PERMETHRIN-TREATED BED NETS IN THE PREVENTION OF MALARIA AND ANEMIA IN ADOLESCENT SCHOOLGIRLS IN WESTERN KENYA

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Abstract. The impact of insecticide (permethrin)-treated bed nets (ITNs) on the health of adolescent schoolgirls was investigated during a community-based, randomized, controlled trial of ITNs in western Kenya. Two school-based cross-sectional surveys were conducted to determine the prevalence of malaria and anemia in 644 schoolgirls 12–18 years old in a rural area with intense perennial malaria transmission. In 12- and 13-year-old schoolgirls, ITNs were associated with a reduced prevalence of all cause anemia (hemoglobin level <12 g/dL, 16.9% versus 31.4%, adjusted odds ratio [OR] = 0.38, 95% confidence interval [CI] = 0.21, 0.69%) and a 0.34 g/dL (95% CI = 0.02, 0.66) increase in mean hemoglobin concentrations. No beneficial effect on all-cause anemia (adjusted OR = 0.79, 95% CI = 0.43, 1.45) or hemoglobin concentrations (difference in mean = 0.14 g/dL, 95% CI = -0.24, 0.53) was evident in older girls. In all age groups, no effect was found on malaria parasite prevalence or density, clinical malaria, all-cause morbidity, standard measures of nutritional status and growth, or the use of antimalarials and other medications. ITNs approximately halved the prevalence of mild anemia in young, school-attending, non-pregnant, adolescent girls, but had no impact in older girls or on other malaria-associated morbidity or nutritional status.

INTRODUCTION

Several large-scale trials have shown that insecticide (permethrin)-treated bed nets (ITNs) reduce all-cause morbidity and mortality in children less than five years of age in areas of sub-Saharan Africa with high or low, but seasonal malaria transmission. More recently, trials in areas of intense perennial transmission have been completed in western Kenya and Tanzania, and demonstrate similar beneficial impacts. The ITN trials have predominantly focused on pre-school children and pregnant women, the two main risk groups for severe disease caused by malaria in sub-Saharan Africa. However, the impact of ITNs on the health of adolescents, particularly in areas of intense and perennial malaria transmission, remains unknown.

In holoendemic malarious areas, such as our study site in western Kenya, immunity against clinical malaria is acquired during the first few years of life. School-age children are at a markedly reduced risk of the adverse consequences of malaria because most children who survive their pre-school years have acquired sufficient immunity to prevent severe disease associated with Plasmodium falciparum infection. Earlier studies in this age group have indicated that, on average, up to 60% of young adolescents may be parasitemic at any time. A recent study in adolescent males in western Kenya suggests that further development of anti-parasite immunity against malaria occurs during puberty. This implies that apart from accumulated recognition of parasite variants through childhood, host development during puberty, possibly mediated by adrenal-hormones, is required to attain adult levels of immunity against malaria. Despite incomplete development of the immune system, the majority of infections in adolescents is controlled and associated with low parasite densities only, does not result in fever, and is thus likely to remain undetected and untreated. Such low-density infections, however, have been associated with an increased risk of severe anemia in children less than two years of age in western Kenya. It is not known if chronic low-density infection among older children and adolescents results in similar hematologic consequences, or if malaria in this age group is truly mostly asymptomatic. Potential hematologic adverse effects are particularly relevant for the health of adolescent girls, where pre-pregnancy hemoglobin levels may be a major determinant of the risk of anemia related morbidity and mortality during possible later teenage pregnancy. Chronic anemia, especially when associated with concomitant micro-nutrient deficiencies, may also affect the adolescent’s physical performance, growth, as well as school performance and attendance, although there is little evidence that chronic malaria-induced anemia in the absence of iron deficiency leads to decreased productivity and performance.

