TRANSACTIONS OF THE ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE (2000) 94, 357–360

Evidence for a mass community effect of insecticide-treated bednets on the incidence of malaria on the Kenyan coast

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Abstract

The use of insecticide-treated bednets (ITBNs) has been shown to be effective in reducing mortality and morbidity from malaria. However, there is mixed evidence as to whether or not community-wide use of ITBNs engenders a 'mass effect', such that those not sleeping under bednets are offered protection from widespread ITBN use in the area in which they live. We have analysed data collected in Kilifi, Kenya, from a cohort of children followed from birth to investigate how the degree of net usage in the locality of a child affects the risk of developing malaria. This effect was explored using a Cox proportional hazards model. For those not using ITBNs, we found that an increasing level of ITBN usage within the area surrounding each child was associated with a decreasing risk of developing malaria, thus providing evidence in support of a mass community effect. The size and significance of this effect were found to decrease as non-overlapping areas of increasing distance away from a child's home were considered. The effect was significant for areas at distances of up to 1·5 km away from each child.

Keywords: malaria, disease control, insecticide-treated bednets, permethrin, disease risk, children, community effect, Kenya

Introduction

The success of insecticide-treated bednets (ITBNs) in reducing mortality and morbidity from malaria has been well documented (ALONSO *et al.*, 1993; D'ALESSANDRO *et al.*, 1995; NEVILL *et al.*, 1996). However, whilst it is intuitively obvious that the use of ITBNs offers individual users protection, less clear is the impact of widespread ITBN use on the wider community of users and non-users of ITBNs. The extent to which ITBNs exert a 'mass effect', whereby the impact of ITBNs on the local vector population is such that the risk of developing malaria is also reduced for those living in the same community who are not sleeping under ITBNs, remains uncertain. The relative magnitudes of individual and mass community effects will have important implications for the design of community control strategies where optimal levels of coverage can be predicted.

The analysis presented here concerns a cohort of children living in the Kilifi District on the Kenyan coast, who were part of a randomized controlled trial of ITBNs (MBOGO *et al.*, 1996; NEVILL *et al.*, 1996; SNOW *et al.*, 1996, 1999). The main findings were reductions in the indoor resting densities of malaria vectors, but no change in the sporozoite rate or survival of the vectors; a 50% reduction in the force of infection; a >40% reduction in the number of admissions to hospital with a primary diagnosis of malaria or a definition of severe malaria; and a 33% reduction in mortality among children aged 6–59 months. In this paper we examine how the risk of developing malaria is influenced by the degree of net usage in the surrounding area for both ITBN users and non-ITBN users.

Materials and Methods

Study area and design

The study area selected for the present study represented a sub-population at Kilifi, on the Kenyan Coast, described in detail by NEVILL *et al.* (1996). This sub-area consisted of 4020 rural scattered households lying within 16 km of Kilifi District Hospital (KDH). In May 1992 a full census was undertaken and all resident individuals were assigned a unique identifying number. Children born into the study area between 1 May 1992 and 30 April 1995 were recruited as part of a long-term follow-up cohort study (R. W. Snow *et al.*, in press). Children remained in the cohort whilst they were living in their natal household and exited the cohort if they moved to another household > 0·5 km from their original home or died. Demographic surveillance was maintained by 6-weekly household visits and bi-annual re-enumerations throughout the study. In addition a linked system of hospital admission surveillance was maintained. Children from the cohort who were admitted to KDH were identified at admission and a primary diagnosis was made on the basis of detailed clinical and laboratory procedures (R. W. Snow *et al.*, in press).

In August 1993 half of the enumeration zones within the area of the controlled trial were randomly allocated to receive ITBNs (NEVILL *et al.*, 1996); the sub-set of the area considered here consisted of 21 zones designated as intervention zones and 21 zones designated as control zones. At this time, nets were issued to ensure coverage of every individual resident in the intervention zones. The nets were impregnated with 25% emulsifiable concentrate permethrin to achieve a concentration of 0·5 g permethrin/m^2 of netting and were re-impregnated every 6 months (SNOW *et al.*, 1999). For a variety of reasons, including absence at the time of net issue and refusal to accept a net, several children in these intervention zones were never issued with a net. This incomplete coverage provided an opportunity to assess the experiences of those who slept without ITBNs in areas of widespread ITBN usage. The zones which did not receive any intervention for 2 years served as contemporaneous controls.

