REDUCTION OF CHILDHOOD MALARIA BY SOCIAL MARKETING OF INSECTICIDE-TREATED NETS: A CASE-CONTROL STUDY OF EFFECTIVENESS IN MALAWI

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Abstract. Use of an insecticide-treated net (ITN) is now the central focus for the Roll Back Malaria campaign, and disease-endemic countries have embarked on large-scale ITN distribution programs. We assessed the impact of an ITN social marketing program on clinical malaria in children less than five years of age. A case-control study was undertaken at Ndirande Health Center in the peri-urban area of the city of Blantyre, Malawi. Cases were defined by an axillary temperature ≥ 37.5°C or a history of fever within the last 48 hours and a positive blood smear for Plasmodium falciparum. The individual effectiveness of ITN use was 40% (95% confidence interval [CI] = 10–60%) when cases were compared with clinic controls and 30% (95% CI = 0–60%) in comparison with community controls. With ITN coverage of 42%, the community effectiveness of this program was estimated to range from 17% to 21%. This represents 1,480 malaria cases averted by the intervention in a population of 15,000 children. Our results show that the benefits of ITN social marketing programs in reducing malaria are enormous. Targeting the poor could increase those benefits.

INTRODUCTION

The efficacy of insecticide-treated nets (ITNs) has been conclusively demonstrated, and the focus in ITN research has shifted to estimating effectiveness under program conditions. Because the impact of ITN programs depends on coverage, the low ITN coverage achieved so far in program settings and the emerging insecticide resistances mean that the effectiveness of ITN programs should be monitored continuously in different epidemiologic settings.

However, the evaluation of ITN program impact is complicated by the need to identify appropriate control groups. Randomized ITN trials are no longer acceptable because they are considered unethical. Lengeler and Snow have argued for the use of case-control studies in evaluating the impact of ITN programs, with non-users serving as a comparison group. Such studies can be quickly undertaken, are relatively inexpensive, and avoid many of the ethical issues inherent in longitudinal and randomized studies. Using this approach, the community effectiveness (CE) of ITN programs, defined as the impact of ITN programs on malaria morbidity and mortality rates in the community, can be estimated.

To date, there have been very few case-control studies published that have evaluated the community effectiveness of ITN programs in Africa and Asia.

In Malawi, ITNs are distributed through a social marketing program, where the public contributes to the cost of the program by paying for subsidized nets and insecticides. In this report, we present results from a prospective clinic-based case-control study conducted in Blantyre, Malawi to evaluate the impact of an ITN social marketing program on clinical malaria in children less than five years old.

METHODS

Study setting. The investigation was conducted at the Ndirande Health Center in the peri-urban area of the city of Blantyre, Malawi. This government-run clinic is the only health unit offering free pediatric services and routine diagnostic procedures in the town. Approximately 30% of all children seen at the clinic are treated for malaria (Mkandala C, unpublished data).

Malaria transmission occurs year round in Blantyre, peaking during the rainy season, typically from November through May. Malaria control is based on prompt diagnosis and treatment of cases and on use of ITNs. Since 1998, ITNs have been distributed in Blantyre through a social marketing program administered by Population Services International. Two types of nets (blue and green) and net re-treatment insecticide are distributed through private shops and clinics. The blue conical net is available to all through the commercial sector, while the rectangular green nets are available at health clinics for pregnant women or mothers with children less than five years of age. At the time of our study, the consumer prices were approximately US $6.00 for the blue net, US $2.00 for the green nets, and US $0.20 for the insecticide re-treatment kit.

Study design. Study participants were recruited between January 2002 and May 2002. Informed consent was obtained from parents or caregivers of each study child before data collection began. The Institutional Review Boards of the University of Michigan, the University of Malawi, and the Centers for Disease Control and Prevention reviewed and approved the entire protocol.

The study was designed as a prospective case-control study based in a single clinic in which controls were matched to cases for age (± 6 months), sex, and location. To be eligible, cases and controls had to be less than five years old and living in the study area at the time of recruitment. For each case, one clinic control was selected from the clinic and another control from the community, both within 14 days of identifying the case. Cases were defined as children who had an axillary temperature ≥ 37.5°C or a history of fever within the last 48 hours and a positive blood smear (any parasitemia) for Plasmodium falciparum. Clinic controls were defined as children who came to the same clinic with an illness that was not malaria and had a negative blood smear. Children with diarrhea and acute respiratory infections were excluded from be-
ing either cases or controls because previous studies have shown the relationship between these conditions and malaria illness.9,10

Community controls were randomly selected by escorting malaria cases to their homes, after which a random direction was chosen by spinning a marked ball. The fifth household in the chosen direction was selected. Subsequent households were approached if necessary, until a matching control was found. Community controls were defined as children with a negative blood smear and an axillary temperature < 37.5°C who had not been ill within the last two weeks.

Blood samples from participants were tested for hemoglobin concentration (HemoCue, Angelholm, Sweden) and for malaria parasites. Giemsa-stained thick blood smears were examined for malaria parasites. Parasite density was calculated by counting the number of asexual parasites per 200 white blood cells, assuming a white blood cell count of 8,000/μL of blood. Slides were considered negative if no parasites were found after examining 100 high-power fields.

