Insecticide-impregnated bed nets for malaria control: a review of the field trials*

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Insecticide-impregnated bed nets act as a physical barrier to repel and kill mosquitos. Community intervention trials suggest that these nets are effective in preventing malaria-related mortality and morbidity—but not malaria infection—in areas of low and moderate transmission; the results from areas of high transmission are not so encouraging. Comparison of the results from these trials and their interpretation are difficult because of variations in the epidemiology of malaria and several methodological flaws. Problems such as defining appropriate health indicators, monitoring bed-net usage, introducing bed nets randomly, selecting adequate controls, performing statistical analysis, and comparing bed nets with other available interventions are considered. Further community intervention trials are needed, paying attention to the methods and to assessment of their impact on malaria.

Malaria is by far the most important insect-borne disease, 100 million persons being infected each year (*1*). Since most malaria-transmitting mosquitos bite indoors at night, insecticide-impregnated bed nets might provide useful protection. The assessment of community interventions which aim at malaria control is fraught with difficulties. Variations in the epidemiology of malaria and the use of diverse clinical and entomological measures make it difficult to compare and interpret the results. Consequently, the value of impregnated bed nets is still a matter of controversy (*2*). This review of field trials that assessed the potential of impregnated bed nets and curtains for malaria control summarizes their findings and highlights the methodological problems and areas where more research is needed.

Mode of action

Pyrethroid-impregnated bed nets and curtains reduce man–vector contact by acting as a physical barrier and by repelling mosquitos and driving them out of houses (*3, 4*). Impregnation improves the effectiveness of a torn bed net (*5*) and prevents mosquitos from feeding on a limb which may touch the bed net during the night (*6*). Community-wide distribution of impregnated bed nets, besides providing individual protection to the persons sleeping under them, can have a profound effect on the transmission of malaria ("mass effect") by killing mosquitos and thus reducing the mosquito population. Such a reduction in mosquito density, which has been seen in several studies (*7–11*), would benefit the entire community, even people who do not use nets.

Field trials

Results

The degree to which impregnated bed nets protect against malaria depends on local circumstances. The reduction in the number of infective bites is greater in areas where mosquitos bite indoors, late at night, and where they are not exclusively anthropophilic (*12*). These characteristics may be modified by the intervention; a significant trend towards outdoor biting, earlier in the evening, has been observed (*10, 11*) but the evidence is inconclusive. Entomological studies show that impregnated bed nets reduce man–vector contact and diminish mosquito populations. To assess if this is of any health benefit, their impact on malaria morbidity and mortality has been measured.

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In some studies (*13–15*) impregnated bed nets were distributed to some individuals, with others in the same community as controls. However, in most field trials impregnated nets (*7–9*, *16–19*) or curtains (*20*) were distributed to entire communities in order to include the "mass effect" in the assessment of their health impact. Table 1 summarizes the impact on malaria morbidity and mortality found in the latter series of trials. The Table includes those studies which provide enough information to evaluate the method.

The results showed consistent decline in the prevalence of malaria infection, but parasite density and malaria incidence were significantly reduced in most trials. These results suggest that the widespread impregnation of bed nets or curtains is more effective in reducing the number of 'heavy' infections that result in clinical episodes than in preventing infection. The only trial that measured malaria mortality showed that the protection was greater against malaria-related mortality than malaria morbidity (*17*). The reasons for this are not fully understood; it could be due to a reduction in the average sporozoite load from infective mosquitos (*8*) or to protection against super-infection, which would account for the severity of the episode in areas of high transmission. Further research is needed to clarify the relationship between sporozoite inoculum (size, number and frequency) and infection, disease, and mortality (*21*). In areas of high transmission, protection against clinical episodes and malaria death may be the best outcome since the harmful effects of malaria are reduced without affecting the acquisition of immunity to the disease (*22*).

Table 1: **Summary of the indicators that measured the health impact of impregnated nets in eight trials (*7–9, 16–20*) in which nets were distributed to entire communities**

Indicator	References of studies whose results were: Significant (P <0.05)	Not significant
Spleen rate	*8*	*20*
Prevalence of malaria infection	*19* [a], (*16* [a]) [b]	*7, 8, 18, 19* [a], *20*, (*16* [a])
Parasite density	*7, 20*, (*16* [a])	(*16* [a])
Incidence of clinical malaria	*7, 8, 16* [a], *20*, (*9*)	*18* [c]
Child mortality	*17*	

[a] Significant in some age groups or communities but not in others.
[b] References in parentheses indicate that significance tests were not done, the results showing a marked or no marked decline.
[c] Incidence of malaria infection.

Methodological problems

Randomized controlled trials are the standard way of evaluating new therapeutic agents and procedures at the individual level (*23*). Extending this method to interventions at community level is difficult, particularly when trying to measure the health impact of malaria control interventions. Several methodological flaws hamper the drawing of definite conclusions from the trials. There are discussed below.

(i) *Health indicators*. The most commonly used indicator of health impact is the incidence of clinical malaria. Neither the definition of a clinical attack of malaria nor methods of case detection are standardized. One trial (*8*) actively looked for people with fever (> 37.5 °C) and > 5000 parasites/ml, while another (*7*) used self-referred fever cases (> 38 °C) and > 10 000 parasites/ml. Given that in areas of holoendemic malaria healthy parasite carriers are common and that impregnated bed nets provide better protection against 'heavy' infections, differences between the results of some of the trials could partly be accounted for by the different way they looked for cases (*12*).

