# IMPACT OF PERMETHRIN-TREATED BED NETS ON GROWTH, NUTRITIONAL STATUS, AND BODY COMPOSITION OF PRIMARY SCHOOL CHILDREN IN WESTERN KENYA

JENNIFER F. FRIEDMAN, PENELOPE A. PHILLIPS-HOWARD, WILLIAM A. HAWLEY, DIANNE J. TERLOUW,
MARGARETTE S. KOLCZAK, MARLENE BARBER, NORMAN OKELLO, JOHN M. VULULE,
CHRISTOPHER DUGGAN, BERNARD L. NAHLEN, AND FEIKO O. TER KUILE

*Division of Parasitic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia;
Centre for Vector Biology and Control Research, Kenya Medical Research Institute, Kisumu, Kenya; Division of Gastroenterology
and Nutrition, Boston Children's Hospital, Boston, Massachusetts; Department of Infectious Diseases, Tropical Medicine and AIDS,
Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands; Roll Back Malaria, World Health Organization,
Geneva, Switzerland*

*Abstract.*    Insecticide-treated bed nets (ITNs) have been demonstrated to reduce morbidity and mortality in children less than five years of age. They have also been shown to improve the nutritional status of these children, but little is known about their impact on the nutritional status of school-age children. We evaluated the impact of ITNs on growth, nutritional status, and body composition of primary schoolchildren less than 13 years of age living in an area of intense perennial malaria transmission in western Kenya. The ITNs did not have a significant impact on linear growth or summary measures of protein-energy malnutrition in this age group. This lack of efficacy most likely relates to the reduced burden of malaria in this age group in a setting of stable transmission pressure. Use of ITNs was associated with a change in body composition with an increase in percent lean body mass (1.2%; $P = 0.04$). This may be consequent to reduced exposure to malaria with subsequent reduced elaboration of pro-inflammatory cytokines known to promote muscle wasting.

## INTRODUCTION

The clinical spectrum of *Plasmodium falciparum* infection is wide, ranging from asymptomatic parasitemia to death, secondary to severe anemia and cerebral malaria. In malaria-endemic settings in sub-Saharan Africa, children less five years of age suffer the burden of severe morbidity and mortality.[1–3] Largely for this reason, investigators have focused attention on this age group when exploring more subtle morbidities of malaria infection. Several observational studies suggest that malaria has a detrimental effect on the nutritional status of children less than five years old.[4–8] Most of these studies examined the impact of acute episodes of malaria infection on nutritional status.[6–8] In addition, several randomized controlled interventions, including two insecticide-treated bed net (ITN) trials, have demonstrated beneficial effects of malaria interventions on nutritional status in children less than five years old.[2,8–10] There is, in contrast, a dearth of information available regarding the impact of malaria infection on school-age children. Only two randomized controlled trials, both chemoprophylaxis trials conducted in areas with stable malaria transmission patterns,[1] examined the impact of malaria infection on measures of child well-being in older children. One study demonstrated a positive impact of malaria chemoprophylaxis on weight but not height,[11] and the other observed an impact on rates of school absenteeism and weight gain, although the latter was not statistically significant.[12]

In the past two decades, ITNs have generated enthusiasm as an intervention against malaria that has been demonstrated to reduce morbidity and mortality in children less than five years old.[9,13–16] In the setting of extremely limited resources in sub-Saharan Africa, data regarding potential benefits of interventions across different populations may be useful in establishing public health priorities. In this study, we evaluated the impact of ITNs on the longitudinal growth, nutritional status, and body composition of primary schoolchildren 5–12 years of age.