We conducted a study to determine the prevalence of and risk factors for anemia, malaria, and malnutrition in adolescent schoolgirls. Although this study was not originally designed to determine the impact of ITNs, it was conducted in the same geographic location as a concurrent population-based study to determine the impact of ITNs on mortality and morbidity in children less than five years of age. We took the opportunity to assess whether ITNs would have any significant effect on clinical parameters in adolescent schoolgirls, particularly anemia. Evaluation of the magnitude and risk factors associated with anemia in this age group will be presented elsewhere.

MATERIALS AND METHODS

Study site and population. This study was conducted at the ITN trial site in Rarieda Division (Asembo) in Bondo District, located on the shores of Lake Victoria in Nyanza Province in western Kenya. The study site and the resident population have been described in detail elsewhere. Briefly, approximately 55,000 people live in Asembo in an area covering 200 km². The population is widely dispersed. They are culturally homogeneous, predominantly Luo subsistence farmers who practice some animal husbandry. Generally, the rainfall pattern is bimodal, with a long rainy season between March and May, and a short rainy season from October to December. Malaria is holoendemic and since some rain falls
in each month, transmission occurs throughout the year. More than 90% of malarial infections are due to *P. falciparum*, infection with *P. malariae* making up most of the balance, along with an occasional *P. ovale* infection. The number of infective bites per person varies substantially at the household level, but is calculated as a crude yearly average to range between 60 and 300 per year. Anopheles gambiae and An. funestus are responsible for more than 90% of the transmission, with the remainder transmitted by An. arabiensis. The ITNs have been shown to reduce transmission by up to 90%. High-grade chloroquine resistance is widespread in the area.

There are 58 primary schools in Asembo. Primary school starts at the age of five years and teaches children for a total of eight years (standard 1 to standard 8). Tuition is charged each trimester and parents decide when their child will start school. Until recently, some parents have waited for their child to reach the age of seven before sending them to school. If children fail exams or misses schooling, for example when unable to pay tuition, they may repeat years, with the result that some children may remain in primary school up to the age of 18. Girls may drop out of school because of pregnancy or if they become orphaned. A concurrent prospective school-based study of younger children from the same area saw a larger number of girls than boys lost to follow-up in the course of two years, suggesting that girls are more likely to drop out of school.

**Bed net trial.** Details of the randomized controlled trial of ITNs are presented elsewhere. Bed nets (Siamdutch Mosquito Netting Co., Bangkok, Thailand) pre-impregnated with the target dose of 0.5g of permethrin/m² of netting were randomly distributed to half the villages in Asembo during the fourth quarter of 1996. The ITNs were re-treated twice annually. The trial was implemented from January 1997 to March 1999. An ITN coverage rate of 1.46 persons per ITN was achieved, with an overall compliance (persons observed to be sleeping under ITNs) of 72%. Residents in the control villages received ITNs in April 1999.

**Study design.** The school-based study used a multi-stage random sample design, with primary schools as the first stage unit and schoolgirls as the second stage unit. Prior to randomization, information on the number and size of schools in the study area was obtained from the district education authority and entered into a computerized database. Information on the longitude and latitude of each school was added to the database using mapping data obtained using global positioning system (GPS) hardware and a geographic information system (ATLAS-GIS). Schools were selected by random sampling proportional to size ranked by geographic location to allow for equal distribution of the schools over the study area. Schools with less than 30 girls in the relevant age category were joined with the closest neighboring school to form one school unit. In each school unit, 30 girls 12−18 years of age were then randomly selected using the computerized list. A total of 840 girls in 28 schools were selected.

