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Effect of expanded insecticide-treated bednet coverage on child survival in rural Kenya: a longitudinal study

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Summary

Background—The potential of insecticide-treated bednets (ITNs) to contribute to child survival has been well documented in randomised controlled trials. ITN coverage has increased rapidly in Kenya from 7% in 2004 to 67% in 2006. We aimed to assess the extent to which this investment has led to improvements in child survival.

Methods—A dynamic cohort of about 3500 children aged 1–59 months were enumerated three times at yearly intervals in 72 rural clusters located in four districts of Kenya. The effect of ITN use on mortality was assessed with Poisson regression to take account of potential effect-modifying and confounding covariates.

Findings—100 children died over 2 years. Overall mortality rates were much the same in the first and second years of the study (14.5 per 1000 person-years in the first year and 15.4 per 1000 person-years in the second). After adjustment for age, time period, and a number of other possible confounding variables, ITN use was associated with a 44% reduction in mortality (mortality rate ratio 0.56, 95% CI 0.33–0.96; $p=0.04$). This level of protection corresponds to about seven deaths averted for every 1000 ITNs distributed.

Interpretation—A combined approach of social marketing followed by mass free distribution of ITNs translated into child survival effects that are comparable with those seen in previous randomised controlled trials.

Introduction

The benefit of using insecticide-treated bednets (ITNs) in Africa has been shown through carefully controlled efficacy trials, resulting in a pooled estimate of a 20% reduction in all cause mortality in children aged under 5 years. However, when delivered outside experimental settings as part of national programmes, the impressive results obtained during

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efficacy trials might be constrained by lower coverage, poor compliance, or differentials in use by wealthier communities at lower risk of child mortality. The difference between efficacy and effectiveness has implications for the cost-effectiveness of ITN distribution in Africa. The effect of ITNs on mortality when delivered under operational conditions has only been measured in The Gambia, as part of a national campaign, and in one district in Tanzania after the promotion of socially marketed ITNs. Here, we assess the effect on child survival of a combined approach of social marketing and free distribution of ITNs in Kenya that resulted in a rapid increase in ITN use by children aged less than 5 years from 7% in 2004, to 23.5% in 2005, to 67% in 2006.

Methods

Participants and procedures

The establishment of prospective surveillance in a sample of rural communities in four sentinel districts (Bondo, Kwale, Makueni, and Kisii) has been described in detail elsewhere. In brief, all homesteads within 18 randomly selected communities in each district were mapped with GPS (Garmin etrex, Garmin [Europe] Ltd, Southampton, UK). Homesteads that agreed to participate were recruited into the homestead cohort and de-jure resident homestead members were enumerated, including details of date of birth and sex, and each homestead member issued a unique identifier. All children aged less than 5 years, resident at a census in December, 2004, to January, 2005, were recruited into the cohort and were revisited in 2005–06 and 2006–07 to track the ownership and use of bednets. Free mass distribution of bednets occurred in Kisii and Bondo in July, 2006, integrated with a measles campaign, and in Kwale and Makueni in Sept, 2006, as a stand-alone campaign. Children exited the cohort if at subsequent census rounds they had out-migrated, their parent or guardian refused continued participation, or they had reached their fifth birthday, or had died. Children who in-migrated or were born during the interval between census rounds were added to the cohort. New births that did not survive the interval between census rounds were also included in the cohort. In-migrants who out-migrated between the census rounds were not included in the cohort.

At each cross-sectional survey, bednet use among surviving children was ascertained, including whether the child was reported as usually using a net, and if so, whether they used a net the previous night. For all those who were reported as usually using a net, whether this net had been treated with insecticide, and if so, whether it had been treated within 6 months, was also recorded. Deaths were investigated separately through interviews with bereaved relatives. During these interviews net use and net treatment before the terminal illness was ascertained in a manner similar to that for surviving children. Deaths that occurred after 28 days of life and before the fifth birthday were the focus of the present study, consistent with efficacy trials done in the 1990s.

Child years of exposure were calculated after subdividing the study period into four 6-month periods from baseline until the last enumeration, and a child was deemed to have used an ITN if the enumeration identified a child as usually using a net that had either been treated within the last 6 months or was a longlasting ITN. Since the re-enumeration rounds took place once a year, there were no data on whether the net was retreated at the midpoint of a year. Thus, an assumption was made that a net was continuously effective, and thus the child exposed to the effect of a net, if the net had been retreated in the two adjacent 6-month periods. Within a period where a child was indicated to have started to use an ITN, based on the date of net acquisition provided during interviews with mothers or guardians, the date of acquisition was used to define the months of use. For example, a child born before July 1, 2006, and who survived to the end of the study and began to use an effective net in September, 2006, contributed 3 months of non-net use to the period July–December, 2006,

and 3 months of net use to the same period. The exposure time was calculated for each of the age categories a child passed through during each of the four periods. For children who out-migrated or were age-censored we assumed that their net status did not change between the last time they were enumerated and the date they exited the cohort.

