Community Coverage with Insecticide-Treated Mosquito Nets and Observed Associations with All-Cause Child Mortality and Malaria Parasite Infections

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Abstract. Randomized trials and mathematical modeling suggest that insecticide-treated mosquito nets (ITNs) provide community-level protection to both those using ITNs and those without individual access. Using nationally representative household survey datasets from 17 African countries, we examined whether community ITN coverage is associated with malaria infection prevalence in children < 5 years old and all-cause child mortality (ACCM) among children < 5 years old in households with one or more ITNs versus without any type of mosquito net (treated or untreated). Increasing ITN coverage (> 50%) was protective against malaria infections and ACCM for children in households with an ITN, although this protection was not conferred to children in households without ITNs in these data. Children in households with ITNs were protected against malaria infections and ACCM with ITN coverage > 30%, but this protection was not significant with ITN coverage < 30%. Results suggest that ITNs are more effective with higher ITN coverage.

BACKGROUND

Randomized controlled trials and observational studies have shown that insecticide-treated mosquito nets (ITNs) reduce exposure to infectious mosquito bites, thereby reducing malaria parasite infection prevalence and all-cause child mortality (ACCM).^{1,2} The insecticide in ITNs kills mosquitoes seeking a blood meal, which reduces indoor vector densities.³ Furthermore, if the person under the net is already infected with the malaria parasite, the ITN reduces transmission by preventing gametocyte uptake by mosquitoes. Based on these mechanisms, there is evidence from trials that ITNs at high population coverage levels (> 90%) provide community-wide protection, whereby individuals living in households without ITNs in these communities are conferred protection from infectious bites.^{3–7} Mathematical models support these studies, showing that, when ITN use in a community reaches between 35% and 65%, individuals in that community without an ITN are afforded protection at a similar level as those using ITNs.⁸ It is logical, therefore, to infer that, because of the observed community protection conferred by high ITN coverage, the effectiveness of ITNs for personal protection against infection and child death will increase as community coverage increases.

Until recently, low ITN coverage in most African countries limited investigations into potential ITN community-level protection. Before widespread ITN scale-up across much of Africa, a study in Tanzania with community coverage of ITN household ownership < 10% found no community-level protection from untreated mosquito nets.⁹ ITN availability, however, has increased rapidly throughout the continent; the pool of countries with > 50% national ITN coverage is now sufficient for a rigorous assessment of community-level protection under routine program conditions.¹⁰

In this paper, we used nationally representative household survey datasets from 17 African countries to examine whether community ITN coverage is associated with malaria parasite

prevalence in children < 5 years old and ACCM among children < 5 years old in households with one or more ITNs versus without any type of mosquito net (treated or untreated). We also assessed if increased community ITN coverage affects the association between ITN household possession and infection and mortality outcomes in children.

METHODS

Data sources. We considered nationally representative household surveys that were publicly available in December of 2010 that met the following conditions: the surveys measured either malaria parasite prevalence or ACCM, and the surveys were performed in countries with endemic *Plasmodium falciparum* malaria transmission in sub-Saharan Africa. We excluded surveys conducted before 2006 from the analysis, because before this time, too few countries had achieved sufficient ITN coverage to assess community ITN protection.¹⁰ For the analysis of the association between community ITN coverage and malaria parasite infection prevalence in children, we included only surveys with a rapid diagnostic test (RDT) for diagnosing a parasite infection among all children sampled; six surveys were included (Table 1). For the analysis of ACCM, we included only surveys with a complete birth history as well as a net roster and procurement date that allowed past household exposure to ITNs to be ascertained; 15 surveys were included (Table 2). In total, 14 demographic and health surveys (DHSS), 4 malaria indicator surveys (MISs), and 1 acquired immunodeficiency syndrome (AIDS) indicator survey (AIS) across 17 countries met the inclusion criteria for either analysis (Figure 1); all data are available through www.measuredhs.com.

Measures of exposure to household ITN ownership and community ITN coverage. We assessed the association between community ITN coverage levels and primary outcomes with two different strategies. First, we tested for community-level protection among children in households stratified by ITN ownership. The effect of community ITN coverage levels on primary outcomes was analyzed among households with one or more ITNs to estimate the added benefit of household ITN ownership plus high community

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TABLE 1
Parasite prevalence and sample size in parasite prevalence analysis

Country	RDT parasite prevalence (n)		
	Children ages 1–11 months	Children ages 12–59 months	All children
Total	13.5% (3,548)	22.7% (24,322)	21.5% (27,870)
Angola 2006	16.1% (273)	23.3% (2,385)	22.5% (2,658)
Liberia 2009	22.5% (546)	38.9% (4,414)	37.1% (4,960)
Rwanda 2007–2008	1.4% (907)	2.1% (4862)	2.0% (5,769)
Senegal 2008–2009	7.0% (359)	12.4% (3,673)	13.1% (4,032)
Tanzania 2007–2008	7.0% (733)	13.8% (5,720)	13.1% (6,453)
Uganda 2009	30.7% (730)	58.0% (3,268)	53.1% (3,998)

ITN coverage. The effect of community ITN coverage levels on primary outcomes was then analyzed among households without any mosquito nets to determine if unprotected children benefit from high community ITN coverage compared with their unprotected counterparts in communities with lower community coverage. Second, we examined whether community ITN coverage modified the effect of ITN ownership that has been shown to be protective against infections and mortality in children.