**Data collection.** Two cross-sectional surveys were performed at the 28 selected schools at the end of the two-year ITN trial; 14 schools in October–November 1998 and 14 schools in February–March 1999. At each survey, participants were interviewed by a female study nurse to document age, date of birth, school standard, village of residence, and reported ITN use. Participants were asked about their recent medical history, including febrile and non-febrile illnesses in the previous month, menstrual history, and any recent medication. The study nurse performed a clinical examination on all participants to measure height, weight, and axillary temperature. Sexual development was also assessed, using a modified Tanner score based on breast development only. Anthropometric measurements were performed according to standard procedures of the World Health Organization. Weight was measured to the nearest 0.1 kg on a battery-powered digital scale (Seca, Inc., Columbia, MD). Heights were measured to the nearest 0.1 cm using a wooden length-measuring board with sliding head. All measurements were taken in duplicate and the mean computed. Z-scores for height-for-age were calculated using Epi-Info2000 (Centers for Disease Control and Prevention, Atlanta, GA). The 1977/1985 U.S.-based National Centers for Health Statistics/World Health Organization reference data were used.

A finger prick blood sample was drawn into heparinized capillary tubes (250−500 μL) for hematology and parasitology. Hemoglobin concentrations were measured in the field using a portable battery-powered photometer (HemoCue AB, Angelholm, Sweden). A full blood count, including repeat hemoglobin, was determined the same afternoon using a Coulter Counter (Coulter, Hialeah, FL). The hemoglobin concentrations assessed by Coulter Counter were used in this analysis, but if a hemoglobin result was missing (n = 7 of 650), it was replaced with the HemoCue reading. Blood slides were stained with Giemsa and examined for the presence of malaria parasites at a magnification of ×1,000. Parasites and leukocytes were counted in the same fields until 300 leukocytes were counted. Parasite densities were estimated using an assumed leukocyte count of 8,000/mm³ of blood. Slides were considered negative if no asexual parasites were found in 200 high-power ocular fields of the thick blood smear.

Study participants were asked to bring fresh (<24 hours old) stool and urine samples to be examined for the presence of geohelminths (hookworm, *Ascaris lumbricoides*, *Trichuris trichiura*, and *Strongyloides stercoralis*) and *Schistosoma mansoni*. Samples were stored at 4°C and processed within 24 hours after collection. Stool was microscopically examined by concentration, using a modification of the formol-ether and acetate techniques, and by Kato-Katz methods. Urine was examined using a filtration-based concentration method.

Participants found to be anemic (hemoglobin level < 12 g/dL) during survey at their school were given iron supplementation. Those having a documented fever (axillary temperature ≥ 37.5°C) were given presumptive treatment with sulfadoxine-pyrimethamine (SP), antibiotics, or both, as indicated. Intestinal helminth infections and schistosomiasis were treated with albendazole and praziquantel, respectively.

**Definitions.** Adolescence was defined as an age of 12−18 years. Girls with a hemoglobin level less than 12 g/dL and 7 g/dL were considered to have anemia and severe anemia, respectively. Malaria was defined as the presence of asexual blood stage parasites in the blood smear (any species). Clinical malaria was defined as a positive malaria smear with a concurrent axillary temperature ≥ 37.5°C. Body mass index (BMI)-for-age (measure of thinness) and height-for-age (measure of stunting) were used to measure nutritional status. The BMI was calculated as weight (kilograms) divided by height (meters) squared, and thinness was defined as a
BMI below the fifth percentile for age. Stunting was defined as height-for-age Z-score less than -2 standard deviations from the mean of a reference population. Age was calculated from date of birth as reported, and when possible, date of birth was checked with school records. If the exact day of birth was unknown (in 41% of the participants), the 15th day of the month was used. If month of birth was unknown (in 28%), the midpoint of the year of birth was used.

Statistical analysis. Analysis was done using the SAS system for Windows, version 8.01 (SAS, Inc., Cary, NC) and Epi-Info 2000 (Centers for Disease Control and Prevention, Atlanta, GA) SUDAAN software (SAS callable version; Research Triangle Institute, Research Triangle Park, NC) was used to allow for correlation among observations taken from the same village (cluster-unit). Use of village as the cluster unit, as opposed to school, was based on the assumption that participants coming from one village were more alike concerning risk factors of the main end points (malaria, anemia, and malnutrition) than those attending the same school since malaria is more likely to be acquired at the villages after sunset than during school hours. In addition, randomization of the exposure variable of interest (ITNs) was based on village cluster. To maintain the assumption of an equal probability sample, weighting was used to adjust for unequal cluster size resulting from variation in the number of absentees or refusals between clusters.

