (three studies), Madagascar, Sierra Leone, United Republic of Tanzania), six in the Americas (Colombia, Ecuador, Nicaragua (two studies), Peru and Venezuela) and four in South-East Asia (India, Myanmar, Thailand (two studies)) and one in the Eastern Mediterranean (Pakistan).

ITNs versus no ITNs:

ITNs reduce the rate of all-cause child mortality compared to no nets (Rate Ratio: 0.83; 95% CI (0.77–0.89); five studies; high

certainty evidence) ITNs reduce the rate of uncomplicated episodes of P. falciparum compared to no nets (Rate Ratio: 0.54; 95% CI (0.48-0.60); five studies; high certainty evidence) ITNs reduce the prevalence of P. falciparum infection compared to no nets (Rate Ratio: 0.69; 95% CI (0.54-0.89); five studies; high certainty evidence) ITNs may have little or no effect on the prevalence of P. vivax infection compared to no nets (Risk Ratio: 1.00; 95% CI (0.75-1.34); two studies; low certainty evidence) ITNs reduce the incidence rate of severe malaria episodes compared to no nets (Rate Ratio: 0.56; 95% CI (0.38-0.82); two studies; high certainty evidence)

Outcome Timeframe	Study results and measurements	Comparator No nets	Intervention Insecticide- treated nets or curtains	Certainty of the Evidence (Quality of evidence)	Plain language summary
All-cause mortality	Relative risk 0.83 (Cl 95% 0.77 — 0.89) Based on data from 129,714 patients in 5 studies. (Randomized controlled)	33 per 1000 Difference:	27 per 1000 6 fewer per 1000 (Cl 95% 8 fewer – 4 fewer)	High	ITNs or curtains reduce the child mortality from all causes.
P. falciparum uncomplicated episodes	Relative risk 0.54 (Cl 95% 0.48 — 0.6) Based on data from 32,699 patients in 5 studies. (Randomized controlled)	178 per 1000 Difference:	96 per 1000 82 fewer per 1000 (CI 95% 93 fewer – 71 fewer)	High	ITNs or curtains reduce the incidence of uncomplicated episodes of P falciparum malaria compared to no nets.
P. falciparum uncomplicated episodes (cumulative incidence)	Relative risk 0.44 (Cl 95% 0.31 — 0.62) Based on data from 10,964 patients in 2 studies. (Randomized controlled)	137 per 1000 Difference:	60 per 1000 77 fewer per 1000 (CI 95% 95 fewer – 52 fewer	Moderate Due to serious indirectness ¹	ITNs or curtains probably reduce the incidence of uncomplicated episodes of P falciparum malaria compared to no nets.

Outcome Timeframe	Study results and measurements	Comparator No nets	Intervention Insecticide- treated nets or curtains	Certainty of the Evidence (Quality of evidence)	Plain language summary
P. falciparum prevalence	Relative risk 0.69 (Cl 95% 0.54 — 0.89) Based on data from 17,860 patients in 5 studies. (Randomized controlled)	120 per 1000 Difference:) 83 per 1000 37 fewer per 1000 (CI 95% 55 fewer – 13 fewer)	High	ITNs or curtains reduce the prevalence of P falciparum malaria compared to no nets.
P. vivax uncomplicated episodes (cumulative incidence)	Relative risk 0.61 (Cl 95% 0.48 — 0.77) Based on data from 10,972 patients in 2 studies. (Randomized controlled)	149 per 1000 Difference:	91 per 1000 58 fewer per 1000 (CI 95% 77 fewer – 34 fewer)	Moderate Due to serious indirectness ²	ITNs or curtains probably reduce the incidence of uncomplicated episodes of P vivax malaria compared to no nets.
P. vivax prevalence	Relative risk 1 (Cl 95% 0.75 — 1.34) Based on data from 9,900 patients in 2 studies. (Randomized controlled)	130 per 1000 Difference:	130 per 1000 0 fewer per 1000 (CI 95% 32 fewer – 44 more)	Low Due to serious indirectness, Due to serious imprecision ³	ITNs or curtains may have little or no effect on the prevalence of P vivax malaria compared to no nets.
Any Plasmodium spp. uncomplicated episodes	Relative risk 0.5 (Cl 95% 0.28 – 0.9) Based on data from 5,512 patients in 1 studies. (Randomized controlled)	256 per 1000 Difference:	128 per 1000 128 fewer per 1000 (CI 95% 184 fewer – 26 fewer)	Low Due to very serious indirectness ⁴	ITNs or curtains may reduce the incidence of uncomplicated episodes of any Plasmodium species compared to no nets.
Severe malaria episodes	Relative risk 0.56 (CI 95% 0.38 — 0.82) Based on data from 31,173 patients in 2 studies. (Randomized controlled)	15 per 1000 Difference:	8 per 1000 7 fewer per 1000 (Cl 95% 9 fewer – 3 fewer)	High	ITNs or curtains reduce the incidence of severe malaria episodes compared to no nets.