Household possession of one or more ITNs and ITN use the previous night have been shown to yield similar estimates for the association of ITN exposure and malaria parasite prevalence.² For the analyses of parasite prevalence, a child was considered exposed to an ITN if the household owned at least one ITN at the time of the survey. For the analyses of ACCM, which is retrospective in nature, the net roster was used to assess when the household obtained an ITN; a child was considered exposed to an ITN from the point at which the ITN was procured going forward. We classified a net as an ITN if it was a long-lasting insecticide-treated net (LLIN) obtained within the past 36 months, a pre-treated but not long-lasting net obtained within the past 12 months, or any net retreated within the past 12 months.¹¹

Community ITN coverage was derived as the proportion of households in a primary sampling unit (PSU) owning at least one ITN at the time of the survey. Primary sampling units are administrative units, typically a standard enumeration area (SEA) consisting of one to five villages. We compared children above and below a community ITN coverage threshold of 30% based on previous findings.⁸ We then examined cov-

erage levels above 30% at 10% increments (all compared with $\leq 30\%$; i.e., we compared children in PSUs with $> 40\%$ coverage with children in communities with $\leq 30\%$, children in PSUs with $> 50\%$ versus $\leq 30\%$, and so forth up to the comparison of children in PSUs with $> 70\%$ coverage with those in communities with $\leq 30\%$ coverage).

Outcome measures. Presence of a malaria parasite infection in children < 5 years old was measured by an RDT among all children in sampled households. ACCM was ascertained from each survey dataset from the mother's self-reported complete birth history. This resultant retrospective cohort was limited to 36 months before the survey date to remain concurrent with the net roster, which references household net possession only within the prior 3 years. A child death was defined as a death between 1 and 59 months old.

Measures of potential confounding factors. In all statistical models, we included individual-, household-, and community-level covariates either known or hypothesized to be associated with malaria parasite prevalence and ACCM. At the child and household levels, they included child's age, household socioeconomic status, urban versus rural residence, mother's education, mother's age at first pregnancy, birth spacing, and type of birth (e.g., single, twin, or triplet). At the PSU and district levels, they included malaria transmission intensity, malaria transmission season, and access to healthcare (individual treatment-seeking behavior aggregated to the PSU level was used as a proxy).

We categorized child's age for the parasite prevalence analysis as 1–11, 12–23, 24–35, 36–47, and 48–59 months. The same was done for the child mortality analysis, with age serving as a time-varying covariate and 1–11 months disaggregated into 1–5 and 6–11 months. We measured household socioeconomic status using principle components analysis of durable assets registered in each survey to derive relative wealth quintiles.¹² We categorized mother's education as none, some primary school, or completed primary school or higher. Mother's age at first pregnancy was categorized as < 18 or ≥ 18 years old. Birth spacing was categorized as firstborn, < 24 months, or ≥ 24 months.

At the district level, we determined malaria transmission intensity using the Malaria Atlas Project estimates of the *P. falciparum* prevalence rate in 2–10 year olds ($PfPR_{2-10}$) for 2007 aggregated to the mean for each district and matched to

TABLE 2
Mortality rates and sample size in child mortality analysis

Country	Mortality rate per 1,000 person-years (n)		
	Children ages 1–11 months	Children ages 12–59 months	All children
Total	39.63 (107,066)	13.28 (179,842)	18.09 (207,219)
Benin	38.06 (11,532)	13.37 (18,869)	18.14 (21,901)
Democratic Republic of the Congo	59.96 (6,014)	14.25 (9,834)	22.56 (11,371)
Ghana	27.42 (2,009)	6.69 (3,577)	10.17 (4,096)
Kenya	23.20 (3,636)	5.13 (6,352)	8.16 (7,279)
Madagascar	24.42 (8,211)	4.72 (15,211)	7.86 (17,199)
Malawi	35.29 (14,229)	8.95 (23,787)	13.69 (27,368)
Mali	50.34 (9,453)	22.80 (15,473)	28.19 (17,997)
Namibia	25.91 (2,800)	5.78 (5,388)	8.85 (6,161)
Niger	43.98 (6,471)	23.54 (11,198)	27.09 (12,746)
Nigeria	41.53 (20,250)	19.47 (32,805)	23.74 (38,227)
Rwanda	34.84 (3,138)	7.25 (5,219)	12.48 (5,951)
Sierra Leone	53.81 (3,901)	12.57 (6,633)	19.91 (7,742)
Tanzania	28.04 (5,813)	6.47 (9,100)	10.61 (10,560)
Uganda	51.73 (5,195)	13.36 (9,008)	20.04 (10,260)
Zambia	40.10 (4,476)	11.38 (7,428)	16.77 (8,496)

FIGURE 1. Map of countries included in the analyses.

PSUs in ArcGIS by latitude and longitude¹³ (included as a continuous variable). Using publicly available Mapping Malaria Risk in Africa (MARA) maps based on a climate susceptibility model,¹⁴ we aggregated malaria transmission seasons over districts and matched them to PSUs by latitude and longitude. We then included monthly malaria transmission season in the parasite prevalence analysis as binary (yes or no at the time of survey) and the child mortality analysis as a time-varying covariate (yes or no during each child-month). District shape files were obtained from www.maplibrary.org.

In the malaria parasite prevalence analysis, we included the proportion of children with fever in the past 2 weeks who were taken for treatment in each PSU as a proxy for access to healthcare. In the child mortality analysis, many PSUs without child fevers in the past 2 weeks prevented including it as a covariate. Diphtheria, pertussis, and typhoid (DPT₃) vaccine along with prenatal coverage, instead, were used as proxies for treatment-seeking behavior.