Differences in proportions between ITN and control groups were compared with the Cochran-Mantel-Haenszel chi-square test (Table 1). Multivariate logistic and linear regression were used to estimate the effect of ITN use on various laboratory and clinical end points using the backward elimination approach to assess interaction and confounding.

The presented means for hemoglobin concentrations, parasite density, and height-for-age Z-score are adjusted for the co-variates using linear regression (Table 2).

Analysis suggested potential effect modification by age of the impact of ITNs on anemia ($P$ value of interaction term = 0.07). Results of the effect of ITNs are given stratified by age (age × ITN interaction term in the model with two age categories: 12 and 13 years old and ≥14 years old), as well as pooled for all study participants (main effect model without the interaction term).

The analysis of ITN efficacy was based on the intent-to-treat principle; groups are compared based on randomization status (reported village of residence) rather than reported bed net use. Two-sided $P$ values < 0.05 were considered statistically significant.

Ethical clearance and informed consent. The ITN project was reviewed and approved by the institutional review boards of the Kenya Medical Research Institute (Nairobi, Kenya) and the Centers for Disease Control and Prevention (Atlanta, GA). The study of the prevalence and risk factors of anemia in adolescent schoolgirls was approved by the institutional review boards of the Kenya Medical Research Institute and the Academic Medical Center, University of Amsterdam (Amsterdam, The Netherlands). Written consent was obtained from the individual student and her parents.

### RESULTS

Of 840 schoolgirls randomized, 669 (79.6%) were enrolled (321 in survey 1 and 348 in survey 2). The remainder had either moved out of the study area or was not present at survey ($n = 55$) or consent was not obtained ($n = 116$). Of the 669 girls present, 25 were excluded from the analysis: 21 because further analysis using date of birth revealed they were younger than 12 years old (despite their reported age), three because they had a history of recent blood transfusions (two from ITN villages and one from a control village), and one because the village of residence (randomization status) was unknown. Age and sexual development of the 644 participants were comparable by randomization status, except that more girls from control villages had started menstruating.

### Table 1

Characteristics of the study population overall and stratified by age and randomization group

<table>
<thead>
<tr>
<th>Age groups</th>
<th>ITN† Control ITN Control ITN Control</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>12–13 years</td>
<td>163</td>
<td>131</td>
</tr>
<tr>
<td>14–18 years</td>
<td>55</td>
<td>44</td>
</tr>
<tr>
<td>Overall</td>
<td>218</td>
<td>175</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Maturity level; no. (%)</th>
<th>ITN† Control ITN Control ITN Control</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modified tanner breast stage</td>
<td>50 (30.3)</td>
<td>44 (34.6)</td>
</tr>
<tr>
<td>B1</td>
<td>50 (32.1)</td>
<td>40 (30.8)</td>
</tr>
<tr>
<td>B2</td>
<td>51 (30.8)</td>
<td>34 (25.4)</td>
</tr>
<tr>
<td>B3</td>
<td>7 (4.0)</td>
<td>9 (7.0)</td>
</tr>
<tr>
<td>B4</td>
<td>5 (2.8)</td>
<td>3 (2.2)</td>
</tr>
<tr>
<td>B5</td>
<td>9 (5.5)</td>
<td>11 (8.4)</td>
</tr>
<tr>
<td>Normal</td>
<td>0</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Menstruation; no. (%)</td>
<td>25 (15.0)</td>
<td>55 (51.2)</td>
</tr>
<tr>
<td>Scabies, no. (%)</td>
<td>19 (13.2)</td>
<td>16 (15.0)</td>
</tr>
<tr>
<td>Schistosoma mansoni, no. (%)</td>
<td>25 (18.3)</td>
<td>11 (10.3)</td>
</tr>
<tr>
<td>Trichuris trichiura, no. (%)</td>
<td>30 (21.5)</td>
<td>22 (21.0)</td>
</tr>
<tr>
<td>Ascaris lumbricoides, no. (%)</td>
<td>32 (22.1)</td>
<td>31 (27.6)</td>
</tr>
<tr>
<td>Strongyloides stercoralis, no. (%)</td>
<td>1 (0.7)</td>
<td>0</td>
</tr>
<tr>
<td>Schistosoma haematobium, no. (%)</td>
<td>1 (0.7)</td>
<td>0</td>
</tr>
</tbody>
</table>