A number of covariates potentially related to mortality were recorded during the study: the child's age and sex; their mother's age and education; and indicators of homestead economic status. District-specific wealth quintiles were created by use of principal components analysis, on the basis of the education level and occupation of the homestead head, housing characteristics (type of wall, roof, and floor), source of drinking water; type of sanitation facility, homestead size, and number of people per sleeping room. Within each district, transport routes and topography, government, mission and private health services, and physical barriers to travel (hills, rivers, and protected areas) were all mapped with GPS and assembled in ARCGIS version 9.0. A travel time algorithm developed in C++ code was used to define speed differentials along the various footpath and road surfaces to curative services to estimate each homestead's physical access to treatment in minutes. Previous work has suggested indirect benefits to non-users of bednets at the community level, and a community-level ITN density measure was constructed on the basis of the number of ITNs per head per cluster and classified in quartiles in the Poisson regression analysis.

The longitudinal surveys were approved by the KEMRI National Ethical Review Committee (KEMRI SSC numbers 906 and 1107).

Statistical analysis

All statistical analyses were done with Stata version 9.2. Mortality rates were calculated for ITN users and non-users, and Poisson regression was used to control for potential confounding of the association between ITN use and mortality, with a random effect term used to model variation between communities. To estimate the number of deaths averted as recommended we applied the rate ratios obtained to the unexposed group.

Role of the funding source

The funding source had no role in the design, conduct, data collection, analysis, or interpretation of this study. GWF had full access to all the data. RWS had final responsibility for the decision to submit for publication.

Results

Between January, 2005, and December, 2006, there were 133 deaths in total, with 100 deaths in children aged 1–59 months identified among a mean cohort of 3484 children seen over the 2 years of observation. 17 of the 33 neonatal deaths occurred in the first year, with the remaining 16 in the second year. These neonatal deaths were excluded from our analyses. The median follow-up time per child was 1.74 (IQR 1.00–1.94) years, with a total time at risk for the whole cohort of 6706 years. Out-migration rates among the cohort were 9.4% (n=390) in the first year and 9.2% (338) in the second year. Refusal rates were 0.8% (33) during the first year and 0.9% (33) in the second year. There were 257 in-migrants; 193 in year 1 and 64 in year 2. 659 new births were identified in the first year and 517 in the second. 52 deaths occurred before the end of the first year of observation (mortality rate 14.5 deaths per 1000 person-years). By the end of the second year, a further 48 deaths had occurred (mortality rate 15.4 deaths per 1000 person-years). 87 of the deaths occurred in Bondo and Kwale, which are located in areas that support high levels of *Plasmodium falciparum* transmission compared with the semi-arid (Makueni) or epidemic prone (Kisii) districts.

Mortality rates by age, district, calendar year, and ITN use are shown in table 1. In the first year, the mortality rate in users of ITNs was 13.7 per 1000 person-years of follow-up, compared with 14.9 per 1000 person-years in non-users, which corresponds to a rate ratio of 0.92 (95% CI 0.39–2.15). Controlling for district and age-group resulted in an adjusted rate ratio of 0.60 (0.25–1.43). In the second year the mortality rates were 11.3 per 1000 person-years in ITN users compared with 17.9 per 1000 person-years in non-users, corresponding to a rate ratio of 0.63 (0.34–1.20). Adjustment for district and age-group resulted in an adjusted rate ratio of 0.57 (0.30–1.09). The combined, adjusted rate ratio for the 2 years was 0.58 (0.35–0.98; $p=0.04$). Poisson regression was used to adjust for possible confounding factors (table 2). When district was not included in the model (model B) there was strong evidence of between-cluster variation ($p<0.0001$). However, after inclusion of district in the model (model A) there was no evidence of between-cluster variation ($p=1.0$), indicating that although mortality rates vary substantially between districts, there is no evidence of important between-cluster variation within a district. Over the 2-year observation period, after controlling for potential confounding factors and using a random effect to account for the cluster sampling framework, ITN use was associated with a 44% reduction in mortality (95% CI 4–67; $p=0.04$; table 2, model B). Restricting this analysis to the two more malaria-prone areas yielded a rate ratio of 0.50 (0.28–0.90; $p=0.02$). We examined whether the effect of ITNs varied between districts or from year to year. There was little or no evidence of such variation (likelihood ratio χ^2 0.16, df 1, $p=0.69$ for district; likelihood ratio χ^2 4.15, df 3, $p=0.5$ for year).