1. Inconsistency: no serious. Indirectness: serious. Imprecision: no serious. Publication bias: no serious.

2. Inconsistency: no serious. Indirectness: serious. Imprecision: no serious. Publication bias: no serious.

3. Inconsistency: no serious. Indirectness: serious. Imprecision: serious. Publication bias: no serious.

4. Inconsistency: no serious. Indirectness: very serious. Imprecision: no serious. Publication bias: no serious.

References

44. Pryce J, Richardson M, Lengeler C : Insecticide-treated nets for preventing malaria. Cochrane Database of Systematic Reviews 2018;(11): Pubmed Journal Website

Clinical Question/ PICO

compared to untreated nets

(Rate Ratio: 0.67; 95% CI (0.36-1.23); two studies;

Population:	Adults and children living in areas with ongoing malaria transmission
Intervention:	Insecticide-treated nets or curtains
Comparator:	Untreated nets

Summary

Summary of evidence from systematic review	moderate certainty evidence)
Of the 23 included studies, 21 were cluster RCTs (six	ITNs reduce the rate of uncomplicated episodes of P.
with households as the cluster and 15 with villages as	falciparum compared to untreated nets
the cluster) and two were individual RCTs; 12 studies	(Rate Ratio: 0.58; 95% CI (0.43–0.79); five studies; high
compared ITNs with untreated nets, and 11 studies	certainty evidence)
compared ITNs with no nets. Based on WHO regions, 12	ITNs reduce the prevalence of <i>P. falciparum</i> compared to
studies were conducted in Africa (Burkina Faso, Cote	untreated nets
d'Ivoire, Cameroon, Gambia (two studies), Ghana, Kenya	(Risk Ratio: 0.81; 95% CI (0.68–0.97); four studies; high
(three studies), Madagascar, Sierra Leone, United	certainty evidence)
Republic of Tanzania), six in the Americas (Colombia,	ITNs may reduce the rate of uncomplicated episodes of
Ecuador, Nicaragua (two studies), Peru and Venezuela)	P. vivax compared to untreated nets
and four in South-East Asia (India, Myanmar, Thailand	(Rate Ratio: 0.73; 95% CI (0.51–1.05); three studies; low
(two studies)) and one in the Eastern Mediterranean	certainty evidence)
(Pakistan).	The effect of ITNs on the prevalence of <i>P. vivax</i> ,
	compared to untreated nets, is unknown
ITNs versus untreated nets:	(Risk Ratio: 0.52; 95% CI (0.13–2.04); two studies; very
ITNs probably reduce the rate of all-cause child mortality	low certainty evidence)
This probably reduce the rate of diffeause child mortality	IOW CEILAITLY EVICETICE

Outcome Timeframe	Study results and measurements	Comparator Untreated nets	Intervention Insecticide- treated nets or curtains	Certainty of the Evidence (Quality of evidence)	Plain language summary
All-cause mortality	Relative risk 0.67 (Cl 95% 0.36 — 1.23) Based on data from 32,721 patients in 2 studies. (Randomized controlled)	19 per 1000 Difference:	13 per 1000 6 fewer per 1000 (CI 95% 12 fewer – 4 more)	Moderate Due to serious imprecision ¹	ITNs or curtains probably reduce all-cause child mortality compared to untreated nets.
P. falciparum uncomplicated episodes	Relative risk 0.58 (CI 95% 0.43 — 0.79) Based on data from 2,084 patients in 5 studies. (Randomized controlled)	180 per 1000 Difference:	104 per 1000 76 fewer per 1000 (CI 95% 103 fewer – 38 fewer)	High	ITNs or curtains reduce the incidence of uncomplicated P falciparum malaria episodes compared to untreated nets.