## MATERIALS AND METHODS

**Study area and population.** A detailed description of the study area and population is presented separately.[17] Briefly, this study was conducted in the context of a large randomized controlled trial of ITNs, for which the primary outcome was mortality in children less than five years old. Randomization took place at the village level, and ITNs were provided to cover all bed spaces in intervention villages. The ITNs (Siam-dutch Mosquito Netting Co., Bangkok, Thailand), pre-impregnated to a target dose of 0.5 grams of permethrin per m$^2$ of netting, were distributed for use by January 1997 in 40 of 79 villages in Asembo, Kenya. Participants in all control villages received ITNs in early 1999 after the two-year intervention period. The ITNs were re-treated biannually by the study staff. The project achieved an ITN coverage rate of 1.46 persons per ITN, and an adherence rate (persons observed to be sleeping under ITNs) of 66% in children less than five years old.[18] The morbidity components of the ITN trial were conducted over a two-year period in Asembo, which covers an area of 200 km$^2$ in the Bondo District in Nyanza province in western Kenya. In most years, there is a long rainy season from March to May and a short rainy season from October to December. This pattern of rainfall is sufficient to maintain malaria transmission perennially, and the average number of infective bites ranges from 60 to 300 per person per year.[19] Previous studies conducted in 15 villages contained within this study area found average monthly *P. falciparum* parasite prevalences among children 5–9 and 10–14 years of age of 75% and 60%, respectively, and monthly fever prevalence means of 8% and 5%, respectively.[3]

The study area is populated predominantly by individuals of the Luo ethnic group. Polygamy is a common practice with

a number of wives and their children living in separate houses within the family compound. The principal occupation is subsistence farming. Maize, sorghum, cassava, millet, and a few other vegetables are cultivated and some animal husbandry (primarily cattle) is done. Fishing on Lake Victoria supplements the diet and is used to earn cash.

At the outset of the trial, 58 primary schools were recorded within the boundaries of the study area. Most schools have a catchment area of three to five villages. School fees are generally equivalent to approximately $8.00 US dollars per trimester. Approximately 80% of the children 5–12 years of age attend primary school at any given time (District Education Officer, unpublished data). Discontinuity in school attendance is common. Children may miss entire semesters due to prohibitive school fees or if the family needs the child's assistance at home.

**Assembly of subjects.** Primary schools in the study area were visited in order of selection by a random number generator after randomization status of each village had been defined, but before ITNs had been distributed. Schools were eligible to participate if the headmaster agreed and allowed study staff to explain the study to parents. In addition, eligible schools had a mixture of children from ITN and control villages within a range of 40–60%. Thirteen schools were approached before the desired sample size of approximately 1,000 children less than 13 years old was achieved with seven primary schools. Ineligibility of six schools was due to unequal proportions of students from ITN and control villages rather than headmaster refusal.

The seven recruited schools were visited in October 1996, before ITNs were distributed, to obtain baseline measurements. Follow-up measurements were then obtained at three subsequent time points: after the long rains in July 1997, just before the subsequent long rains in February 1998, and at the end of the study in October 1998. At each follow-up visit, measurements were obtained at all seven schools within a three-week time frame. In addition, each school was visited a second time at each follow-up within two weeks of the initial measurement to capture any children who were absent at the time of the first visit. Children absent at both baseline visits were not included in the cohort.

To be included, children had to be in standards I–VI (grades 1–6) and less than 13 years of age at the time of the baseline measurements. With the assistance of teachers, children provided their village of residence and date of birth. Each child was also provided with a form on which a parent recorded the child's date of birth and the house location code number that had been written on the door of his/her home during mapping.[17] This code number indicated the village, compound, and house number. The child's randomization status, defined on an intention to treat basis (village of residence), and date of birth were determined based upon these data, or by that provided by the child and teacher if the form was not returned. To be included, subjects had to live in a village within the boundaries of the Asembo study area, be less than 13 years of age, and provide village of residence information. Of 1,093 subjects initially recruited, 31, 13, and 173 subjects were excluded from subsequent analyses for the listed reasons, respectively.

**Nutritional assessment.** The height and weight of children were measured while wearing light clothing and no shoes according to procedures described by Jelliffe.[20] The child's height was recorded to 0.1 cm using a wooden height board with a sliding headpiece parallel to the base. The same height board, which was constructed by a local carpenter according to United Nations specifications,[21] was used throughout the study. Weight was measured to 0.1 kg on a Seca model 770 scale (Seca, Inc., Columbia, MD). Mid-upper arm circumference (MUAC), a composite measure of upper arm muscle and subcutaneous fat reserves, was measured to 0.1 cm at the midpoint of the left upper arm, between the acromion process and the tip of the olecranon, using a non-stretch MUAC insertion tape (UNICEF, Copenhagen, Denmark).[22] Triceps skinfold thickness, a measure of subcutaneous fat stores, was measured at the same location using Holtain skinfold calipers (Holtain, Ltd., Crymych, United Kingdom) to 0.2 mm.[22] Triceps skinfold measurements were made in duplicate by one of two trained field staff who performed the triceps skinfold measure throughout the study. If differences between the two measurements were greater than 0.2 mm, a third measurement was taken and the two closest measurements were recorded.[23] The mean of these two measurements was used in all statistical analyses. Field staff conducting the nutritional assessments were blinded to the child's randomization status.