If ITN use is indeed associated with a 44% reduction in mortality, the scaling-up of ITN coverage could avert seven (95% CI 1–11) deaths for every 1000 ITNs used. However, there is considerable mortality variation by area, ranging from 22 (2–34) averted deaths per 1000 ITNs distributed in Bondo to one (0–2) averted death per 1000 ITNs distributed in Makueni.

Discussion

ITN coverage in the four Kenyan districts reported here rose from 7% at the end of 2004 to 67% by the end of 2006. This alone represents a substantial improvement in coverage of one of the most efficacious and cheap evidence-based child survival tools to have emerged in recent years. However, national governments and bilateral and multinational agencies often cannot determine whether increasing disease-specific intervention coverage contributes to improvements in child survival. Here, we have assembled data on child mortality and ITN use in an effort to determine the effect of changes in coverage to risk of death among children aged 1–59 months. The estimated rate of mortality in children reported to have used a recently treated bednet was about 56% of that for children who did not use an ITN, a protective efficacy of 44%. Using these estimates of protection, we estimate that the scaling-up of ITN coverage might have averted about seven deaths for every 1000 ITNs used. However, there is considerable mortality variation by area—the effects were greatest in areas of reported high malaria transmission. This finding has implications for future estimation of possible numbers of deaths averted through the combined campaigns between 2003 and 2006. Clearly, despite high coverage across the varied malaria ecologies in Kenya, the numbers of lives saved will be greatest in high endemic settings and least in areas where transmission is low or very over-dispersed.

Despite the estimated mortality rate for children who used ITN being about half that of those who did not use an ITN, the overall mortality rate in the child population did not change appreciably over the 2 years of observation. One possible explanation for these apparently contradictory results is that there was a drought during the first year of observation that would have affected malaria transmission, and that during this period the effects of wealth status were most marked. During the second year rainfall was more than twice that recorded

during the first year and the mass distribution of free ITNs, which took place in the second half of the second year, removed all inequities in use.

Our study design did not seek to measure specifically the relative contribution of a mass effect on local vector population survival or disease risks. However, our results did not show evidence of a mass effect over and above that of individual protection when adjusted for quartiles of community enumerated net coverage (table 2). Another possible confounding effect could have been the introduction of new antimalarial drugs, especially the arthemether-containing treatments that are known to have anti-gametocyte activity and hence have the potential to reduce malaria transmission. Artemether-lumefantrine was starting to be deployed in government clinics between July and September, 2006, with nationwide coverage achieved during the last quarter of 2006. We have done a cross-sectional survey in the same four districts as described here in August, 2006. During this survey the proportion of children reporting a fever in the last 14 days who were treated with arthemether-lumefantrine was 1.3% (unpublished data), and the proportion reporting being treated within 48 hours with arthemether-lumefantrine was only 0.6%. Neither indicator suggests that changing access to effective arthemether-containing medicines would have greatly affected the mortality effects reported here.

The size of effect is particularly striking because it is greater than the pooled estimate of protection under conditions of efficacy trials. We attempted to control for several important covariates associated with child survival, but there will be covariates we have not included and our definition of exposure might have an element of bias. Unlike carefully controlled trials, and given the ethical constraints of repeated investigations of cohorts of children not sleeping under nets, we cannot be completely certain about the reported use of the ITNs by children who died. A further possible source of bias is that some of those who had either out-migrated or were age-censored by reaching age 5 between the midpoint survey and the last cross-sectional survey could have been deaths. However, among this subset of children the proportion of ITN users at the time of the midpoint survey was the same as the overall population and any bias that such missed deaths could have introduced is likely to be non-differential. Further, given the advanced age of these children, the probability of death among such children has to be fairly small (table 2).

The national estimate of protection afforded through the expansion of the Kenyan ITN delivery programme might be more conservative than we have shown in districts that were able to achieve over 67% coverage. We are nevertheless confident that a substantial effect on child survival was achieved during the expansion phase of the ITN strategy and might have reduced by over a third the numbers of childhood deaths in high coverage districts in 2006. Donor agencies should regard this as money well spent and recognise that the challenge is now to maintain and increase funding to expand coverage further.

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GWF was responsible for the data assembly, analysis, and producing the final manuscript. AMN was responsible for design and implementation of the data collection, collation, and preparation, and assisted in the preparation of the manuscript. WSA is head of the Division of Malaria Control, Kenyan Ministry of Health, and provided the necessary interface with community leaders and helped prepare the manuscript. SC assisted with the statistical analysis, interpretation of the results, and assisted in the preparation of the manuscript. RWS was responsible for the conception and continued funding of the project and its overall scientific management, analysis, interpretation and preparation of the final manuscript.