We also stratified the analyses of community ITN coverage (> 50% ITN community coverage or not) by urban versus rural and low versus high malaria transmission ($PfPR_{2-10}$ < 25% or not) to assess if the community-level protection differed within these strata.

Statistical analysis. *Parasite prevalence analyses.* To examine the added benefit of community ITN coverage levels among households with ITNs and households without any mosquito nets, we used random effects logistic regression to model parasite prevalence as a function of community ITN coverage and other individual, household, and community characteristics. We ran separate models for children in households with ITNs, with non-treated mosquito nets, and without any mosquito nets to measure additive effects of community ITN coverage among households both with and without nets or ITNs as well as account for selection bias of owning a net or ITN. We included the survey PSU nested within country as a random intercept in each model and tested the association between various com-

munity ITN coverage levels and malaria parasite prevalence after controlling for potential confounders as defined above.

To examine the potential effect modification of community ITN coverage on the effectiveness of ITN ownership against malaria infections in children, we first matched children within country on the following covariates in an attempt to mitigate selection bias: mother received any intermittent preventive treatment (IPT) with sulfadoxine-pyrimethamine during previous pregnancy, mother attended antenatal care (ANC) during previous pregnancy, mother's education (some versus none), household wealth (rich versus poor), place of residence (urban versus rural), district $PfPR_{2-10}$ (above versus below median), and treatment-seeking behavior (above versus below median). We used a mixed effects logistic regression model with matched group as a random intercept and tested the interaction between ITN ownership and various community ITN coverage levels on the outcome of malaria parasite prevalence after controlling for potential confounders. We conducted the parasite prevalence analyses using the lme4 package¹⁵ in R, version 3.0.2¹⁶; matching was performed with the MatchIt package in R, version 3.0.2.^{16,17}

Child mortality analyses. To examine the added benefit of community ITN coverage levels among households with ITNs and households without mosquito nets, we performed survival regression analyses with a Cox proportional hazard model for all children ages 1–59 months old stratified *a priori* by infants ages 1–11 months old and older children ages 12–59 months old. We used a Weibull distribution, which is recommended, for the analysis of infant mortality; an exponential distribution was used for older children, which better fits the risk of mortality at ages beyond infancy.¹⁸ We included country as a shared frailty in the survival models. A shared frailty in a survival model is comparable with a random effect in a logistic model and can be used to account for unobserved heterogeneity between clusters of observations in a manner similar to the inclusion of the community-level random effect in the parasite

prevalence models.¹⁹ A sensitivity analysis conducted with country as a covariate and PSU as a shared frailty showed no difference in results when using country of PSU as a shared frailty. In addition to the aforementioned covariates, time-varying covariates included household ITN ownership, household ownership of non-treated mosquito net, community ITN coverage, malaria transmission season, child age, and year.

To examine the potential effect modification of community ITN coverage on the effectiveness of ITN ownership against ACCM, we first matched children within a country on the following covariates in an attempt to mitigate confounding bias: mother receiving any IPT with sulfadoxine-pyrimethamine during previous pregnancy, mother receiving neonatal tetanus vaccine during previous pregnancy, mother receiving iron supplementation during previous pregnancy, mother attended ANC during previous pregnancy, mother's education (some versus none), household wealth (rich versus poor), place of residence (urban versus rural), district $PfPR_{2-10}$ (above versus below median), PSU coverage of three doses of DPT₃ vaccine (above versus below median), PSU measles vaccination coverage (above versus below median), PSU polio vaccination coverage (above versus below median), and PSU Bacillus Calmette-Guerin (BCG) vaccination coverage (above versus below median). Effect modification between ITN household effectiveness and community ITN coverage was tested using a Cox proportional hazard model, with the matched group included as the shared frailty. We conducted the child mortality analyses using Stata, version 13.1 (Stata Corporation, College Station, TX); matching was performed with the MatchIt package¹⁷ in R, version 3.0.2.¹⁶

Exploration of interactions. Modeling suggests that high coverage of ITNs has a greater effect on malaria trans-

mission in low-transmission areas.²⁰ For this reason, we explored the interaction between community ITN coverage and urban or rural residence using a likelihood ratio test to determine if inclusion of the interaction term improved the model. We also explored the interaction between community ITN coverage and low or high $PfPR_{2-10}$ ($< 25\%$ or $\geq 25\%$, respectively) using a likelihood ratio test to determine if inclusion of the interaction term improved the model.

RESULTS

Community ITN coverage varied across surveys. Surveys with low ITN coverage ($< 20\%$; Democratic Republic of Congo, Nigeria, and Uganda) showed a great deal of overdispersion with 0% coverage in many PSUs, whereas other PSUs had ITN coverage exceeding 50%. Surveys with relatively higher ITN coverage ($> 50\%$), such as Kenya, Madagascar, Mali, Tanzania, and Zambia, also had many communities with $< 50\%$ ITN coverage. In total, 27,870 children < 5 years of age were included in the parasite prevalence analysis, with an average parasite prevalence of 21.6% (Table 1). In the child mortality analysis, 207,219 children < 5 years of age provided 371,591 person-years and 6,723 deaths, with an average child mortality of 18 deaths/1,000 person-years (Table 2).