Height-for-age (HAZ), weight-for-height (WHZ), and weight-for-age (WAZ) Z-scores were calculated from Centers for Disease Control (National Center for Health Statistics [NCHS])/World Health Organization (1977/1985) reference values using Epi-Info 2000 software (Centers for Disease Control and Prevention, Atlanta, GA). Stunting, wasting and undernourishment were defined as HAZ, WHZ, and WAZ < -2 SD from the NCHS median respectively. Body mass index (BMI), which is the weight in kilograms divided by height square meters, was also calculated. The BMI was the primary weight-for-stature measure used because Epi-Info will not calculate WHZ for girls > 10 years of age and boys > 11.5 years of age due to variability in this index based on pubertal status. A triceps skinfold Z-score was calculated based on age- and sex-specific means and standard deviations from the National Health and Nutrition Examination Surveys I and II.[24] In addition, two measures of body composition, upper arm fat area and upper arm muscle area, were derived from MUAC and triceps skinfold thickness as described by Frisancho.[25] Upper arm fat area provides a summary measure of body fat that is more highly correlated with total body fat than a single site skinfold thickness.[25,26] Upper arm muscle area provides a summary measure of protein and bone or lean body mass that is an indicator of protein reserves.[25,27] To explore shifts in body composition, estimates of percent body fat and lean body mass were also determined. The triceps skinfold thickness, which is the most valid skinfold estimate of percentage body fat in children,[28] was used to calculate body density from regression equations developed for pre-adolescent girls and boys.[29] Body density was then used to calculate percent body fat and lean body mass.[30,31] Comparison of these equations as an estimate of lean body mass to total body water content,[32] densitometry,[33] and potassium dilution techniques[34] in children demonstrated they provide an accurate estimate of lean body mass.

**Confounding/mediating covariates.** Age was calculated from date of birth. If month and year, or only year were available for a child's date of birth, the 15th of the known month or the mid-year day were used, respectively. Global positioning system data were available for all children whose

parent provided the study number from the door of the child's house, which supplied compound elevation and distances to water bodies.[35] Socioeconomic status and hygiene variables were also available at the level of the compound including whether animals were owned, the number of cows, and whether there was a pit latrine.

**Informed consent.** Village-based ITN *barazas* (open community meetings) were held at the time of ITN distribution to discuss the project, provide information, and answer questions in Dholuo, the native language. The ITN trial was approved by the institutional review boards of the Kenya Medical Research Institute (Nairobi, Kenya) and the Centers for Disease Control and Prevention (Atlanta, GA). Informed consent was obtained from all parents after explanation of the study procedures. In addition, information sessions were conducted at all seven schools explaining the details of this project.

**Data analysis.** Most statistical analyses were performed using SAS version 8.1 (SAS Institute, Cary, NC). Bivariate analyses were performed to assess baseline differences between the control and intervention group and to explore predictors of nutritional status at baseline. For normally distributed data, confidence intervals (CIs) and significance tests (Student's $t$-test) are presented after adjusting the standard errors for clustering at the village level. Chi-square tests adjusted for clustering at the village level were done using SUDAAN 8.0 (Research Triangle Institute, Research Triangle Park, NC). Non-parametric tests used in bivariate analyses such as Spearman correlation avoid distribution assumptions and are not adjusted for clustering.