Acknowledgments

We declare that we have no conflict of interest.

Table 1

Deaths, person-years of observation, and mortality rates by period of follow-up, district, and age

	Dec 04–Jan 05 to Dec 05–Jan 06			Dec 05–Jan 06 to Dec 06–Jan 07			Combined follow-up time			
	Total*	With ITN	No ITN	Total*	With ITN	No ITN	Total*	With ITN	No ITN	
Bondo										
1–5 months	8/64.2 (124.6)	1/15.4 (65.0)	7/45.7 (153.2)	4/54.3 (73.7)	2/18.5 (108.1)	2/35.7 (56.0)	12/118.5 (101.3)	3/33.9 (88.48)	9/108.5 (101.3)	
6–11 months	9/81.2 (110.8)	3/20.4 (147.4)	6/57.9 (103.6)	8/61.5 (130.0)	2/32.7 (61.2)	6/28.9 (207.6)	17/142.8 (119.0)	5/53.0 (94.3)	12/119.0 (119.0)	
1–5 years	13/563.2 (23.1)	0/111.2 (0.0)	13/442.6 (29.4)	16/465.1 (34.4)	6/197.7 (30.4)	10/265.4 (37.7)	29/1028.3 (28.2)	6/308.9 (19.4)	23/1028.3 (28.2)	
Rate ratio [†]		0.50 (0.17–1.47; p=0.20)			0.70 (0.33–1.48; p=0.35)			0.62 (0.33–1.14; p=0.12)		
Kisii										
1–5 months	1/87.0 (11.5)	0/10.5 (0.0)	1/75.0 (13.3)	2/65.5 (30.5)	2/27.4 (72.9)	0/38.1 (0.0)	3/152.6 (19.7)	2/37.9 (52.8)	1/75.0 (13.3)	
6–11 months	0/109.4 (0.0)	0/14.1 (0.0)	0/94.2 (0.0)	0/72.9 (0.0)	0/33.4 (0.0)	0/39.5 (0.0)	0/182.3 (0.0)	0/47.5 (0.0)	0/72.9 (0.0)	
1–5 years	5/708.9 (7.1)	1/93.3 (10.7)	4/607.6 (6.6)	1/639.6 (1.6)	0/260.8 (0.0)	1/375.8 (2.7)	6/1348.5 (4.4)	1/354.1 (2.8)	5/708.9 (7.1)	
Rate ratio [†]		1.32 (0.15–11.39; p=0.80)			2.84 (0.25–32.04; p=0.38)			1.91 (0.39–9.30; p=0.43)		
Kwale										
1–5 months	2/93.8 (21.3)	0/9.1 (0.0)	2/83.0 (24.1)	0/73.2 (0.0)	0/21.5 (0.0)	0/51.6 (0.0)	2/167.0 (12.0)	0/30.6 (0.0)	2/93.8 (21.3)	
6–11 months	2/132.2 (15.1)	0/11.6 (0.0)	2/117.8 (17.0)	2/101.0 (19.8)	0/31.1 (0.0)	2/69.0 (29.0)	4/233.2 (17.1)	0/42.7 (0.0)	2/132.2 (15.1)	
1–5 years	9/1003.6 (9.0)	0/78.1 (0.0)	9/904.2 (10.0)	14/898.5 (15.6)	1/258.3 (3.9)	13/638.2 (20.4)	23/1902.1(12.1)	1/336.4 (3.0)	9/1003.6 (9.0)	
Rate ratio [†]		0 (0–3.67; p=0.27) [‡]			0.16 (0.02–1.23; p=0.04) [§]			0.13 (0.02–1.02; p=0.16)		
Makueni										
1–5 months	1/66.8 (15.0)	1/7.7 (129.9)	0/58.4 (0.0)	0/47.7 (0.0)	0/20.7 (0.0)	0/27.0 (0.0)	1/114.5 (8.7)	1/28.4 (35.2)	0/66.8 (15.0)	
6–11 months	0/87.4 (0.0)	0/11.8 (0.0)	0/74.0 (0.0)	0/59.9 (0.0)	0/26.4 (0.0)	0/33.5 (0.0)	0/147.3 (0.0)	0/38.2 (0.0)	0/87.4 (0.0)	
1–5 years	2/595.7 (3.4)	0/55.6 (0.0)	2/521.1 (3.8)	1/572.8 (1.7)	0/218.7 (0.0)	1/350.5 (2.9)	3/1168.4 (2.6)	0/274.3 (0.0)	2/595.7 (3.4)	
Rate ratio [†]		4.58 (0.38–55.8; p=0.19)			0 (0–60.3; p=0.43) [‡]			1.53 (0.21–10.95; p=0.72)		
Overall										
1–59 months	52/3593.6 (14.5)	6/438.9 (13.7)	46/3081.7 (14.9)	48/3112.9 (15.4)	13/1147.2 (11.3)	35/1953.2 (17.9)	100/6705.6 (14.9)	19/1586.1 (12.0)	84/3593.6 (14.5)	
Rate ratio [¶]		0.60 (0.25–1.43; p=0.24)			0.57 (0.30–1.09; p=0.09)			0.58 (0.35–0.98; p=0.04)		