Effect of community ITN coverage on malaria infection. Among children in households with one or more ITNs, community ITN coverage $\geq 50\%$ was associated with decreased odds of a malaria parasite infection compared with their counterparts in households with one or more ITNs in communities with $< 30\%$ community ITN coverage (Figure 2). No level of community ITN coverage (compared with $\leq 30\%$ community coverage) was significantly associated with prevention of malaria

FIGURE 2. Comparison of adjusted odds ratios of community ITN coverage against a malaria infection among six pooled surveys in sub-Saharan Africa for (A) children in households without ITNs and (B) children in households with ITNs. All odds ratios are compared with $< 30\%$ coverage. *Community ITN coverage was statistically significant at $P < 0.05$.

TABLE 3

Logistic regression models for malaria parasite prevalence among children in households without any type of mosquito net in six pooled datasets

Factor/categorization	Odds ratio (95% CI)		
	Children ages 1–59 months	Infants ages 1–11 months	Children ages 12–59 months
Sample size (PSUs)	7,603 (1,087)	1,020 (550)	
Community ITN coverage (%)			
≤ 30	Reference	Reference	Reference
> 30 and ≤ 50	1.070 (0.797–1.436)	1.568 (0.977–2.518)	0.986 (0.728–1.336)
> 50	0.993 (0.725–1.360)	1.210 (0.698–2.097)	0.936 (0.675–1.298)
Wealth quintile			
1	Reference	Reference	Reference
2	0.937 (0.774–1.133)	0.748 (0.461–1.213)	0.954 (0.779–1.169)
3	0.790* (0.630–0.992)	0.891 (0.521–1.524)	0.740* (0.579–0.945)
4	0.631† (0.483–0.823)	0.994 (0.543–1.819)	0.562† (0.421–0.751)
5	0.352† (0.246–0.503)	0.347* (0.133–0.907)	0.346† (0.236–0.509)
Mother's education			
None	Reference	Reference	Reference
Some primary	0.919 (0.782–1.081)	0.998 (0.653–1.524)	0.910 (0.765–1.083)
Completed primary or higher	0.687* (0.509–0.928)	0.785 (0.379–1.626)	0.667* (0.480–0.927)
Child's age (months)			
1–11	Reference	–	–
12–23	1.718† (1.351–2.185)	–	Reference
24–35	2.524† (1.986–3.206)	–	1.476† (1.201–1.814)
36–47	2.803† (2.213–3.552)	–	1.653† (1.353–2.018)
48–59	3.166† (2.498–4.013)	–	1.867† (1.528–2.281)
Place of residence			
Urban	Reference	Reference	Reference
Rural	2.300† (1.646–3.215)	2.717‡ (1.405–5.253)	2.275† (1.606–3.222)
Season at the time of survey			
Not malaria transmission season	Reference	Reference	Reference
Malaria transmission season	1.382* (1.071–1.785)	0.755 (0.499–1.141)	1.430* (1.096–1.864)
Malaria transmission intensity			
2007 <i>P. falciparum</i> prevalence rate (continuous)	772.3† (266.9–2,234.4)	736.0† (107.1–5,055.9)	852.9† (283.3–2,568.0)
Healthcare access to fever treatments			
Continuous	0.568* (0.367–0.879)	0.396* (0.185–0.850)	0.601* (0.383–0.943)

Models included PSUs nested within country as random effects.

* $P < 0.05$.† $P < 0.001$.‡ $P < 0.01$.

parasite infections among children unprotected by any type of mosquito net: ≤ 30% versus 30–50% community ITN coverage (adjusted odds ratio [AOR] = 1.07, 95% confidence interval [95% CI] = 0.80–1.44) and < 30% versus ≥ 50% community ITN coverage (AOR = 0.99, 95% CI = 0.73–1.36) (Table 3).

The test for interaction between community ITN coverage and urban versus rural or low- versus high-transmission areas showed no difference in the effect of community ITN coverage on the odds of a malaria parasite infection among children in household protected by ITNs ($P = 0.75$ and $P = 0.99$, respectively) and those in non-net households ($P = 0.15$ and $P = 0.95$, respectively).

Effect of community ITN coverage on ACCM. Malaria transmission season, malaria transmission intensity, wealth quintile, mother's education, mother's age at first pregnancy, child age, birth interval, being a twin, and level of DPT₃ coverage were all associated with child mortality (Table 4). Higher community ITN coverage was significantly associated with decreased risk of ACCM among children in households with one or more ITNs when community ITN coverage exceeded 30% or higher compared with communities with ITN coverage ≤ 30%. Among unprotected children in households without any mosquito nets, community ITN coverage was not associated with reduced risk of ACCM at any community ITN coverage level compared with those without ITNs in areas with < 30% coverage (Figure 3 and Table 4).

The test for interaction between community ITN coverage and urban versus rural or high- versus low-transmission level

showed no differences in the effect of community ITN coverage on the risk of ACCM by strata for children protected and unprotected by ITNs.

Effect modification of community ITN coverage on association of household ITN possession with malaria parasite infection and mortality in children. Matching reduced the sample size in the parasite prevalence analysis by 14% to 23,952 individuals and 5,335 malaria infections. After controlling for potential confounding factors with exact matching and fixed effects in the logistic regression model, household ITN ownership was not associated with the odds of a malaria infection in areas with ≤ 30% ITN coverage (AOR = 1.00, 95% CI = 0.83–1.20) (Table 5). In areas with > 30% ITN coverage, household ITN ownership was associated with decreased odds of a malaria infection (AOR = 0.87, 95% CI = 0.80–0.95). Including an interaction term of household ITN ownership by community ITN coverage at ≤ 30% or > 30% was not statistically significant ($P = 0.22$).