Hierarchical mixed effects models that included data from all four time points were created for each nutritional outcome. Given this was a randomized, controlled trial, the baseline measure was included as a covariate, rather than in the response vector. Covariates that were ($P < 0.10$) associated with either randomization status or a nutritional outcome in bivariate analyses were evaluated for inclusion. Clustering was taken into account at the level of the school and village together, and then each individually. With clustering at both levels, none of the models were able to converge, reflecting

the small proportion of the overall variance attributable to these clusters (proportion of variance = 2.1–3.2% for different outcomes). Models were dropped if they did not converge. Thus, clustering was taken into account only at the village level for all outcomes. Subject and village level random intercepts and slopes were evaluated in each model and were dropped if they did not explain a significant ($P < 0.10$) amount of the variance.

## RESULTS

At the baseline measurement, 867 children from 39 villages were eligible to participate. The following numbers of subjects were available for measurement at the three follow-up time-points: 704 (81%) after the rainy season in July 1997, 643 (74%) just before the subsequent rainy season in February 1998, and 541 (62%) at the end of the study in October 1998. Using the last measurement time point to define lost to follow-up, there were no significant baseline differences with respect to age or nutritional status between those who were followed for the whole study and those who were ultimately lost to follow-up. However, there were sex differences with girls more likely than boys to be lost to follow-up (43.0% versus 33.4% lost to follow-up, respectively; $P < 0.03$, by adjusted chi-square test). This pattern was also seen using the third time point to define lost to follow-up (29.3 versus 23.9%; $P = 0.12$, by adjusted chi-square test). There was no difference with respect to randomization status and loss to follow-up at the final measurement (36.7% of children from ITN control versus 40.1% from control villages were ultimately lost to follow-up; $P = 0.52$, by adjusted chi-square test).

Baseline characteristics of the pooled cohort and by randomization status are shown in Table 1. At study inception, the children were 4.0–12.9 years of age (mean ± SD age = 9.3 ± 1.7 years) and 51.8% were female. The observed standard deviations of the Z-scores for HAZ, WAZ, and WHZ were 1.24, 0.90, and 0.90, respectively. These fell within the World Health Organization recommended ranges and suggested that the quality of the data was good.[36] Relative to a healthy ref-

TABLE 1
Baseline characteristics of study participants by randomization status controlling for clustering by village*

| | Pooled (n = 876) | ITN villages (n = 455) | Control villages (n = 421) | P |
|---|---|---|---|---|
| Demographic/socioeconomic status | | | | |
| Age (months)† | 108.4 [107.1, 109.7] | 109.1 [107.3, 110.7] | 107.6 [105.8, 109.6] | NS |
| Female‡ | 454/876 (51.8) | 237/455 (52.1) | 217/421 (51.5) | NS |
| Animals present on compound‡ | 317/832 (38.1) | 186/440 (42.3) | 131/392 (33.4) | <0.05 |
| Pit latrine on compound‡ | 576/832 (69.2) | 301/440 (68.4) | 275/392 (70.2) | NS |
| Nutritional status | | | | |
| WAZ† | −1.13 [−1.23, −1.05] | −1.16 [−1.27, −1.05] | −1.10 [−1.25, −0.97] | NS |
| Undernourished (WAZ < −2 SD)‡ | 132/835 (15.8) | 74/443 (16.7) | 58/392 (14.8) | NS |
| HAZ† | −0.96 [−1.07, −0.86] | −0.98 [−1.11, −0.85] | −0.95 [−1.15, −0.76] | NS |
| Stunted (HAZ < −2 SD)‡ | 155/838 (18.5) | 79/445 (17.8) | 76/393 (19.3) | NS |
| WHZ†§ | −0.70 [−0.81, −0.58] | −0.72 [−0.86, −0.58] | −0.67 [−0.86, −0.47] | NS |
| Wasted (WHZ < −2 SD)§ | 42/715 (5.9) | 25/368 (6.8) | 17/347 (4.9) | NS |
| Body mass index (kg/m²)† | 14.74 [14.56, 14.92] | 14.73 [14.48, 14.97] | 14.76 [14.51, 15.01] | NS |
| Mid upper arm circumference (cm)† | 17.31 [17.91, 17.42] | 17.36 [17.24, 17.47] | 17.26 [17.05, 17.47] | NS |
| Triceps skin fold thickness Z-score†¶ | −0.99 [−1.04, −0.94] | −0.98 [1.05, −0.90] | −1.01 [−1.07, −0.95] | NS |