Household geo-positions

Hand-drawn maps were developed for the entire area by walking transects of the study area and positioning households in association with major landmarks defined from ariel photographs. Subsequently latitude and longitude were determined for each household using a combination of at least 2 recordings from a hand-held global positioning system (GPS; SatNav®, Trimble Navigational Europe Ltd, UK). The GPS did not allow for a geo-stationary reference point and consequently had an element of error corresponding to ±30 m. A process of digitizing the hand-drawn maps and comparing with GPS positions was used to derive a more reliable longitude and latitude measurement for each household. The spatial data were used to produce digital maps of the study area using Mapinfo Professional version 6.0 (Mapinfo Corporation, Troy, New York, USA). In addition to the positioning of the households all of the roads, bus stages and health service providers, including

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KDH, within the area were also positioned. Access to the district hospital for most children is by bus. For each child in the cohort the nearest bus stage used by the family of the child to reach Kilifi town was recorded.

Statistical methods

Statistical analysis was carried out using S-Plus (version 3.4, 1996, Mathsoft Inc., Cambridge, MA, USA). The data analysed concern those children in the cohort who were at risk of a hospital admission with malaria between 1 August 1993 and 1 October 1995, after which time ITBNs were also issued to those resident in the control zones.

In order to assess the evidence for a mass effect, we defined a variable to reflect the level of net usage in the areas surrounding a child at risk. The area immediately surrounding a child was defined by a circle of a given radius centred on his/her household. Areas further away were defined as non-overlapping concentric rings. For each child in the cohort the level of net usage within an area was estimated by calculating the proportion of all households within a specified area that were selected to receive ITBNs. The exact proportion of net users within any area was not available since not all households in the study area contained children recruited into the cohort; for those living in the study area who were not involved in the cohort only allocation to receive ITBN was known. Defining the variable in this way captured the geographical realities that some children resident in control zones live 'closer' to intervention zones than others, and therefore live in an area of higher net usage than children living in the centre of control zones. The distance between households was calculated from the measurements of latitude, a_1 and a_2, and longitude, b_1 and b_2, of each household respectively, using the following formula:

$$\text{Distance (km)} = 111{\cdot}23 \times \cos^{-1}(\sin(a_1)\sin(a_2) + \cos(a_1)\cos(a_2)\cos(|b_1 - b_2|))$$

In an analysis of the geographical distribution of severe malaria in Kilifi District SCHELLENBERG *et al.* (1998) found that admission rates were significantly higher in children with easier access to the hospital, as measured by the distance they lived from the hospital. SNOW *et al.* (1994) found that children who had been admitted to hospital with a fatal condition tended to live nearer a bus stage than those who died at home. In order to control for these potentially confounding factors the distance from each household to KDH and the distance to the nearest bus stage used by the family were calculated using the above formula.

The proportion of intervention households was calculated within non-overlapping concentric rings of increasing distance from the centre, ranging from the proportion within 0·5 km (excluding the individual's own household) to the proportion 2·5–3 km away. The significance of this variable upon the risk of developing malaria was investigated using a Cox proportional hazards model. Survival time was taken to be the time between the beginning of the risk period (1 August 1993 or subsequent birth date) and the first hospital admission with a primary diagnosis of malaria. Observations were treated as censored if the child died, migrated or the end of observation was reached before an admission with malaria. Age at the beginning of the risk period was controlled for, as was the distance from KDH, and the distance from the nearest bus stage to the household. The analysis was carried out for all children together and separately for ITBN users and non-ITBN users.