Matching reduced the sample size in the child mortality analysis by 17% to 167,555 children followed over 308,022 person-years and 5,769 deaths at 1–59 months of age. After controlling for potential confounding factors with exact matching and fixed effects in the Cox proportional hazard model, including an interaction term of household ITN ownership by community, ITN coverage at ≤ 30% or > 30% was statistically significant at the $P < 0.05$ level (Table 6). Household ITN ownership was not associated with ACCM in areas with ≤ 30% ITN coverage (hazard ratio [HR] = 0.96,

TABLE 4
HRs of various covariates against ACCM among non-ITN-owning households in 14 pooled datasets

Factor/categorization	HR (95% CI)		
	Children ages 1–59 months	Infants ages 1–11 months	Children ages 12–59 months
Sample size (deaths)	147,141 (4,496)	69,160 (1,880)	126,063 (2,616)
Community ITN coverage (%)			
≤ 30	Reference	Reference	Reference
> 30 and ≤ 50	1.030 (0.905–1.173)	1.151 (0.958–1.384)	0.941 (0.794–1.128)
> 50	0.932 (0.748–1.163)	1.062 (0.783–1.441)	0.825 (0.598–1.136)
Wealth quintile			
1	Reference	Reference	Reference
2	0.962 (0.885–1.046)	0.971 (0.852–1.105)	0.958 (0.860–1.067)
3	0.959 (0.876–1.050)	1.002 (0.873–1.151)	0.930 (0.826–1.047)
4	0.939 (0.846–1.042)	0.949 (0.809–1.112)	0.935 (0.815–1.072)
5	0.754* (0.653–0.869)	0.770† (0.622–0.954)	0.745‡ (0.617–0.900)
Mother's education			
None	Reference	Reference	Reference
Some primary	1.046 (0.958–1.143)	1.041 (0.912–1.187)	1.046 (0.928–1.178)
Completed primary or higher	0.834* (0.758–0.918)	0.841† (0.728–0.972)	0.822‡ (0.724–0.933)
Mother's age at first pregnancy (years)			
≥ 18	Reference	Reference	Reference
< 18	1.068† (1.004–1.135)	1.034 (0.940–1.139)	1.099† (1.015–1.191)
Previous birth interval (months)			
≥ 24	Reference	Reference	Reference
< 24	1.575* (1.466–1.692)	1.771* (1.583–1.982)	1.430* (1.303–1.570)
Child is first born	1.119‡ (1.032–1.213)	1.275* (1.129–1.440)	1.006 (0.903–1.121)
Child is twin or triplet			
No	Reference	Reference	Reference
Yes	2.405* (2.127–2.719)	3.048* (2.568–3.618)	1.931* (1.618–2.305)
Child's sex			
Female	Reference	Reference	Reference
Male	0.945 (0.891–1.003)	0.945 (0.863–1.035)	0.942 (0.872–1.018)
Child's age (months)			
1–5	Reference	Reference	–
6–11	0.737* (0.667–0.815)	0.358* (0.316–0.405)	–
12–23	0.427* (0.383–0.477)	–	Reference
24–35	0.283* (0.249–0.322)	–	0.695* (0.635–0.760)
36–47	0.143* (0.123–0.166)	–	0.363* (0.324–0.406)
48–59	0.072* (0.060–0.086)	–	0.187* (0.161–0.215)
Place of residence			
Urban	Reference	Reference	Reference
Rural	1.012 (0.919–1.115)	1.019 (0.883–1.177)	1.008 (0.889–1.143)
Season			
Not malaria transmission season	Reference	Reference	Reference
Malaria transmission season	1.029 (0.966–1.097)	0.989 (0.896–1.092)	1.054 (0.970–1.145)
Malaria transmission intensity			
2007 <i>P. falciparum</i> prevalence rate (continuous)	2.012* (91.440–2.811)	1.652† (1.011–2.700)	2.380* (1.534–3.692)
DPT ₃ vaccination coverage			
Continuous	0.693* (0.585–0.821)	0.779 (0.606–1.003)	0.646* (0.519–0.804)
Prenatal care coverage			
Continuous	0.875 (0.734–1.043)	1.045 (0.796–1.373)	0.797† (0.640–0.992)

Models included year as a covariate and country as a shared frailty.

* $P < 0.001$.

† $P < 0.05$.

‡ $P < 0.01$.

95% CI = 0.83–1.20), whereas in areas with > 30% ITN coverage, it was associated (HR = 0.87, 95% CI = 0.80–0.96).

DISCUSSION

Using nationally representative cross-sectional household surveys conducted in sub-Saharan Africa from 2006 to 2010, we attempted to examine the community-level protection provided by ITNs against the outcomes of malaria parasite prevalence and ACCM as well as assess if community ITN coverage modified the effect of ITN household possession on these outcomes. Among children in households with one or more ITNs, living in communities with ITN coverage ≥ 30% conferred protection against malaria infection and ACCM

significantly more than living in communities with < 30% community ITN coverage. These data were unable to show a protective effect of community ITN coverage among children in households without an ITN by comparing unprotected children between areas of high and low community ITN coverage. Results also show that community ITN coverage modifies the effect of ITNs as assessed with a community ITN coverage × ITN exposure interaction, with children in households with one or more ITNs having significant protection against parasite infections and ACCM compared with unprotected children, whereas no effect of ITNs was observed in areas with < 30% community ITN coverage.