* NS = not significant; WAZ = weight-for-age Z-score; HAZ = height-for-age Z-score; WHZ = weight-for-height Z-score; ITN = insecticide-treated bed nets.
† Mean [95% confidence interval]. $P$ value from difference in means adjusted for clustering by village.
‡ Number yes/denominator for covariate (%). $P$ value from adjusted chi-square (SUDAAN 8.0).
¶ Arithmetic mean of two measurements on each subject.
§ Calculable only for girls <10 years of age and boys <11.5 years of age (n = 715).

erence population, the pooled cohort was malnourished with mean Z-scores for adjusted nutritional outcomes approximately one standard deviation below the median. Overall, 18.5%, 5.9%, and 15.8% were stunted, wasted, and undernourished (HAZ, WHZ, and WAZ < -2 SD from the NCHS median), respectively. There were no significant differences by randomization status with respect to age, sex, or nutritional status (Table 1). The ITN group was more likely to live on a compound that owned animals (42.3% versus 33.4; $P < 0.03$ by adjusted chi-square test). Of note, there were no significant relationships between animal ownership and nutritional status, reducing the potential for confounding by this variable.

Baseline nutritional measures were used in bivariate analyses to explore potentially mediating/confounding covariates. Older children were more malnourished than younger children with respect to long term indicators of malnutrition, with 11.7% of younger children versus 25.2% of older children stunted at baseline ($P < 0.01$, by adjusted chi-square test). Girls experienced less linear growth faltering than boys, as demonstrated by higher mean HAZ (-1.07 versus -1.26; $P = 0.03$, by adjusted $t$-test) and a lower proportion of stunting, with 14.7% of the girls and 22.5% of the boys stunted at baseline ($P < 0.04$, by adjusted chi-square test).

**Impact of ITNs on standard nutritional parameters.** The crude mean values over time for four growth and nutritional outcomes adjusted for clustering by village are shown by ran-

domization status in Figure 1. For the nutritional outcomes that are adjusted for age and sex (HAZ and triceps skinfold z-score), there was a general trend toward lower Z-scores following the rainy season compared with baseline. For MUAC, a general upward trend was observed that is likely related to the cohort aging across time points.[24] There were no significant differences by randomization status for any unadjusted nutritional outcomes at any time point.

The results from repeated measures regression models using data from all four time points adjusted for mediating covariates are shown in Table 2. Over the course of the trial, ITNs did not have a significant impact on any standard measures of growth or nutritional status. Interaction terms were also explored to assess the impact of ITNs in specific subgroups including younger children (age < median for cohort), those who began the study malnourished (stunted, wasted, or undernourished at baseline), and those who lived closest to the lake shoreline (closest tertile of distance). The ITNs did not have a significant impact on the linear growth or nutritional status of any of these subgroups.