Results

A total of 3853 children were at risk of a first admission with malaria for some or all of the period 1 August 1993–1 October 1995; 2048 children living in control zones were at risk during the study period. Of the 1805 'intervention' children at risk of hospitalization, 179 children were never issued with a bednet. This represents an overall coverage of 90·1% amongst the members of the cohort living in the intervention zones; within the separate intervention zones coverage amongst the cohort children ranged from 76·8% to 97·3%. The actual coverage during the randomized controlled trial for households in the intervention areas was 96% at the beginning of the trial and 80% in April 1995 (NEVILL *et al.*, 1996).

The Table shows the numbers of first malaria admissions amongst those using and not using ITBNs in the intervention zones and those in the control zones. Within the intervention zones, the proportion of malaria admissions (as a percentage of total children studied) did not differ significantly between ITBN users and non-ITBN users. However, the Table shows that the proportion of malaria admissions amongst children not using ITBNs in the intervention zones is significantly lower than the rate amongst children in the control zones ($\chi^2 = 3{\cdot}84$, d.f. = 1, $P = 0{\cdot}05$). This suggests that those not using ITBNs in areas of widespread use have a lower risk than those not using ITBNs in areas of no use.

The Cox proportional hazards analysis was firstly carried out for all children at risk in the cohort. The effect of the following variables was assessed in separate models: individual ITBN usage, proportion of net usage within 0·5 km (excluding the individual's own household), proportion between 0·5 and 1 km, proportion between 1 and 1·5 km, between 1·5 and 2 km, between 2 and 2·5 km and between 2·5 and 3 km. Within the circles of radius 1-km centred on each child the median number of households was 77 (interquartile range = 63–103). Figure (a) shows the odds ratios and 95% confidence intervals for each of the variables after controlling for the effects of both age and distance from KDH (the distance to the nearest bus stage was not found to be significantly associated with the risk of admission). The horizontal line corresponds to an odds ratio of 1. On the distance axis, a distance of zero corresponds to individual ITBN

Table. Children with first malaria admissions to Kilifi District Hospital (Kenya) amongst insecticide-treated bednet (ITBN) users and non-ITBN users in the intervention zones and those in the control zones in 1 August 1993–1 October 1995

Group	Number admitted with malaria	Total	% admitted with malaria (95% CI)
Intervention zones			
ITBN users	95	1626	5·84 (4·75–7·10)
Non-ITBN users	13	179	7·26 (3·92–12·10)
Control zones	257	2048	12·55 (11·14–14·06)

95% CI, 95% confidence interval.

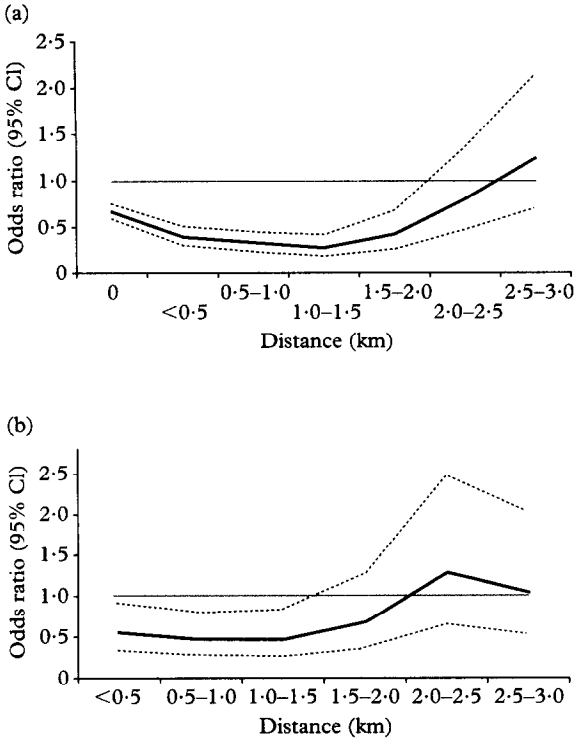

Figure. Odds ratio and 95% confidence interval (95% CI) for the variable representing the degree of net usage within areas of given distances away from the child against distance for (a) all children in the cohort and (b) non-ITBN users only. An odds ratio of significantly less than 1 implies that an increasing level of the variable is associated with a decreasing risk of developing malaria.