Outcome Timeframe	Study results and measurements	Comparator Untreated nets	Intervention Insecticide- treated nets or curtains	Certainty of the Evidence (Quality of evidence)	Plain language summary
P. falciparum prevalence	Relative risk 0.81 (Cl 95% 0.68 — 0.97) Based on data from 300 patients in 4 studies. (Randomized controlled)	85 per 1000 Difference:	69 per 1000 16 fewer per 1000 (CI 95% 27 fewer – 3 fewer)	High	ITNs or curtains reduce the prevalence of P falciparum malaria compared to untreated nets.
P. vivax uncomplicated episodes	Relative risk 0.73 (Cl 95% 0.51 — 1.05) Based on data from 1,771 patients in 3 studies. (Randomized controlled)	143 per 1000 Difference:	104 per 1000 39 fewer per 1000 (CI 95% 70 fewer – 7 more)	Low Due to serious indirectness, Due to serious imprecision ²	ITNs or curtains may reduce the incidence of uncomplicated P vivax malaria episodes compared to untreated nets.
P. vivax uncomplicated episodes (cumulative incidence)	Relative risk 0.58 (CI 95% 0.3 — 1.14) Based on data from 17,910 patients in 3 studies. (Randomized controlled)	168 per 1000 Difference:	97 per 1000 71 fewer per <u>1000</u> (CI 95% 118 fewer – 23 more)	Low Due to serious imprecision, Due to serious inconsistency ³	ITNs or curtains may reduce the incidence of uncomplicated P vivax malaria episodes compared to untreated nets.
P. vivax prevalence	Relative risk 0.52 (Cl 95% 0.13 — 2.04) Based on data from 300 patients in 1 studies. (Randomized controlled)	85 per 1000 Difference:	44 per 1000 41 fewer per 1000 (CI 95% 74 fewer — 88 more)	Very low Due to very serious imprecision, Due to very serious indirectness ⁴	it is unclear if the proportion of people infected with P vivax parasites is any lower in those using an ITN than those using an untreated net.
Any Plasmodium spp. uncomplicated episodes (cumulative incidence)	Relative risk 0.47 (Cl 95% 0.17 — 1.28) Based on data from 7,082 patients in 2 studies. (Randomized controlled)	69 per 1000 Difference:	32 per 1000 37 fewer per 1000 (Cl 95% 57 fewer – 19 more)	Moderate Due to serious imprecision ⁵	ITNs or curtains probably reduce the incidence of uncomplicated malaria episodes of any species compared to untreated nets.
Any Plasmodium spp. prevalence	Relative risk 0.17 (Cl 95% 0.05 — 0.53) Based on data from 691 patients in 1 studies. (Randomized controlled)	104 per 1000 Difference:	18 per 1000 86 fewer per 1000 (CI 95% 99 fewer – 49 fewer)	Very low Due to serious imprecision, Due to very serious indirectness ⁶	It is unclear if ITNs reduce the prevalence of malaria, regardless of species, compared to untreated nets.

- 1. Imprecision: serious.
- 2. Indirectness: serious. Imprecision: serious.
- 3. Inconsistency: serious. Imprecision: serious.
- 4. Indirectness: very serious. Imprecision: very serious.
- 5. Imprecision: serious.
- 6. Indirectness: very serious. Imprecision: serious.

References

44. Pryce J, Richardson M, Lengeler C : Insecticide-treated nets for preventing malaria. Cochrane Database of Systematic Reviews 2018;(11): Pubmed Journal Website

Clinical Question/ PICO

Population:	Adults and children living in areas with ongoing malaria transmission
Intervention:	Pyrethroid-PBO nets
Comparator:	LLIN

Summary

Summary of evidence from systematic review Fifteen trials met the inclusion criteria: two laboratory trials, eight experimental hut trials, and five cluster-randomized controlled village trials. endpoint at 21 months post-intervention showed that malaria prevalence probably decreased in the intervention arm (OR 0.40, 95% CI 0.20 to 0.80; 1 trial, 1 comparison, moderate-certainty evidence).

One village trial examined the effect of pyrethroid-PBO Other trials report nets on malaria infection prevalence in an area with highly pyrethroid-resistant mosquitoes. The latest Other trials report of the trials report included here).

Other trials reported entomological outcomes (not included here).

Outcome Timeframe	Study results and measurements	Comparator LLIN	Intervention PBO	Certainty of the Evidence (Quality of evidence)	Plain language summary
Prevalence of malaria	Odds Ratio 0.4 (CI 95% 0.2 — 0.8) Based on data from 3,966 patients in 1 studies.	527 per 1000 Difference:	211 per 1000 316 fewer per 1000 (CI 95% 422 fewer – 105 fewer)	Moderate Due to serious indirectness ¹	Prevalence of malaria is probably decreased with pyrethroid-PBO nets compared to standard LLINs in areas of high insecticide resistance.

1. Indirectness: serious.

References

45. Gleave K, Lissenden N, Richardson M, Choi L, Ranson H : Piperonyl butoxide (PBO) combined with pyrethroids in insecticide-treated nets to prevent malaria in Africa. The Cochrane database of systematic reviews 2018;11 CD012776 Pubmed Journal

Clinical Question/ PICO

Population:	Adults and children living in areas with ongoing malaria transmission
Intervention:	IRS
Comparator:	no IRS

Summary

IRS versus no IRS in areas with unstable transmission: IRS may reduce malaria incidence compared to no IRS (Risk Ratio: 0.12; 95% CI (0.04–0.31); one study; low certainty evidence) IRS may reduce parasite prevalence compared to no IRS (Risk Ratio: 0.24; 95% CI (0.17–0.34); one study; low certainty evidence)