**Impact of ITNs on body composition.** To explore the impact of ITNs on body composition, multivariate repeated measures models were made. The impact of ITNs on measures of body composition is shown in Table 2. Over the course of the trial, there were no significant differences in upper arm muscle area between children from ITN and control villages (ITN group 4.7 mm$^2$ adjusted higher, $P = 0.84$). Those from
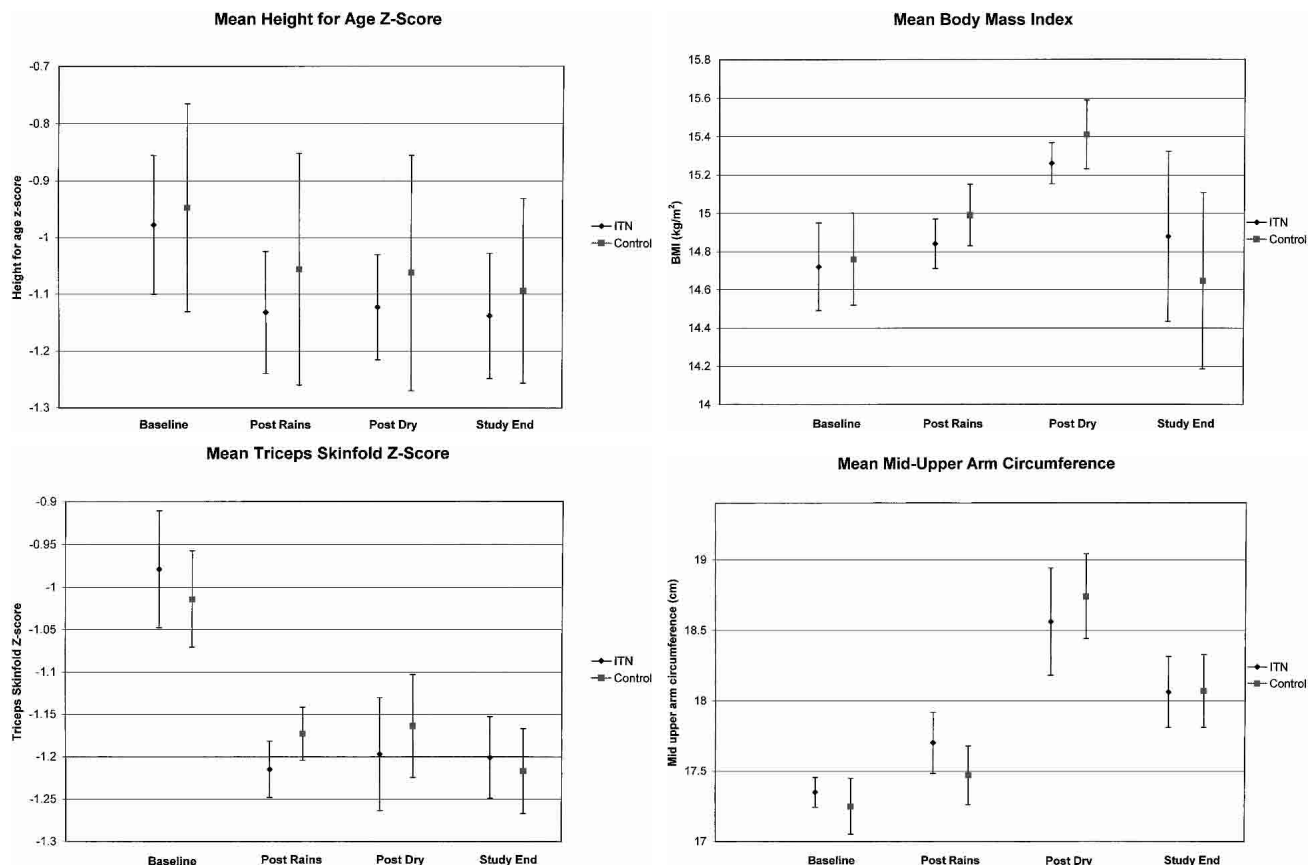


FIGURE 1. Nutritional status over time by randomization status. No significant differences were seen between any groups for any nutritional measure at any time point. Significant test results by the Student's $t$-test were clustered by village. Error bars show ± 95% confidence intervals adjusted for village level clustering.

TABLE 2
Hierarchical repeated measures models: impact of insecticide-treated bed nets (ITN) on nutritional status and body composition*

| | Mean difference* | 95% CI | P |
|---|---|---|---|
| Nutritional status | | | |
| HAZ | −0.0053 | [−0.7, 0.06] | 0.87 |
| WAZ | −0.011 | [−0.10, 0.06] | 0.64 |
| BMI (kg/m²)† | −0.121 | [−0.32, 0.07] | 0.22 |
| MUAC (cm)† | −0.051 | [−0.26, 0.15] | 0.63 |
| Triceps skinfold Z-score† | −0.007 | [−0.04, 0.03] | 0.70 |
| Body composition | | | |
| Upper arm area (mm²)† | −10.87 | [−64.5, 42.7] | 0.69 |
| Upper arm muscle area (mm²)† | 4.73 | [−41.6, 51.1] | 0.84 |
| Upper arm fat area (mm²)† | −20.30 | [−40.7, 0.07] | 0.06 |
| Percent lean body mass† | 1.18 | [0.06, 2.30] | 0.04 |

* Bed net status forced into all models (ITN = 1, control = 0) Above models also adjusted for baseline measure ($P < 0.0001$ for all outcomes) and age ($P < 0.05$ for all outcomes). Beta coefficient for age was negative for height-for-age Z-score (HAZ) and weight-for-age Z-score (WAZ) and positive for body mass index (BMI), mean upper-arm circumference (MUAC), triceps z-score, total upper arm area, and upper arm muscle and fat areas. Beta coefficients displayed are with these three covariates in model and sex when this was included. CI = confidence interval.