Because of the fact that individuals use ITNs, ITNs can easily be thought of as an individual-level intervention. Previous

FIGURE 3. Comparison of HRs of community ITN coverage against ACCM among 14 pooled surveys in sub-Saharan Africa for (A) children in households without ITNs and (B) children in households with ITNs. *Community ITN coverage was statistically significant at $P < 0.05$.

studies have estimated the effect that individual-level coverage has had on health outcomes independent of community ITN coverage.^{2,21} We have found, however, that the effect that individual ITN ownership has on reducing risk of ACCM depends on the ITN coverage in the community. Universal coverage of individuals will ensure that communities have a high ITN coverage, but until universal coverage is attained, malaria control programs should seek to assure minimum community ITN coverage.

Previous studies by Hawley and others⁴ and Rowland and others²² failed to find a statistically significant community-level protection among children without ITNs when ITN coverage was $< 25\%$ and 10% , respectively. We find no statistically significant community-level protection for children without ITNs when ITN coverage is as high as 70% compared with children in communities with $\leq 30\%$ ITN coverage. The only documented finding of community-level protection among non-ITN-owning households is from an RCT, when coverage was above 90% . Failure to find a statistically significant community-level protection may suggest that relatively high ITN coverage, perhaps exceeding 70% , is needed for

measurable community-level protection among children in households without any type of mosquito net. It should be noted, however, that, since the year 2010, multiple DHS and MIS datasets have been made publicly available. Inclusion of these datasets in the analysis could potentially change the results and conclusions.

An important limitation of this analysis is the absence of measures of small-scale (PSU-level) time-varying measures of vector population composition and behavior, which may have contributed to not finding a community-level protection among non-ITN users. ITNs will presumably have a greater impact on more anthropophilic and endophilic mosquito populations, such as *Anopheles gambiae* and *An. funestus*; if the prevalent vector is a less anthropophilic species, such as *An. arabiensis*, area-wide effects of ITNs are likely weaker. Furthermore, the failure to find a protective effect among households without nets may be because of a lack of sensitivity of measured indicators. In higher ITN coverage communities, the lack of an ITN may act as a proxy for a general lack of healthcare access.²³ Households in higher ITN coverage communities that lack ITNs may also lack economic resources or

TABLE 5

AORs of household ITN ownership against malaria infection among households in communities with $\leq 30\%$ ITN coverage and communities with $> 30\%$ ITN coverage in six pooled datasets

	AOR of household ITN ownership in communities with $\leq 30\%$ ITN coverage (95% CI)	AOR of household ITN ownership in communities with $> 30\%$ ITN coverage (95% CI)	Likelihood ratio test for interaction between community ITN coverage and household ITN ownership
Children 1–59 months	0.997 (0.827–1.203)	0.874* (0.802–0.955)	1.521
Infants 1–11 months	1.114 (0.643–1.931)	0.632† (0.490–0.815)	3.227
Children 12–59 months	0.977 (0.801–1.193)	0.911‡ (0.830–1.000)	0.386

* $P < 0.01$.

† $P < 0.001$.

‡ $P < 0.05$.

TABLE 6

HRs of household ITN ownership against ACCM among households in communities with $\leq 30\%$ ITN coverage and communities with $> 30\%$ ITN coverage in 14 pooled datasets

	HR of household ITN ownership in communities with $\leq 30\%$ ITN coverage (95% CI)	HR of household ITN ownership in communities with $> 30\%$ ITN coverage (95% CI)	Likelihood ratio test for interaction between community ITN coverage and household ITN ownership
Children 1–59 months	0.959 (0.863–1.065)	0.697* (0.609–0.797)	13.246*
Infants 1–11 months	0.842† (0.713–0.994)	0.579* (0.472–0.709)	7.76‡
Children 12–59 months	1.043 (0.910–1.195)	0.807† (0.674–0.968)	4.686†

* $P < 0.001$.

† $P < 0.05$.

‡ $P < 0.01$.

social capital not captured in our measures socioeconomic status and as such, may suffer differentially from causes of child mortality unrelated to malaria. This relationship is accentuated in infants. A large proportion of ITNs are distributed through ANC, and lack of ownership in high-coverage areas is an indicator of lack of access to life-saving interventions, like neonatal tetanus vaccine, IPT, and iron fortification. Community ITN coverage was protective but not significant at reducing the risk of ACCM among older children without ITNs. Even in sub-Saharan Africa, where malaria is a leading cause of death, it only accounts for approximately 16% of all deaths in children 1–59 months,²⁴ making ACCM a relatively weak indicator when trying to assess the relationship between varying levels of community ITN coverage and child mortality in a dataset with few deaths in key exposure categories.

Higher community ITN coverage often results from villages or districts being targeted by the malaria control program, which would lead to selection bias in this analysis. These data, however, show no association between high community ITN coverage and $PfPR_{2-10}$, higher wealth quintile, mother's education, or being in an urban area. Communities targeted for ITN distributions could still differ in a manner not measured by the covariates included in the analysis. Matching has been previously used to adjust for selection bias,^{2,25} and it was used to assess the degree of protection that household ITN ownership provides at varying degrees of ITN coverage. For the community-level protection analyses, matching was not used; rather, stratifying by ITN ownership removed selection bias at the individual level, and including community as a random effect in the parasite prevalence analysis allowed the intercept estimates to vary among communities and thereby, capture unobserved heterogeneity. We additionally attempted to control for potential selection bias and confounding caused by differential access to healthcare proxied through the proportion of children with fever in the past 2 weeks who received treatment for fevers in the parasite prevalence analysis and the level DPT₃ and ANC coverage in the mortality analysis. Higher levels of treatment-seeking in the community and higher levels of community DPT₃ coverage were associated with decreased odds of parasite prevalence and decreased risk of ACCM, respectively.