Outcome Timeframe	Study results and measurements	Comparator no IRS	Intervention IRS	Certainty of the Evidence (Quality of evidence)	Plain language summary
Incidence of malaria in children under 5 years in areas of intense malaria transmission	Relative risk 0.86 (Cl 95% 0.77 — 0.95) Based on data from 884 patients in 1 studies. (Randomized controlled)	650 per 1000 Difference:	560 per 1000 90 fewer per 1000 (CI 95% 150 fewer – 40 fewer)	Low Due to serious indirectness, Due to serious imprecision ¹	
Parasite prevalence in children under 5 years in areas of intense malaria transmission	Relative risk 0.94 (Cl 95% 0.82 — 1.08) Based on data from 452 patients in 1 studies. (Randomized controlled)	680 per 1000 Difference:	630 per 1000 50 fewer per 1000 (CI 95% 130 fewer – 50 more)	Low Due to serious indirectness, Due to serious imprecision ²	
Incidence of malaria in all ages in areas of unstable malaria	Relative risk 0.12 (Cl 95% 0.04 — 0.31) Based on data from 18,261 patients in 1 studies. (Randomized controlled)	50 per 1000 Difference:	10 per 1000 40 fewer per 1000 (CI 95% 50 fewer – 40 fewer)	Low Due to serious indirectness, Due to serious imprecision ³	
Parasite prevalence in children aged 5–15 years in areas of unstable malaria	Relative risk 0.24 (Cl 95% 0.17 — 0.34) Based on data from 2,359 patients in 1 studies. (Randomized controlled)	110 per 1000 Difference:	30 per 1000 80 fewer per 1000 (CI 95% 90 fewer – 70 fewer)	Low Due to serious indirectness, Due to serious imprecision ⁴	

- 1. Indirectness: serious. Imprecision: serious.
- 2. Indirectness: serious. Imprecision: serious.
- 3. Indirectness: serious. Imprecision: serious.
- 4. Indirectness: serious. Imprecision: serious.

Clinical Question/ PICO

Population:	Adults and children living in areas with ongoing malaria transmission
Intervention:	IRS
Comparator:	ITNs

Summary

IRS versus ITNs in areas with intense transmission: IRS may reduce malaria incidence compared to ITNs (Rate Ratio: 0.88; 95% CI (0.78–0.98); one study; low certainty evidence)

There may be little or no difference between IRS and ITNs in terms of parasite prevalence

(Risk Ratio: 1.06; 95% CI (0.91–1.22); one study; very low certainty evidence)

IRS versus ITNs in areas with unstable transmission: IRS may increase malaria incidence compared to ITNs (Rate Ratio: 1.48; 95% CI (1.37–1.60); one study; low

certainty evidence) IRS may increase parasite prevalence compared to ITNs (Risk Ratio: 1.70; 95% CI (1.18–2.44); one study; low certainty evidence)

Outcome Timeframe	Study results and measurements	Comparator ITNs	Intervention IRS	Certainty of the Evidence (Quality of evidence)	Plain language summary
Incidence of malaria in children under 5 years in areas of intense malaria transmission	Relative risk 0.88 (Cl 95% 0.78 — 0.98) Based on data from 818 patients in 1 studies. (Randomized controlled)	630 per 1000 Difference:	550 per 1000 80 fewer per 1000 (CI 95% 140 fewer - 10 fewer)	Low Due to serious indirectness, Due to serious imprecision ¹	
Parasite prevalence in children under 5 years in areas of intense malaria transmission	Relative risk 1.06 (Cl 95% 0.91 — 1.22) Based on data from 449 patients in 1 studies. (Randomized controlled)	600 per 1000 Difference:	640 per 1000 40 more per 1000 (CI 95% 50 fewer — 140 more)	Low Due to serious indirectness, Due to serious imprecision ²	
Incidence of malaria in all ages in areas of unstable malaria	Relative risk 1.48 (Cl 95% 1.37 – 1.6) Based on data from 88,100 patients in 1 studies. (Randomized controlled)	20 per 1000 Difference:	30 per 1000 10 more per 1000 (CI 95% 10 more – 20 more)	Low Due to serious imprecision, Due to serious indirectness ³	
Parasite prevalence in all ages in areas of unstable malaria	Relative risk 1.7 (Cl 95% 1.18 – 2.44) Based on data from 52,934 patients in 1 studies. (Randomized controlled)	0 per 1000 Difference:	0 per 1000 0 fewer per 1000 (Cl 95% 0 fewer – 0 fewer)	Low Due to serious indirectness, Due to serious imprecision ⁴	

1. Indirectness: serious. Imprecision: serious.

2. Indirectness: serious. Imprecision: serious.

- 3. Indirectness: serious. Imprecision: serious.
- 4. Indirectness: serious. Imprecision: serious.