† Sex also a significant predictor and was included in model. The female estimate was higher for BMI, MUAC, total upper arm area, upper arm muscle, and fat areas. The male estimate was higher for triceps z-score and percent lean body mass.

the control group had greater absolute upper arm fat areas over the course of the study, although the difference was not statistically significant (adjusted mean difference = 20.3 mm²; $P = 0.06$). This increase in upper arm fat area among control subjects occurred without a concomitant increase in total upper arm area. To explore this, we examined differences in percent lean body mass (see Materials and Methods). Children from ITN villages had significantly higher percent lean body mass compared with children from control villages (1.2% lean body mass difference, $P < 0.04$).

## DISCUSSION

This study reconfirms several findings from studies exploring the nutritional status of school-age children in sub-Saharan Africa. Chronic undernutrition, as shown by a high proportion of stunted children, was prevalent in this cohort (18.5% at baseline), while acute undernutrition was less common, as supported by the relatively low proportion of wasted children (5.9% at baseline).

With respect to the impact of ITNs on growth and nutritional status, we did not find any significant improvement in the linear growth or protein-energy nutritional status, of children from ITN villages when averaged over the entire study period. The ITNs did not have a significant impact on linear growth, the most important outcome we measured due to its implications for attained adult size and consequent adult work capacity,[37] pregnancy outcomes,[37–39] and fertility.[38,39] There are a number of possible explanations for this lack of efficacy. First, compliance with ITN use in this age group may be less than that observed among other age groups. In the setting of stable malaria transmission, parents may not enforce ITN use in children more than five years old because they often sleep away from their parents, and parents may not perceive any need to protect against malaria in this age group. Furthermore, children in this age group retire to bed at a later hour, thus reducing the protection conferred by ITNs. Second, there was significant attrition of study participants during the course of this study. Although we might expect that

those lost to follow-up were from lower income households, and perhaps less well nourished, we did not have any differential loss to follow-up between control and ITN children, and apart from sex, children lost to follow-up did not differ in baseline characteristics from those followed successfully. Thus, the most likely explanation is that malaria has a much smaller impact on the growth and nutritional status of children more than five years old, compared with younger children, due to the vastly reduced burden of malarial disease under conditions of stable transmission.[1] This reduced burden of disease relates to acquired immunologic resistance to malaria and results in a reduced risk of high-density parasitemias and clinically apparent illness in this age group. Studies conducted in 15 villages within Asembo found average monthly fever prevalence means of 32%, 8%, and 5% and average monthly prevalence means for clinical malaria of 20%, 1%, and 0.3% among children 6–11 months old, 5–9 years old, and 10–14 years old, respectively.[3] Thus, variability in growth and nutritional status attributable to malaria is likely to be much less among older children in this setting than among younger children, for whom a significant impact of ITNs on nutritional status has been demonstrated.[2,9,10] A study of the impact of ITNs on the growth and nutritional status of adolescent school girls during the trial found that ITN use reduced anemia among young adolescent girls, without any evidence of improved growth or nutritional status.[40]

In this study, ITNs had a significant impact on percent lean body mass. Children in the control group had relatively higher upper arm fat areas over the course of the study. This occurred without a concomitant difference in overall upper arm area, a summary measure of lean body mass and fat mass. This suggests that there might be a shift in body composition, with children under ITNs maintaining increased lean body mass and losing fat mass compared with the control group. This pattern of body composition difference is indicative of a relative sarcopenia, or decreased muscle mass with maintenance of total body mass,[41] among control children compared with ITN children.

