World Health Organization

GLOBAL MALARIA PROGRAMME

# WHO guidance for countries on combining indoor residual spraying and long-lasting insecticidal nets

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## Summary


1. In settings where there is high coverage with long-lasting insecticidal nets (LLINs) and LLINs remain effective, indoor residual spraying (IRS) may have limited utility in reducing malaria morbidity and mortality. However, IRS may be implemented in areas where there are LLINs as part of an insecticide resistance management strategy.[1]

2. If LLINs and IRS are to be deployed together in the same geographical location, the IRS should use non-pyrethroid insecticides.

3. Malaria control and elimination programmes should prioritize delivering either LLINs or IRS at high coverage and to a high standard rather than introducing the second intervention as a means of compensating for deficiencies in the implementation of the first.

4. Evidence is needed to determine the effectiveness of combining IRS and LLIN in malaria transmission foci, including in low transmission settings. Evidence is also needed from different eco-epidemiological settings outside of Africa.

5. All programmes in any transmission setting that invest in the combined use of LLINs and IRS should include a rigorous programme of monitoring and evaluation (e.g. a stepped wedged introduction of the combination) to confirm whether the additional inputs have the desired impact. Countries that are already using both interventions should similarly undertake an evaluation of the effectiveness of combining versus either LLINs or IRS alone.


## Background

The reduction in disease burden of malaria in recent years has in large part been attributed to the massive scale up of the two main vector control interventions, LLINs and IRS, particularly in Africa south of the Sahara. A number of countries have deployed the two interventions in combination in an attempt to further reduce transmission.

The evidence for enhanced protection against malaria resulting from the combination of IRS and ITNs is currently not clear even though several trials and observational studies have attempted to answer this question. Cluster randomized trials, which provide the best evidence for the effectiveness of an intervention, have been conducted in Benin, Tanzania, The Gambia and Sudan. All but one (Benin) are currently unpublished. However, the results

[1] World Health Organization. *Global plan for insecticide resistance management in malaria vectors*. Geneva, 2012. http://www.who.int/malaria/publications/atoz/gpirm/en/

of the other three trials have been presented at international conferences, and detailed data of two of the unpublished trials have been accessible for the purpose of this technical review.

The Benin trial[2] showed no evidence of added protection from the combination of IRS and LLINs, compared to LLINs alone. However, this trial does not provide adequate guidance on this question since: (a) it had low statistical power with only seven clusters per study arm (compared to 25, 35 and 70 in the Tanzania, Gambia and Sudan trials, respectively); (b) its reference arm had ITNs for targeted groups only, instead of universal coverage; and (c) spraying was conducted at intervals considerably longer than the residual life of the insecticide used (bendiocarb). The trial in The Gambia (completed but unpublished) compared LLINs in combination with IRS using DDT versus LLINs alone, and showed no evidence that the IRS offered increased protection compared to the use of LLINs alone. The Sudan study ( ongoing) is being conducted in a setting of very low transmission; results to date show some additional protection in the combination arm, but the evidence for this is very weak (non-significant).

The Tanzania study[3] showed significant additional protection provided by the combined use of LLINs and IRS, but the generalizability of this result is complicated by the fact that LLIN usage was modest (between 53% and 36%). However, per protocol analysis of the trial data showed a large additional reduction in prevalence in the subgroup that used LLINs and also received IRS, compared to those who were protected by LLINs alone. Whether this additional benefit would have been seen if net use had been at universal coverage level, is unknown. Furthermore, available data suggest some level of resistance in local vector populations to the insecticide used on nets.

Overall, therefore, the trial evidence so far remains inconclusive. It should be noted that none of the trials were non-inferiority studies attempting to show equivalence of LLIN only versus LLIN plus IRS combined interventions. Observational studies have similarly given contradictory results. However, the benefit of adding LLINs to IRS has been consistently shown in Bioko over several years where the effective coverage of IRS was less than complete for the full transmission period.

Insecticide resistance is undoubtedly an additional factor that may determine whether the combined use of IRS and LLINs provides additional protection, but there are currently not enough data to determine the impact of resistance on the effectiveness of such combinations. In areas of high pyrethroid resistance it may be particularly beneficial to add IRS with non-pyrethroids to areas with high coverage of LLINs , to (a) provide protection against biting by pyrethroid-resistant mosquitoes, particularly when nets have already acquired holes, and (b) for resistance management purposes.

IRS may also have some utility in areas with low resistance as part of an overall resistance management strategy aimed at preserving the effectiveness of pyrethroids.

[2] Corbel V, Akogbeto M, Damien GB, Djenontin A, Chandre F, Rogier C, Moiroux N, Chabi J, Banganna B, Padonou GG, Henry MC. *Combination of malaria vector control interventions in pyrethroid resistance area in Benin: a cluster randomised controlled trial.* Lancet Infect Dis. 2012 Aug;12(8):617-26.

[3] West PA, Protopopoff N, Wright A, Kivaju Z, Tigererwa R, Mosha F, Kisinza W, Rowland M, Kleinschmidt I. *Indoor residual house spraying in combination with insecticide treated nets compared to insecticide treated nets alone for protection against malaria: Results of a cluster randomised trial in Tanzania.* PLOS Medicine. 2014. (*In Press*)

## Current evidence

1. Three trials have compared LLINs alone versus LLINs plus IRS with bendiocarb:
    - One showed significant added protection of the combination against malaria infection; this was in a setting of intermediate transmission intensity, high pyrethroid resistance and modest LLIN use.

    - Two showed no additional protection of the combination. One of these had low power and targeted LLIN coverage only, while the other was in a setting of very low transmission intensity but high LLIN coverage.

2. One large trial that compared LLINs alone versus LLINs plus IRS using DDT found no evidence of additional protection of the combination against malaria.

3. There is evidence from several non-randomized observational studies and from mathematical models that the combined use of LLINs and IRS offers added protection versus LLINs alone. Findings from observational studies may be subject to confounding, and those from models are clearly sensitive to the assumptions upon which the models are based.

4. A number of non-randomized observational studies have shown no added protection resulting from the combination of IRS and LLINs. Negative findings do not constitute proof of no effect, but may indicate that, if present, the effect is small.

5. At least three additional cluster randomized trials investigating the combined use of LLINs plus IRS versus one alone are in progress.

## Conclusions

1. In settings where there was high LLIN use and susceptibility of vectors to pyrethroids, there was no evidence that adding IRS would provide additional protection against malaria.

2. In settings of high pyrethroid resistance there is limited evidence that combining LLINs and IRS with bendiocarb may give added protection.

3. All studies that have investigated the question of added protection due to combined use of LLINs and IRS were performed in Africa. The above conclusions may therefore not be applicable in other regions.

## Further information

Vector Control Technical Expert Group. *Guidance for countries on combining IRS and LLINs*. Report to MPAC March 2014. [Withheld temporarily pending publication of West et al. (*In press*)].