usage. For areas at distances of up to 1·5–2 km away, the Figure shows that the variable has a significant effect upon the risk of developing malaria. An odds ratio of significantly less than 1 implies that an increasing level of net use within the specified area is associated with a decreasing risk of developing malaria. The graph shows that the smallest odds ratio, corresponding to the largest effect, is for the level of net usage 1·0–1·5 km away from the child. The odds ratio for individual net usage is closer to 1 than the odds ratios within the next 3 areas of increasing distance away; this implies that the level of net usage within each of these areas has a greater effect on the risk of malaria than individual net usage.

To explore these associations further, the analysis was repeated for the sub-set of children not using ITBNs during the observation period. This group of children included all those resident in control zones, together with those resident in intervention zones, who, for whatever reason, were not sleeping under a bednet. This latter sub-set of children would in general have high values for the proportion of net usage in their surrounding area, whereas the values for those living in the control zones were in general much lower. Figure (b) shows how the odds ratio for the level of ITBN usage changed within areas of increasing distance from the child. The effects within the first 3 areas are very similar and, as the distance is further increased, the proportion of intervention households becomes less significant. Thus the level of net usage within areas <1·5 km away from the child has a significant effect on their risk of developing malaria.

Finally, the analysis was carried out for the group of children using ITBNs, all of whom were resident in intervention zones. For all the concentric areas considered, the effect of an increasing proportion of local net usage was to decrease the risk of developing malaria. The effect of the proportion between 2·0 and 2·5 km was of borderline significance, but for all other distances was not significant (data not shown). This suggests that for those protected individually by ITBN use, there is no significant additional benefit of widespread ITBN use in the surrounding area.

Discussion

We have explored possible effects of wide-scale ITBN use upon geographically defined risks of a hospital admission with malaria. The primary observation is that those without ITBNs, but living in intervention zones, have a lower risk of being hospitalized with malaria than those living in control zones. This is an encouraging result, since in theory the converse could be the case if vectors were diverted from those sleeping under ITBNs to their unprotected neighbours. This initial observation was explored in more detail using a Cox proportional hazards model which demonstrates that an increasing level of net usage in the areas immediately surrounding an index child's home is significantly associated with a decreased risk of developing malaria. Both results provide evidence in support of the notion that ITBNs do confer a mass effect in communities where they are used widely. The variable used to reflect the level of net usage within an area, the numbers of households selected to receive ITBNs, provides only an approximation to the true numbers of net users within that area. However, this measurement error will result in the observed effects being underestimates of the 'true' effects (PRENTICE, 1982) and in this sense the estimates obtained in this analysis are conservative.

When all children were considered together, it was interesting to note that the level of net usage within the immediate surrounding areas had a larger effect than that of individual net usage, as indicated by the size of the odds ratios [Figure (a)]. This result is consistent with the observations of the Table, which suggest that zone lived in is a better determinant of outcome than individual net use; there is a significant difference between control and intervention zones, but no significant difference between users and non-users within the same zone. This implies the level of net usage within the area surrounding a child at risk has a greater impact upon his/her risk of developing malaria than whether or not he/she is individually protected.

For those not using ITBNs, the risk of developing malaria is significantly decreased if there is widespread use in the area around them. As areas of increasing distance away from a non-user are considered, the proportion of intervention households within the area becomes less significant and is not significant for areas >1·5 km away. This result is not surprising, as any effect exerted on the local vector population would be expected to operate only over a certain range. For the sub-set of children who were sleeping under ITBNs throughout the study period, we observed no significant effect of the level of net usage upon the risk of developing malaria. However, the direction of the observed effect was the same as for the non-users, in that an increasing proportion was associated with a decreasing risk.