These findings raise interesting questions about the way in which children may use protein and fat reserves in the context of malaria infection, and potential biologic mechanisms underlying this. It is well known that acute symptomatic malaria infection leads to the elaboration of pro-inflammatory cytokines such as tumor necrosis factor-α (TNF-α) or cachectin,[42–46] interleukin-1 (IL-1),[47] and IL-6.[42] Even children with mild malaria elaborate greater amounts of TNF-α than children with other illnesses.[48] Two longitudinal studies, one of which was conducted among adolescent and young adult males in this study area, demonstrated very high levels of plasma TNF-α,[49] and TNF-α elaborated in response to malaria-specific antigens,[50] with seasonal fluctuations in production that mirror malaria transmission pressure. Tumor necrosis factor-α has potent catabolic effects, inducing muscle proteolysis, which lead to the lean body mass wasting seen in many diseases that trigger the elaboration of this cytokine.[41,51–53] In the context of the acute-phase response to infection, pro-inflammatory cytokines deplete structural and transport proteins for use in the immune response and host defense.[54] With maintenance of total body mass, a shift in percent lean body mass may also be partly driven by a relatively higher absolute upper arm fat area in the control group. Many diseases associated with a pro-inflammatory state lead

to preferential loss of protein reserves with sparing of fat reserves;[55,56] however, few have found an actual increase in fat reserves.[57] Although most sources support a net lipolytic effect for pro-inflammatory cytokines,[41,52] many animal models have demonstrated hepatic lipogenesis[58–61] and an increase in adipose tissue.[62] More specific to malaria, malaria toxic antigens have been shown to have a direct lipogenic effect on adipocytes.[63,64] Without data regarding parasitemia levels for this cohort, we can only speculate that the greater lean body mass observed in the ITN group is related to decreased production of pro-inflammatory cytokines consequent to reduced exposure to malaria. Although children in this age group and transmission setting experience relatively few episodes of symptomatic infection, these infections may exact a nutritional price through pro-inflammatory cytokines elaborated in response to infection.

The functional consequences of body composition changes have been evaluated in other disease states, suggesting some impact on health status. Decreased lean body mass predicted disease progression in children infected with human immunodeficiency virus (HIV)[53] and physical functioning and health perceptions in adults infected with HIV.[65,66] Lean body mass, and not body fat, has been correlated with attained height in cross-sectional surveys in the developing world.[67,68] The adjusted difference in percent lean body mass between groups observed in this study was small (1.2%), however, and the biologic significance of this difference is not known.

Although ITN use in an area with intense malaria transmission had an impact on body composition in children 5–12 years old, this study found no evidence to suggest an impact on standard measures of nutritional status, which have more clearly defined functional consequences. More studies are needed to elucidate the mechanisms by which changes in body composition may occur in malaria infection, and more importantly, the functional consequences of such a change in this context.

Authors' addresses: Jennifer F. Friedman, International Health Institute, Brown University, Box G-B495, Providence, RI 02912, Telephone: 401-863-2172, Fax: 401-863-1243, E-mail: Jennifer_Friedman@Brown.edu. Penelope A. Phillips-Howard, William A. Hawley, Dianne J. Terlouw, Margarette S. Kolczak, and Feiko O. ter Kuile, Division of Parasitic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Mailstop F-22, 4770 Buford Highway, Atlanta, GA 30341, Telephone: 770-488-7760, Fax: 770-488-4206. Marlene Barber, Centre for Public Health, School of Medical Education, University of New South Wales, New South Wales 2052, Australia, Telephone: 61-2-9385-2507, Fax: 61-2-9385-1526. Norman Okello and John M. Vulule, Vector Biology and Control Research Centre, Kenya Medical Research Institute, PO Box 1578, Kisumu, Kenya. Christopher Duggan, Division of Gastroenterology and Nutrition, Boston Children's Hospital, 300 Longwood Avenue, Boston, MA 02115, Telephone: 617-355-7612, Fax: 617-713-2892, E-mail: christopher.duggan@tch.harvard.edu. Bernard L. Nahlen, Roll Back Malaria, World Health Organization, Avenue Appia 20, 1211 Geneva 27, Switzerland, Roll Back Malaria, World Health Organization, 1211 Geneva 27, Switzerland.

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