* Significantly different ($P < 0.05$).
† ITN = insecticide-treated bed net group.
There was no difference in the number of girls reporting heavy menstruation ($P=0.771$). Of 339 participants from ITN villages, 49 (14.6%) reported not using an ITN, while 31 (9.7%) of 305 participants from control villages reported sleeping in a house having an ITN. All of the latter ITNS were reported to be study bed nets (identifiable by the green color) supplied by the ITN project to intervention villages. Unlike the study nets in intervention villages, bed nets in control villages were not retreated routinely with insecticide by the study staff.

Positive blood smears for malaria were detected in 27.8% of all girls. The prevalence was lower in 12–13-year-old girls from ITN villages than in girls from control villages, but this difference was not statistically significant. There was no difference in older girls (Figure 1). The geometric mean (95% confidence interval [CI]) parasite density was 209/mm$^3$ (150–290/mm$^3$), with no difference between ITN and control groups overall or between the two age strata (Table 2). The prevalence of high-density parasitemia and clinical malaria were also similar (Table 3).

Overall, 21.1% of the girls were anemic (hemoglobin level < 12 g/dL). Only one girl (from an ITN village) had severe anemia (hemoglobin level < 7 g/dL). Girls in ITN villages were less likely to be anemic than girls in control villages, but this difference was not statistically significant. There was no difference in older girls (Figure 1). The geometric mean (95% confidence interval [CI]) parasite density was 209/mm$^3$ (150–290/mm$^3$), with no difference between ITN and control groups overall or between the two age strata (Table 2). The prevalence of high-density parasitemia and clinical malaria were also similar (Table 3).

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A high proportion (64.4%) of the study participants reported illness in the month prior to survey (Table 3). Among

![Figure 1. Effect of insecticide-treated bed nets (ITNs) on the prevalence of malaria parasitemia (upper graph) and anemia (lower graph) in adolescent schoolgirls in Kenya. Dark bars represent control villages and light bars represent ITN villages. Text boxes contain the odds ratios (95% confidence intervals [CIs]) adjusted for age, cross-sectional survey, menstruation, helminth infections, and use of antimalarials (upper graph) or for age, cross-sectional survey, menstruation, helminth infections, and use of antimalarials (lower graph). Hb = hemoglobin.](image-url)

| Table 2: Effect of insecticide-treated bed nets on hemoglobin (Hb) concentration, malaria parasite densities, and height for age Z-scores using linear regression, by age group |