The results found here are supported by the results of parasitological surveys carried out among infants during the trial (SNOW *et al.*, 1999). The *Plasmodium falciparum* infection rates were very similar amongst children sleeping under treated nets (12%) in communities of high usage and children not sleeping under nets (15%) living in the same communities. However, the infection rate amongst children not using nets in control areas was much higher (25%). Furthermore, MBOGO *et al.* (1996) observed that houses in non-intervention areas that were closest to the intervention area had fewer malaria vectors compared to those further away.

Nevertheless, entomological studies on the effect of ITBNs on local vector populations have produced mixed results leading to some confusion over the relative

contribution of individual versus mass-effects of ITBN use. In an area of Tanzania, MAGESA *et al.* (1991) found that the introduction of impregnated bednets into a village reduced the sporozoite inoculation rates into people not sleeping under nets by over 90%. In other studies, suppression of the local vector population (JANA-KARA *et al.*, 1995) and reduction in vector-biting densities (ROBERT & CARNEVALE, 1991; KERE *et al.*, 1993) have been found. However, these results conflict with those from studies in the Gambia (LINDSAY *et al.*, 1993; QUINONES *et al.*, 1998), where the effects of treated and untreated bednets were compared. These results suggested that the protection offered from treated bednets is primarily on a personal level, rather than due to a mass killing effect on the local vector population.

In light of the conflicting evidence from entomological studies, the added health gains afforded by community ITBN use on non-users is encouraging. These public health impacts are in concert with results from a randomized controlled trial of bednets in rural northern Ghana (BINKA *et al.*, 1998). That study demonstrated that for children not using treated bednets, there was a significant increase in mortality as distance from the nearest compound where bednets were in use increased.

Currently, delivery approaches for ITBNs in Africa, especially those using commercial or social marketing, are likely to provide protection for those in a community who can afford this intervention. It is perhaps of some comfort for those of us concerned about equitable access to health care that less-advantaged members of a community may also benefit from their more-advantaged neighbours.

Acknowledgements

This investigation received financial support from the Wellcome Trust, the UNDP/World Bank/WHO Special Programme for Research and Training and the Kenya Medical Research Institute (KEMRI). We thank all the clinical staff of the KEMRI Unit at Kilifi who made this study possible especially Victor Mung'ala Odera, Kevin Marsh and Norbert Peshu. S.C.H. thanks the Medical Research Council for Studentship funding. C.A.D. thanks the Wellcome Trust for research funding. R.W.S. is supported by the Wellcome Trust as part of a Senior Research Fellowship in Basic Biomedical Science (033340). This paper is published with the permission of the Director of KEMRI.

References

Alonso, P. L., Lindsay, S. W., Armstrong Schellenberg, J. R. M., Keita, K., Gomez, P., Shenton, F. C., Hill, A. G., David, P. H., Fegan, G., Cham, K. & Greenwood, B. M. (1993). A malaria control trial using insecticide-treated bed nets and targeted chemoprophylaxis in a rural area of The Gambia, West Africa. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **87**, 37–44.

Binka, F. N., Indome, F. & Smith, T. (1998). Impact of spatial distribution of permethrin-impregnated bed nets on child mortality in rural northern Ghana. *American Journal of Tropical Medicine and Hygiene*, **59**, 80–85.

D'Alessandro, U., Olaleye, B. O., McGuire, W., Langerock, P., Bennett, S., Aikins, M. K., Thomson, M. C., Cham, M. K., Cham, B. A. & Greenwood, B. M. (1995). Mortality and morbidity from malaria in Gambian children after introduction of an impregnated bednet programme. *Lancet*, **345**, 479–483.

Jana-Kara, B. R., Jihullah, W. A., Shahi, B., Dev, V., Curtis, C. F. & Sharma, V. P. (1995). Deltamethrin impregnated bednets against *Anopheles minimus* transmitted malaria in Assam, India. *Journal of Tropical Medicine and Hygiene*, **98**, 73–83.

