## Insecticide-treated nets for malaria control: real gains

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Insecticide-treated nets (ITNs) have become an important tool in the prevention of malaria in highly endemic areas. At present, large-scale ITN programmes are being implemented in sub-Saharan Africa, Asia and Latin America using a number of operational approaches (1). However, if the targets of the Abuja Declaration, set in April 2000 at the African Summit on Roll Back Malaria, are to be reached, the scale of operations needs to be increased substantially.

No less than 81 trials and over 30 descriptive studies carried out in every type of malaria setting worldwide have documented the positive impact of ITNs on child and adult morbidity and mortality (2). In five randomized controlled trials (RCTs) an overall reduction in child mortality of 17% could be demonstrated, with six lives saved per year for every 1000 children protected. Recently, a reduction of 27% in child mortality could be demonstrated in a social marketing programme (3). Thus, the impact of ITNs seems overwhelming and public investments in ITN programmes fully justified. Does the evidence support this assumption?

From 1995 onwards, coinciding with the results from the main African ITN trials, a vigorous debate arose about the possibility that the short-term mortality improvements observed in trials of 1-2 years' duration could be offset by increased mortality at older ages — a "delayed mortality" effect (4, 5). The underlying hypothesis was that immunity to malaria would develop more slowly under reduced transmission, leading to a longer period of susceptibility. No direct evidence was available at the time either to support or to refute this hypothesis.

The careful follow-up work by Diallo et al. in Burkina Faso reported in this issue (6) provides high-quality evidence on this matter. Although the evidence does not arise from an RCT (which it would be unethical to conduct, as the authors point out), the in-depth analysis of their results provides a convincing case for the absence of a delayed mortality effect in their setting. Overall, there was a 19–24% reduction in child mortality, which was sustained over time. The probability of a child dying before its fifth birthday was reduced from 240 per 1000 to 170 per 1000, a gain of 29%. Few other child survival interventions are currently as effective. Further, no shift in the age pattern of mortality could be detected in children under five years of age.

Similar results for all ages, based on a 5.5-year follow-up, were published recently from a nearby area in Ghana (7). No evidence for a delayed mortality pattern was found there either, despite the fact that the intervention was not maintained systematically during the follow-up period. To a lesser extent the decreased use of treated nets (from over 70% initially to 43% after five years) also affected the intervention in Burkina Faso. Therefore, failing to maintain the intervention after the end of the trial did not lead to a mortality increase in children who spent their early childhood protected by an ITN. This is an important additional finding for large-scale ITN programmes, which will always struggle to maintain high levels of protection. Historically, a similar situation was found with indoor residual spraying programmes, with children protected from birth not experiencing increased mortality after cessation of control (8).

While the evidence from Burkina Faso and Ghana is already very valuable, at least two more follow-up studies are being conducted at the present time: one in Kenya as a continuation of an RCT (9) and one in the United Republic of Tanzania comparing cohorts of users and non-users of ITNs (3). Similar to the procedure for establishing the efficacy of a new intervention, multiple studies in different sites are required to disprove the hypothesis of a delayed mortality effect.

Looking back over the past decade, one can draw two conclusions. Firstly, the point made by the proponents of the delayed mortality hypothesis was important, following on from similar debates in the 1950s and 1960s. Fortunately, this debate gave rise to initiatives aimed at providing good evidence regardless of methodological difficulties. Secondly, the public health community did not wait for the outcome of such long-term studies to advocate the deployment of ITNs. Undoubtedly, thousands of young children owe their survival to action based on evidence of benefit in the face of hypothetical doubt of harm.

- RBM Technical Support Network for Insecticide-Treated Materials. Scaling up insecticide-treated netting programmes in Africa: a strategic framework for coordinated national action. Geneva: World Health Organization; 2002. Geneva, Switzerland; 2002. Available from: URL: http://www.rbm.who.int/ITNs.
- 2. Lengeler C. Insecticide-treated bednets and curtains for preventing malaria (Cochrane Review). Cochrane Database of Systematic Reviews; 2000.
- Armstrong Schellenberg JRM, Abdulla S, Nathan R, Mukasa O, Marchant TJ, Kikumbih N, et al. Effect of large-scale social marketing of insecticide-treated nets on child survival in rural Tanzania. *Lancet* 2001;357:1241-7.
- Snow RW, Marsh K. Will reducing *Plasmodium falciparum* transmission alter malaria mortality among African children? *Parasitology Today* 1995;11:188-90.
- Trape JF, Rogier C. Combating malaria morbidity and mortality by reducing transmission. *Parasitology Today* 1996;12:236-40.
- Diallo DA, Cousens SN, Cuzin-Ouattara N, Nebié I, Ilboudo-Sanogo E, Esposito F. Child mortality in a West African population protected with insecticide-treated curtains for a period of up to 6 years. *Bulletin of the World Health Organization* 2004;82: 85-91.
- Binka FN, Hodgson A, Adjuik M, Smith T. Mortality in a seven-and-a-half-year followup of a trial of insecticide-treated mosquito nets in Ghana. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 2002;96:597-9.
- Bradley DJ. Morbidity and mortality at Pare-Taveta, Kenya and Tanzania, 1954-66: the effects of a period of malaria control. In: Feachem RG, Jamison D, editors. *Disease and mortality in sub-Saharan Africa*. Oxford: Oxford University Press; 1991. p. 248-62.
- Phillips-Howard PA, Nahlen BL, Kolczak MS, Hightower AW, ter Kuile FO, Alaii JA, et al. Efficacy of permethrin-treated bed nets in the prevention of mortality in young children in an area of high perennial malaria transmission in western Kenya. *American Journal of Tropical Medicine and Hygiene* 2003;68:23-9.

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