One of us (DPM) conducted structured interviews with the caregivers during which information on the subjects, socioeconomic status (SES) of the household, parent or caregiver’s knowledge of malaria, health-seeking behavior (availability and use of anti-malarial drugs), mosquito avoidance behavior, travel histories, and ITN use was recorded on a pre-coded standard questionnaire. Use of a net was verified by asking to see that it was present in the house.

Definitions. Use of an ITN was defined as owning and using an ITN. Children using an untreated net or no net were considered non-users of ITNs. Similarly, children that lived in households that owned ITNs but were not using them were classified as non-users. Socioeconomic status was based on household material possessions. Scores were derived for each household based on the presence (scored 1) or absence (scored 0) of the following items: radio, bed, mattress, cycle, refrigerator, telephone, and car. An index of SES was created to classify households as either poor (<3 household possessions) or less poor (>3 household possessions). Knowledge of malaria was evaluated by asking the open-ended question: what are the signs and symptoms of severe malaria? Based on the number of correct answers, each respondent’s knowledge was classified as either poor (no correct answer) or not poor (one or more correct answers).

Community effectiveness has been used to estimate percent reduction in overall morbidity rates in the community as a result of the ITN social marketing program. This CE allows us to estimate the impact of an intervention in the community.5

Statistical analysis and methods. Separate analyses were undertaken comparing cases of malaria with clinic controls and with community controls. Both matched univariate and multivariate analyses were carried out using SAS System for Windows version 6.12 (SAS, Inc., Cary, NC). Only factors that were significant at univariate analysis were included in a matched multivariate analysis using conditional logistic regression. Differences in means were compared using the Student’s t-test and differences in proportions were analyzed using the chi-square test. Odds ratios (ORs), adjusted odds ratios, and 95% confidence intervals (CIs) were calculated in some analyses. For all statistical tests, a P value < 0.05 was considered significant. Protective effectiveness was calculated as (1 - OR) × 100. Community effectiveness, the product of individual effectiveness and ITN coverage in the area,5 was also estimated.

RESULTS

Study population. A total of 246 cases of malaria were identified and successfully matched both to a clinic control and a community control. Of these controls, 6 from the clinic and 13 from the community were subsequently excluded from the analysis because they lacked complete data on ITN use. These few excluded controls were not significantly different from the others in mean age or household characteristics.

Children in the clinic who were asked to participate as controls were being treated for conditions including otitis media (36%), abdominal problems (20%), injuries (13%), scabies (11%), unidentified rash (5%) and other conditions. Cases and both control groups were mostly from poor families, with more than 80% living in simple houses with tin roofs and mud walls. Less than half of the households of both cases and controls had electricity and less than 40% of the household heads were formally employed. The average age for cases was 26.7 months (95% CI = 25.0, 28.3), similar to that for clinic controls (27.1 months; 95% CI = 25.5, 28.8) and community controls (26.8 months; 95% CI = 25.0, 28.6). The mean hemoglobin concentration was significantly lower among cases (8.0 g/dL) than among both clinic controls (9.8 g/dL; P < 0.0001) and community controls (10.1 g/dL; P < 0.0001).

Predictors of clinical malaria. Children with malaria came from households with various exposures that were less often observed among either of the two control groups (Table 1). In matched multivariate analyses comparing cases to clinic controls, important risk factors included poor knowledge of malaria symptoms or signs (OR = 1.8, 95% CI = 1.2, 2.7), recently staying in a rural area (OR = 5.8, 95% CI = 2.3, 14.6), and use of a mosquito repellent (OR = 2.2, 95% CI = 1.4, 3.5), which were all associated with increased risk of malaria. Conversely, the use of ITNs significantly reduced the risk of malaria (OR = 0.6, 95% CI = 0.4, 0.9). In our analysis of cases and clinic controls, other factors such as mother’s education, living in households with electricity, and keeping anti-malarials at home were not significant predictors of malaria illness.

When cases were compared with community controls, use of ITNs (OR = 0.5, 95% CI = 0.3, 0.8) was again a significant protective factor against clinical malaria. As with the other analysis, recently staying in a rural area (OR = 6.6, 95% CI = 2.5, 17.6) and poor knowledge of symptoms of malaria (OR = 1.7, 95% CI = 1.1, 2.5) increased the risk of clinical disease. Again, education of the mother and having electricity in the house were not significant predictors of malaria illness.