Kere, N. K., Parkinson, A. D. & Samrawickerema, W. A. (1993). The effect of permethrin impregnated bednets on the incidence of *Plasmodium falciparum* in children of north Guadalcanal, Solomon Islands. *Southeast Asian Journal of Tropical Medicine and Public Health*, **24**, 130–137.

Lindsay, S. W., Alonso, P. L., Armstrong Schellenberg, J. R. M., Hemingway, J., Adiamah, J. H., Shenton, F. C., Jawara, M. & Greenwood, B. M. (1993). A malaria control trial using insecticide-treated bed nets and targeted chemoprophylaxis in a rural area of The Gambia, West Africa. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **87**, 45–51.

Magesa, S. M., Wilkes, T. J., Mnzava, A. E. P., Njunwa, K. J., Myamba, J., Kivuyo, M. D. P., Hill, N., Lines, J. D. & Curtis, C. F. (1991). Trial of pyrethroid impregnated bednets in an area of Tanzania holoendemic for malaria. *Acta Tropica*, **49**, 97–108.

Mbogo, C. N. M., Baya, N. M., Ofulla, A. V. O., Githure, J. I. & Snow, R. W. (1996). The impact of permethrin-impregnated bednets on malaria vectors of the Kenyan coast. *Medical and Veterinary Epidemiology*, **10**, 251–259.

Nevill, C. G., Some, E. S., Mung'ala, V. O., Mutemi, W., New, L., Marsh, K., Lengeler, C. & Snow, R. W. (1996). Insecticide-treated bednets reduce mortality and severe morbidity from malaria among children on the Kenyan coast. *Tropical Medicine and International Health*, **1**, 139–146.

Prentice, R. L. (1982). Covariate measurement errors and parameter estimation in a failure time regression model. *Biometrika*, **69**, 331–342.

Quinones, M. L., Lines, J., Thomson, M. C., Jawara, M. & Greenwood, B. M. (1998). Permethrin-treated bed nets do not have a 'mass-killing effect' on village populations of *Anopheles gambiae s.l.* in The Gambia. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **92**, 373–378.

Robert, V. & Carnevale, P. (1991). Influence of deltamethrin treatment of bed nets on malaria transmission in the Kou valley, Burkina Faso. *Bulletin of the World Health Organization*, **69**, 735–740.

Schellenberg, J. A., Newell, J. N., Snow, R. W., Mung'ala, V., Marsh, K., Smith, P. G. & Hayes, R. J. (1998). An analysis of the geographical distribution of severe malaria in children in Kilifi District, Kenya. *International Journal of Epidemiology*, **27**, 323–329.

Snow, R. W., Armstrong Schellenberg, J. R. M., Forster, D., Mung'ala, V. O. & Marsh, K. (1994). Factors influencing admission to hospital during terminal childhood illnesses in Kenya. *International Journal of Epidemiology*, **23**, 1013–1019.

Snow, R. W., Molyneux, C. S., Warn, P. A., Omumbo, J., Nevill, C. G., Gupta, S. & Marsh, K. (1996). Infant parasite rates and immunoglobulin M seroprevalence as a measure of exposure to *Plasmodium falciparum* during a randomised controlled trial of insecticide-treated bed nets on the Kenyan Coast. *American Journal of Tropical Medicine and Hygiene*, **55**, 144–149.

Snow, R. W., McCabe, E., Mbogo, C. N. M., Molyneux, C. S., Some, E. S., Mung'ala, V. O. & Nevill, C. G. (1999). The effect of delivery mechanisms on the uptake of bed net re-impregnation in Kilifi District, Kenya. *Health Policy and Planning*, **14**, 18–25.

Snow, R. W., Howard, S. C., Mung'ala-Odera, V., English, M., Molyneux, C. S., Waruiru, C., Mwangi, I., Roberts, D. J., Donnelly, C. A. & Marsh, K. (in press). Paediatric survival and re-admission risks following hospitalisation on the Kenyan Coast. *Tropical Medicine and International Health.*

Received 17 December 1999; revised 27 January 2000; accepted for publication 3 February 2000