A number of additional limitations exist in this study and may have contributed to the null finding of community ITN protection against infection and ACCM among children in households without any mosquito nets. The nature of cross-sectional data makes it impossible to determine if the malaria parasite infection preceded the exposure to community ITN coverage. On average, untreated malaria infections have been estimated to last about 6 months in Africa^{26,27}; most (75%)

ITNs included in this analysis were obtained > 6 months before the malaria parasite test. Misclassification bias caused by poor recall or a definite cutoff of 12 months may have occurred when classifying bed nets as ITNs as well as determining at what age a child died. Because of the lack of available data, we did not include any measurements of indoor residual spraying. Furthermore, the community-level protection observed in households owning ITNs may have been, in part, caused by communities with higher ITN coverage having more ITNs per household, a key factor in determining child ITN use.²⁸

This study did not have sufficient power to detect a saturation effect, where increasing ITN coverage adds no direct health benefit beyond existing ITN coverage, which mathematical models have suggested may be the case.⁸ Identifying the point at which returns for increased ITN coverage are small enough that greater cost-effectiveness could be obtained by investing in case management or other health interventions rather than ITNs will require additional research.

The age of nets was not incorporated as a factor in this analysis because of the high potential for measurement error of retrospective exposure of varying ages of ITNs. Net age is an area for future work. Evidence suggests that the insecticide in LLINs maintains its efficacy up to 3 years^{29,30} or 20 washes³¹; however, holes in nets may decrease their effectiveness,³² and future research should verify that LLINs maintain their effectiveness for preventing both malaria infection and child mortality over time.

These results further reinforce that ITNs seem to provide better protection against infection and ACCM when community ITN coverage of $\geq 30\%$ is achieved. These results, therefore, confirm the importance of malaria control programs to quickly achieve and sustain high universal ITN coverage across communities. Because of the heterogeneity of ITN coverage within a country, malaria control programs should explore ways of monitoring community ITN coverage at the local level rather than relying only on national-level estimates that typically only provide data at the regional level.