The individual effectiveness of ITN use was estimated to be 40% (95% CI = 10–60%) when cases were compared with clinic controls, and similarly was 50% (95% CI = 0–60%) in comparison with community controls. Using results from a different cross-sectional survey previously undertaken in the study area9 that showed ITN coverage of 42% among 1,852 children who responded, we estimate the CE of this program to range from 17% to 21%. This represents approximately 1,480 malaria cases averted over one transmission season in a population of 15,000 children less than five years of age.
DISCUSSION

This clinic-based, case-control study represents the first evaluation of the effectiveness of socially-marketed ITNs in preventing malaria in Malawi, and is one of very few impact reports6,7 of an ongoing program. Our results show that this ITN program dramatically reduced the incidence of clinical malaria, with individual effectiveness estimated to have cut risk by approximately half. The individual effectiveness observed in this study is similar to that found in another case-control evaluation of an ITN social marketing program in Afghanistan, where efficacy was estimated to be 69% (95% CI = 53–79%).7 Overall, the CE produced roughly one-fifth fewer malaria cases, and this did not consider possible indirect effects from ITN users on diminished transmission to non-ITN users due to reduced mosquito survival and decreased infection prevalence.2,11 If 100% coverage were achieved, we estimate that disease episodes could be reduced by at least half. These estimates, even with the relatively low net coverage of 42%, suggest that the benefits of ITN social marketing programs in reducing disease burden in the community are significant.

The risk of clinical malaria increased with poor knowledge of malaria signs and symptoms. Although all caregivers responded that they believed malaria to be transmitted by mosquito bites, more than half of the cases’ parents or caregivers did not know one or more signs or symptoms of severe malaria, compared with approximately one-third of clinic control and community control parents or caregivers. This finding could have important policy implications for ITN programs. Other studies have shown that effective malaria prevention and use of clinical services depends on people’s ability to recognize the nature and severity of malaria illness.12,13 Given the low ITN coverage throughout much of sub-Saharan Africa,3 extensive health education programs on signs or symptoms of malaria and of the benefits of ITN use could lead to increased acceptance and use of these prevention methods.

Our study showed that children who had slept in a rural area anytime during the two weeks prior to questioning were six times more likely to have clinical malaria than children who did not. Although there is evidence suggesting that there is more malaria transmission in urban areas than previously thought,14 increasing bidirectional urban-rural movement of people is likely to result in cases being seen in urban areas that were acquired during rural exposures. Although our results suggest that only 14% of cases were associated with urban-rural travel, other studies in different cities are needed to estimate the burden of urban malaria that can be attributed to such population movement. The implications of population movement on urban ITN programs are likely to be considerable. If most malaria infections in urban areas are imported from rural areas, then ITN programs in urban areas may be rendered ineffective should short-term travelers not use nets in their journeys into rural areas. Social marketing programs should then emphasize the importance of daily use of ITNs even for short-term visits to rural areas. Other preventive measures, such as malaria chemoprophylaxis, should also be considered for the urban-rural traveler to prevent infection and development of severe disease.

Our finding that use of synthetic mosquito repellents (mosquito coils) was associated with increased risk of malaria illness is curious, and contradicts earlier studies demonstrating that mosquito repellents were effective in malaria prevention.15 We are unsure why cases were more likely to have reported using mosquito repellents than controls, except if they perceived a greater need to do so. Perhaps this was due to the fact that cases and clinic controls were interviewed after knowing their diagnosis, thus allowing cases to emphasize their use of mosquito repellents, trying to show that the illness was not their fault. It is also possible that cases could have been coming from areas in Ndirande where mosquito density and biting was more intense, and the community responded by using more repellents. Unfortunately, we were unable to collect information on spatial distribution of the malaria cases that would be required to address this assumption.

Although case-control studies are acceptable in program evaluation, results should be interpreted cautiously given the pitfalls associated with this approach. Case-control studies present more opportunities for selection bias and mistaken inference than longitudinal studies. For example, in this study, the selection of community controls that had no history of recent illness and had no malaria parasites could have had the effect of inflating the true malaria case-community control odds ratio. Abdulla and others8 also found that in using a clinic based case-control study to evaluate an ITN program, children with ITNs were more likely to go to the clinic than those without ITNs, resulting in more observations on a selected group of individuals. Although this may be important in comparing cases with community controls, it may not be as much of a concern when clinic controls are involved because...
they should be subject to similar selection factors. Our results clearly show that ITNs were equally effective when cases were compared with both clinic and community controls, suggesting that attendance bias did not influence our estimates.

Problems of selection bias could also emerge between cases and clinic controls if some of the clinic controls had had malaria but had been treated with anti-malarials before attending clinic, and if the rate of pre-treatment with anti-malarials differed between ITN users and non-users. In this study, the frequency with which pre-treatment with anti-malarials among children attending the clinic was reported was not different between net users and non-users (8.5% versus 7.8%; P = 0.75), suggesting that this source of selection bias was not likely. Another source of selection bias in this study might be differences in SES between users and non-users. However, because wealth, as measured by the education of the caretaker and number of household items, was not associated with the risk of clinical malaria, the risk for this potential selection bias seems minimal.

Although this ITN social marketing program has resulted in a modest increase of ITN coverage in urban Malawi, use has remained very low in rural areas where transmission is high. Our results demonstrate that increased coverage would result in reduced morbidity, and that targeting vulnerable groups such as children, pregnant women, and the poor could increase the impact of ITN programs. These programs would in turn save many lives, assuming that children that survive malaria do not die of other illnesses.

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