<table>
<thead>
<tr>
<th>Randomization group</th>
<th>ITN</th>
<th>Control</th>
<th>Mean difference (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb in g/dL, mean (95% CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All ages</td>
<td>12.98 (12.67, 13.30)</td>
<td>12.85 (12.57, 13.13)</td>
<td>0.23 (−0.06, 0.52)</td>
</tr>
<tr>
<td>12–13 years</td>
<td>13.00 (12.67, 13.33)</td>
<td>12.74 (12.42, 13.06)</td>
<td>0.26 (−0.09, 0.52)</td>
</tr>
<tr>
<td>14–18 years</td>
<td>12.97 (12.59, 13.35)</td>
<td>12.93 (12.62, 13.24)</td>
<td>0.04 (−0.24, 0.32)</td>
</tr>
<tr>
<td>Parasitemia/mm$^3$‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All ages</td>
<td>211 (144, 308)</td>
<td>206 (120, 354)</td>
<td>5 (−95, 189)</td>
</tr>
<tr>
<td>12–13 years</td>
<td>257 (159, 416)</td>
<td>215 (111, 416)</td>
<td>42 (−99, 352)</td>
</tr>
<tr>
<td>14–18 years</td>
<td>176 (104, 302)</td>
<td>200 (110, 361)</td>
<td>22 (−117, 180)</td>
</tr>
<tr>
<td>Height-for-age Z-score, mean (95% CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All ages</td>
<td>−0.77 (−0.89, −0.66)</td>
<td>−0.65 (−0.78, −0.52)</td>
<td>−0.07 (−0.23, 0.09)</td>
</tr>
<tr>
<td>12–13 years</td>
<td>−1.06 (−1.22, −0.91)</td>
<td>−1.10 (−1.30, −0.89)</td>
<td>0.06 (−0.20, 0.32)</td>
</tr>
<tr>
<td>14–18 years</td>
<td>−0.50 (−0.69, −0.31)</td>
<td>−0.30 (−0.41, −0.20)</td>
<td>−0.20 (−0.41, 0.01)</td>
</tr>
</tbody>
</table>

† Mean difference adjusted for age, cross-sectional survey, menstruation, helminth infections, and malaria medication use.
‡ Parasitemic cases included only.
ITN = insecticide-treated bed nets.
them, headache was the most frequently mentioned symptom (84%), followed by abdominal pain (31%), fever/chills (13%), and cough (12%). Medication was reportedly used by 71.4% of the participants in the preceding month. Antimalarials were used by almost one-third of the girls (30.3%), of whom 186 (94.8%) used chloroquine, five (2.5%) used SP alone, four (1.9%) used a combination of chloroquine with SP, one (0.4%) used amodiaquine and one (0.4%) used quinine. Use of iron and folic acid supplementation was rare, with just 5.3% and 1.1% of participants reporting their use, respectively. Reported recent illness, fever, use of traditional or conventional medication, and use of antimalarials in the previous month were equally likely in control and intervention villages (Table 3).

Analysis taking school clustering into account rather than village clustering, or analysis based on reported ITN use rather than intention to treat, did not alter the conclusions.

### DISCUSSION

In this study we explored the effect of ITNs on malaria-associated outcomes in adolescent schoolgirls, as part of a large, community-based, group-randomized, controlled trial.
of ITNs in an area of intense perennial malaria transmission in western Kenya. To our knowledge, this is the first study describing the impact of ITNs in adolescent girls in sub-Saharan Africa. One previous study, which compared the efficacy of ITNs with placebo-treated bed nets in two age groups was conducted in Irian-Jaya, which has hyperendemic malaria. A significant reduction in infection rates and densities of *P. falciparum* was found in children more than 10 years old and adults that used treated bed nets.35

In the current study, we observed a reduction in the prevalence of mild all-cause anemia (hemoglobin level < 12 g/dL) from 31% to 17% in schoolgirls 12–13 years of age. This was associated with a 0.34 g/dL higher mean hemoglobin concentration in girls living in ITN villages. Similarly, the prevalence of mild anemia associated with concurrent parasitemia was reduced from 12% to 3%. This improvement in hematologic status in the 12–13-year-old girls from ITN villages implies that malaria is still a substantial contributor to anemia in these young adolescents and that the ITN intervention can provide hematologic benefit to this age group.