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REFERENCES

- Lengeler C, 2004. Insecticide-treated bed nets and curtains for preventing malaria. *Cochrane Database Syst Rev* 2: CD000363.
- Lim SS, Fullman N, Stokes A, Ravishanker N, Masiye F, Murray CJL, Gakidou E, 2011. Net benefits: a multicountry analysis of observational data examining associations between insecticide-treated mosquito nets and health outcomes. *PLoS Med* 8: e1001091.
- Gimnig JE, Kolczak MS, Hightower AW, Vulule JM, Schoute E, Kamau L, Phillips-Howard PA, Kuile Ter FO, Nahlen BL, Hawley WA, 2003. Effect of permethrin-treated bed nets on the spatial distribution of malaria vectors in western Kenya. *Am J Trop Med Hyg* 68 (Suppl): 115–120.
- Hawley WA, Phillips-Howard PA, Kuile Ter FO, Terlouw DJ, Vulule JM, Ombok M, Nahlen BL, Gimnig JE, Kariuki SK, Kolczak MS, Hightower AW, 2003. Community-wide effects of permethrin-treated bed nets on child mortality and malaria morbidity in western Kenya. *Am J Trop Med Hyg* 68 (Suppl): 121–127.
- Binka F, Indome F, Smith T, 1998. Impact of spatial distribution of permethrin-impregnated bed nets on child mortality in rural northern Ghana. *Am J Trop Med Hyg* 59: 80–85.
- Howard SC, Omumbo J, Nevill C, Some ES, Donnelly CA, Snow RW, 2000. Evidence for a mass community effect of insecticide-treated bednets on the incidence of malaria on the Kenyan coast. *Trans R Soc Trop Med Hyg* 94: 357–360.
- Klinkenberg E, Onwona-Agyeman KA, McCall PJ, Wilson MD, Bates I, Verhoeff FH, Barnish G, Donnelly MJ, 2010. Cohort trial reveals community impact of insecticide-treated nets on malariometric indices in urban Ghana. *Trans R Soc Trop Med Hyg* 104: 496–503.
- Killeen GF, Smith TA, Ferguson HM, Mshinda H, Abdulla S, Lengeler C, Kachur SP, 2007. Preventing childhood malaria in Africa by protecting adults from mosquitoes with insecticide-treated nets. *PLoS Med* 4: e229.
- Gosoni L, Vounatsou P, Tami A, Nathan R, Grundmann H, Lengeler C, 2008. Spatial effects of mosquito bednets on child mortality. *BMC Public Health* 8: 356.
- Flaxman AD, Fullman N, Otten MW, Menon M, Cibulskis RE, Ng M, Murray CJL, Lim SS, 2010. Rapid scaling up of insecticide-treated bed net coverage in Africa and its relationship with development assistance for health: a systematic synthesis of supply, distribution, and household survey data. *PLoS Med* 7: e1000328.
- Roll Back Malaria; MEASURE Evaluation; World Health Organization; Unicef, 2004. *Guidelines for Core Population Coverage Indicators for Roll Back Malaria: To Be Obtained from Household Surveys*. Calverton, MD: MEASURE Evaluation.
- Filmer D, Pritchett LH, 2001. Estimating wealth effects without expenditure data—or tears: an application to educational enrollments in states of India. *Demography* 38: 115–132.
- Hay SI, Guerra CA, Gething PW, Patil AP, Tatem AJ, Noor AM, Kabaria CW, Manh BH, Elyazar IRF, Brooker S, Smith DL, Moyeed RA, Snow RW, 2009. A world malaria map: *Plasmodium falciparum* endemicity in 2007. *PLoS Med* 6: e1000048.
- Craig MH, Snow RW, le Sueur D, 1999. A climate-based distribution model of malaria transmission in sub-Saharan Africa. *Parasitol Today* 15: 105–111.
- Bates D, Maechler M, Bolker B, 2011. *lme4: Linear Mixed-Effects Models Using Eigen and S4*. Available at: <http://CRAN.R-project.org/package=lme4>. Accessed December 1, 2010.
- R Development Core Team, 2010. *R: A Language and Environment for Statistical Computing*. Available at: <http://www.R-project.org/>.
- Ho D, Imai K, King G, Stuart EA, 2007. *MatchIt: Nonparametric Preprocessing for Parametric Causal Inference*. Citeseer. Cambridge, MA: Harvard.
- Choe MK, 1981. Fitting the age pattern of infant and child mortality with the Weibull survival distribution. *Asian Pac Cens Forum* 7: 10–13.
- Andersen PK, Klein JP, Knudsen KM, Tabanera y Palacios R, 1997. Estimation of variance in Cox's regression model with shared gamma frailties. *Biometrics* 53: 1475–1484.
- Griffin JT, Hollingsworth TD, Okell LC, Churcher TS, White M, Hinsley W, Bousema T, Drakeley CJ, Ferguson NM, Basáñez MG, Ghani AC, 2010. Reducing *Plasmodium falciparum* malaria transmission in Africa: a model-based evaluation of intervention strategies. *PLoS Med* 7: e1000324.
- Fegan G, Noor A, Akhwale W, Cousens S, Snow R, 2007. Effect of expanded insecticide-treated bednet coverage on child survival in rural Kenya: a longitudinal study. *Lancet* 370: 1035–1039.
- Rowland M, Bouma M, Ducornez D, Durrani N, Rozendaal J, Schapira A, Sondorp E, 1996. Pyrethroid-impregnated bed nets for personal protection against malaria for Afghan refugees. *Trans R Soc Trop Med Hyg* 90: 357–361.
- Larsen DA, Keating J, Miller J, Bennett A, Changufu C, Katebe C, Eisele TP, 2010. Barriers to insecticide-treated mosquito net possession 2 years after a mass free distribution campaign in Luangwa District, Zambia. *PLoS ONE* 5: e13129.
- Black RE, Cousens S, Johnson HL, Lawn JE, Rudan I, Bassani DG, Jha P, Campbell H, Walker CF, Cibulskis R, Eisele T, Liu L, Mathers C; Child Health Epidemiology Reference Group of WHO and UNICEF, 2010. Global, regional, and national causes of child mortality in 2008: a systematic analysis. *Lancet* 375: 1969–1987.
- Eisele TP, Larsen DA, Anglewicz PA, Keating J, Yukich J, Bennett A, Hutchinson P, Steketee RW, 2012. Malaria prevention in pregnancy, birthweight, and neonatal mortality: a meta-analysis of 32 national cross-sectional datasets in Africa. *Lancet Infect Dis* 12: 942–949.
- Smith DL, Dushoff J, Snow RW, Hay SI, 2005. The entomological inoculation rate and *Plasmodium falciparum* infection in African children. *Nature* 438: 492–495.
- Bretscher MT, Maire N, Chitnis N, Felger I, Owusu-Agyei S, Smith T, 2011. The distribution of *Plasmodium falciparum* infection durations. *Epidemics* 3: 109–118.
- Eisele TP, Keating J, Littrell M, Larsen D, Macintyre K, 2009. Assessment of insecticide-treated bednet use among children and pregnant women across 15 countries using standardized national surveys. *Am J Trop Med Hyg* 80: 209–214.
- Kilian A, Byamukama W, Pigeon O, Atieli F, Duchon S, Phan C, 2008. Long-term field performance of a polyester-based long-lasting insecticidal mosquito net in rural Uganda. *Malar J* 7: 49.
- Erlanger TE, Enayati AA, Hemingway J, Mshinda H, Tami A, Lengeler C, 2004. Field issues related to effectiveness of insecticide-treated nets in Tanzania. *Med Vet Entomol* 18: 153–160.
- Sreehari U, Raghavendra K, Rizvi MMA, Dash AP, 2009. Wash resistance and efficacy of three long-lasting insecticidal nets assessed from bioassays on *Anopheles culicifacies* and *Anopheles stephensi*. *Trop Med Int Health* 14: 597–602.
- Rehman AM, Coleman M, Schwabe C, Baltazar G, Matias A, Gomes IR, Yellott L, Aragon C, Nchama GN, Mzilawo T, Rowland M, Kleinschmidt I, 2011. How much does malaria vector control quality matter: the epidemiological impact of holed nets and inadequate indoor residual spraying. *PLoS ONE* 6: e19205.