Data are deaths/person-years (rate per 1000 person-years) or rate ratio (95% CI; p value).

* Person-year totals are larger than the sum of the nets and non-nets person times due to missing data for net status.

[†] Mantel-Haenszel adjusted on age-group and also year for combined follow-up time.[‡] Not adjusted for age due to lack of data but exact values computed.[§] Test is approximate, hence discrepancy between 95% CI including one and p value being less than 0.05.[¶] Adjusted for age-group and district for the yearly surveys and also for year when combined.

Table 2

Adjusted mortality rate ratios*

	Model A	Model B
Use ITN	0.51 (0.30–0.87; p=0.01)	0.56 (0.33–0.96; p=0.04)
District [†]		
Kisii	0.12 (0.06–0.24; p<0.0001)	..
Kwale	0.26 (0.16–0.41; p<0.0001)	..
Makueni	0.06 (0.02–0.17; p<0.0001)	..
Year (2005 vs 2006)	0.75 (0.50–1.13; p=0.17)	0.75 (0.50–1.13; p=0.18)
Sex (female)	0.68 (0.45–1.02; p=0.06)	0.66 (0.44–0.99; p=0.05)
Child's age [‡]		
6–11 months	0.96 (0.51–1.81; p=0.90)	0.94 (0.50–1.77; p=0.85)
1–2 years	0.87 (0.49–1.52; p=0.62)	0.84 (0.48–1.47; p=0.54)
2–3 years	0.28 (0.14–0.58; p=0.001)	0.28 (0.14–0.57; p=0.0003)
3–4 years	0.14 (0.06–0.35; p<0.0001)	0.14 (0.05–0.35; p<0.0001)
4–5 years	0.09 (0.03–0.30; p<0.0001)	0.09 (0.03–0.30; p<0.0001)
Mother had some education [§]	0.87 (0.44–1.72; p=0.73)	1.11 (0.61–2.03; p=0.73)
Mother >30 years old	0.88 (0.56–1.37; p=0.58)	0.83 (0.53–1.29; p=0.41)
Wealth quintile [¶]		
Second	1.11 (0.60–2.04; p=0.75)	1.12 (0.60–2.10; p=0.73)
Third	1.30 (0.72–2.34; p=0.39)	1.34 (0.72–2.54; p=0.34)
Fourth	1.18 (0.63–2.22; p=0.61)	1.30 (0.66–2.55; p=0.45)
Fifth	1.23 (0.63–2.37; p=0.55)	1.44 (0.71–2.94; p=0.31)
Tertile of distance to health facility		
Middle	1.17 (0.69–1.98; p=0.57)	1.07 (0.59–1.94; p=0.83)
Furthest	1.08 (0.63–1.86; p=0.78)	1.01 (0.52–1.96; p=0.97)
Quartiles of net coverage of each enumeration area ^{**}		
Second	1.01 (0.59–1.72; p=0.98)	1.25 (0.57–2.72; p=0.58)
Third	0.55 (0.28–1.01; p=0.08)	0.58 (0.24–1.41; p=0.23)
Fourth	1.32 (0.73–2.37; p=0.36)	1.11 (0.49–2.54; p=0.80)

Data are rate ratio (95% CI; p value).

* Cluster (ie, community) level random effects parameter (θ) in model A was 0.00 (95% CI 0–0; p=1.0), and in model B was 0.67 (95% CI 0.29–1.53; p<0.0001).

[†] Reference group is Bondo.

[‡] Reference group is 1–5 month olds.

[§] Taken from models with 97 rather than 100 deaths due to missing values of maternal education; all other parameter values remained essentially unchanged.

[¶] Reference group is most poor—ie, first wealth quintile.

^{||} Middle corresponds to a range of about 30 min to 1 h. Furthest corresponds to about 1–5 h.

** Second ranges from 23% to 30%, third ranges from 30% to 35%, fourth from 35% to 62%.