There was no evidence of a beneficial effect on anemia in older adolescent girls 14–18 years old. This provides further observational support for the hypothesis that maximal expression of resistance to infection and morbidity occurs later in adolescence and may depend on age, a proxy for cumulative exposure, and also on host pubertal development independent of age.10

In all of our study adolescents, regardless of age, ITNs did not appear to affect malaria prevalence, parasite density, all-cause morbidity, nutritional parameters, or the use of health care or antimalarial medication. Other malaria intervention studies in sub-Saharan Africa have shown a relationship between malaria and under-nutrition in young children, and in our study site, ITNs resulted in improved weight gain in children less than three years old and improved weight and height gain in infants. A contemporary malaria intervention cohort study in primary school children 5–12 years old conducted in our same study area showed no improvement in nutritional status. However, young adolescent girls experience the highest growth velocity after infancy, and it is plausible that frequent malaria infection could have a negative impact on such growth. We observed no evidence that ITN use resulted in improved linear growth or BMI scores in any of the adolescent girls, including those 12–13 year old.

A considerable proportion of women in developing countries will have their first pregnancy during adolescence, and young primigravidae are at particular risk of the adverse consequences of malaria-associated morbidity, such as severe maternal anemia and low birth weight. The observed improvements in hemoglobin concentrations with the ITN intervention in young adolescents are likely to have important functional benefits for those who might become pregnant. Conversely, while it is well understood that early teenage pregnancies, in which girls have not reached their full growth potential, have been associated with an increased risk of obstructed labor due to cephalo-pelvic disproportion and its associated increased risk of peripartum maternal mortality, our study suggests that antimalarial interventions provided only in adolescents may not alter this scenario.

Several design-related limitations should be considered when interpreting the results of our study. A caveat associated with generalization of these findings concerns the school-based design. No attempt was made to identify adolescents either absent from school on the day of survey (e.g., due to illness) or to evaluate the effect in children who do not attend school at all. Girls may drop out of school if they become orphaned or because of teenage pregnancy. The selected study sample is thus likely to be biased towards healthier girls, possibly with higher socioeconomic status, potentially resulting in an underestimate of the proportion of girls with clinical malaria and more severe anemia. It is also noted that the effect observed in the current study was due to a combination of individual barrier protection by ITNs, and a general reduction in malaria transmission consequent to the observed area-wide community or mass effect of insecticide-treated ITNs on vector populations and sporozoite rates. It is likely that the area-wide reductions in the malaria-transmitting mosquito populations, which benefited at least 23% of the control population in this area, will have resulted in an underestimate of the impact of ITNs. Third, both the ITN trial and this school-based study were group-randomized trials (cluster randomization), which because of the limited number of assignment units, have a greater potential for bias than studies which use randomization by individual. Furthermore, the study in adolescent schoolgirls was conducted in preparation for a nutritional intervention study, independently, but simultaneously with the ITN trial. It was not designed originally to determine the impact of ITNs, hence the lack of a baseline survey to determine if the study groups were comparable before the introduction of ITNs.

Should prevention and intervention programs directed at adolescent health in malarious areas include ITN distribution efforts focused on this population? Our study suggests that the prevention of malaria by ITNs would halve the prevalence of mild anemia in young, school-attending, non-pregnant adolescent girls in this area and in similar areas with intense malaria. However, it also suggests that in older girls little direct health benefits can be expected from school-based ITN programs and would not justify diverting resources from other essential preventive health activities. Conversely, targeting school-age children may have indirect benefits to the community, and may be a practical means to increase ITN coverage and contribute to any area-wide reductions in malaria transmission. Furthermore, our analyses presented elsewhere in this supplement show that the prevention of malaria by ITNs during pregnancy and infancy have a marked beneficial impact on maternal health, birth outcome and subsequent infant survival. However, teenage pregnant girls and their newborns are the least likely to be ITN users. Thus, the additional public health value of such school-based ITN programs could be their potential to reach and educate teenage girls on the benefits of ITNs before they become pregnant and drop out of school. The potential direct and indirect benefits of distributing ITNs through schools, along with other intervention programs for adolescent girls, deserve further study.

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