The use of child mortality as an indicator of health impact is most promising. However, it is confounded by the indirect effect of malaria on mortality and by competing causes of death. A study from Guyana (*24*) suggests that malaria has an indirect impact on mortality from acute and chronic respiratory diseases and on neonatal mortality (through the health of the mother). This fact can explain why the overall reduction in mortality found in Gambia (*17*) was greater than what could be expected from the prevention of deaths directly attributable to malaria. The Garki project illustrates the problem of competing risks. Before the intervention, *Plasmodium falciparum* was the immediate cause of many of the infant deaths, but the control of malaria prevented only a small number of deaths because of increase in mortality from other causes (*25*). This kind of competition limits the possibility of extrapolation from the short-term effects of intervention trials that aim at the removal of a single cause of death.

(ii) *Bed-net usage*. Distribution of bed nets or curtains does not guarantee that they will be used. Failure to record whether the bed nets were actually used (*7–9, 18, 20*) is remarkable; in fact, in one study (*18*) the lack of impact on malaria morbidity was attributed, in a follow-up study (*26*), to a failure to use the bed nets. Malaria is markedly seasonal and has an uneven age distribution, which most trials have taken into consideration; but none of them has taken into account that the use of bed nets and curtains may also be seasonal and age-dependent. Future trials must include this issue.

(iii) *Randomization*. The use of random allocation ensures that confounding factors are equally likely to be allocated to the intervention or comparison groups. Randomization is specially desirable when variables such as child mortality are being measured, as it is very difficult to control for all the possible confounders. In most studies (*7, 9, 16–20*) the intervention was not introduced randomly and they are thus liable to bias. However, the logistical difficulties of introducing community interventions on a random basis should not be overlooked.

A true double-blind trial is not a practical option: the reduction in insect nuisance is likely to be so substantial that neither the study population nor the field staff can remain unaware of which communities had the treated bed nets. However, the blood slides and questionnaires referring to cause of death should be coded before they are read, so as to reduce possible bias at this stage. None of the trials mention whether this was done.

(iv) *Controls*. Malaria transmission varies unpredictably from year to year and from village to village. Because of this annual variation the use of historical controls is inadequate and contemporary controls are required. In three trials (*9, 18, 20*), the baseline data gathered prior to the intervention were insufficient to establish the comparability of the control and intervention communities. In two of the trials (*8, 17*), baseline data showed the two groups to be different from the outset. It is doubtful whether these controls truly estimate what would occur in the intervention communities if impregnated bed nets had no impact—particularly as these nets had not been randomly allocated.

(v) *Sample size*. When assessing the potential of community-wide distribution of impregnated bed nets for malaria control, each individual or household is not an independent unit. The sampling unit is the community or village and analysis should be based on the differences between communities (*23*). Significance tests that assume independence between each person surveyed should not be used.[a] Several studies (*7, 9, 20*) compared one intervention community with one control community, thus drawing their conclusions from a one-to-one comparison. This is analogous to treating one person and using another as a control (*27*). The required sample size depends on the health impact that is measured, the desired power of the study, and the study period. For example, a two-year follow-up of about 40 communities of 1000 people would be required to have a 90% chance of detecting a reduction of 30% in child mortality. The required sample size can be reduced by matching communities with respect to baseline characteristics. Communities should be separated by at least one kilometre in order to have separate mosquito populations.

(vi) *Comparison with other available measures*. There have only been two field trials comparing DDT house-spraying with pyrethroid-impregnated bed nets (*16, 22*). Both suggest that bed nets are more effective than spraying, but more comparative studies are needed before spraying can be replaced by impregnated bed nets.

[a] **World Health Organization**. *The use of impregnated bednets and other materials for vector-borne disease control*. Unpublished document WHO/VBC/89.981, 1989.

Conclusions

Our object was not to criticize particular trials but to summarize their results and highlight the problems that challenge the assessment of the potential of insecticide–impregnated bed nets for malaria control. These problems are particularly important as they will also have to be confronted by malaria vaccine trials.

Impregnated bed nets provide good personal protection against malaria by reducing exposure to mosquitos. Their potential for malaria control depends on factors such as the level of transmission, mosquito characteristics, the immune-status and sleeping habits of the population, and financial constraints. Since these factors are area-specific, caution is necessary when extrapolating the results of one area to another. The evidence suggests that impregnated bed nets are effective in preventing malaria-related mortality and morbidity—but not malaria infection—in areas of low and moderate transmission; the results from areas of high endemicity are not so encouraging. Further trials are clearly needed and much attention needs to be given to the methods of community-intervention trials which aim to assess the malaria impact. Trials should include several communities, far enough apart to have separate mosquito populations. Intervention and control communities should be randomly selected and their comparability established prior to the intervention. The acceptability and actual use of the nets should be monitored systematically. The concepts of malaria infection, clinical malaria, and malaria-related death need to be clarified and their relation with sporozoite inoculum investigated.

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