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Marked Increase in Child Survival after Four Years of Intensive Malaria Control

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Abstract. In malaria-endemic countries in Africa, a large proportion of child deaths are directly or indirectly attributable to infection with *Plasmodium falciparum*. Four years after high coverage, multiple malaria control interventions were introduced on Bioko Island, Equatorial Guinea, changes in infection with malarial parasites, anemia, and fever history in children were estimated and assessed in relation to changes in all-cause under-5 mortality. There were reductions in prevalence of infection (odds ratio [OR] = 0.31, 95% confidence interval [CI] = 0.2–0.46), anemia (OR = 0.11, 95% CI = 0.07–0.18), and reported fevers (OR = 0.41, 95% CI = 0.22–0.76) in children. Under-5 mortality fell from 152 per 1,000 births (95% CI = 122–186) to 55 per 1,000 (95% CI = 38–77; hazard ratio = 0.34 [95% CI = 0.23–0.49]). Effective malaria control measures can dramatically increase child survival and play a key role in achieving millennium development goals.

INTRODUCTION

Reducing under-5 mortality is a target in the Millennium Development Goals (MDG), the Abuja Declaration on Roll Back Malaria, and the Global Malaria Action Plan.[1–3] In malaria-endemic countries in Africa, a large proportion of child deaths are directly or indirectly attributable to infection with *Plasmodium falciparum*.[4,5] Previous studies have shown the effectiveness of insecticide-treated bed nets (ITN), artemisinin-based combination therapy (ACT), and indoor residual spraying (IRS) in controlling malaria transmission.[6–8]

Increased donor funding to combat malaria has resulted in comprehensive integrated malaria control interventions being implemented in a number of sub-Saharan African countries.[9–11] Although malaria-attributable mortality can usually not be measured, there is an expectation that these combined interventions will have a major impact on child survival[4] as a result of the large proportion of deaths caused by malaria.[12] In countries where disease-specific mortality statistics are unavailable, it has been argued that reductions in all-cause child mortality can be attributed to malaria control efforts if improvements are found in steps on the causal pathway between the scaling up of programmatic efforts and mortality.[13]

Bioko, Equatorial Guinea, is an island in the Gulf of Guinea, with ~200,000 inhabitants. The Bioko Island Malaria Control Project (BIMCP) was launched in 2003 with funding from a consortium led by Marathon Oil Corporation and from the Government of Equatorial Guinea. In this study, we report on changes in malaria transmission indicators and in all-cause under-5 mortality that were recorded over a 4-year period after implementation of comprehensive malaria control measures.[14–16]

MATERIALS AND METHODS

Study setting. After the discovery of offshore oil reserves in the 1990s, Equatorial Guinea experienced rapid economic growth, resulting in gross national product per capita exceeding US$10,000/yr by 2007,[17] with concomitant, if not commensurate, overall improvements in living standards. For example, households with access to piped water either in their own home or from a public tap increased from 38% in 2000 (Multiple Indicator Cluster Survey, unpublished data, 2000) to 54% in 2008 (BIMCP household survey, 2008). There are no recent estimates of immunization coverage; WHO Immunization Summary[18] reports coverage of third dose of diphtheria and tetanus toxoid with pertussis vaccine (DTP3) and measles-containing vaccine (MCV) to have remained at 33% and 51%, respectively, from 2000 to 2007, but this may be a result of the data from 2000 being projected forward in the absence of more recent figures. Equatorial Guinea is currently undergoing major development of its infrastructure. However, as recently as 2005, the United Nations Development Program (UNDP) ranked Equatorial Guinea 127th on the Human Development Index.[19]

Mean annual rainfall in Bioko is ~2,000 mm/yr, peaking at ~300 mm/mo in August and September. Before the introduction of intensive malaria control measures in 2004, transmission intensity exceeded 700 infective bites per person per year,[20] and estimates of community prevalence of infection in children younger than 10 years of age generally exceeded 50%.[21] Malaria transmission is year round, but pre-intervention outpatient records from the Luba district hospital suggested that transmission was highest in the month of October.

Malaria control measures. BIMCP intervention activities were launched in March 2004 with a comprehensive IRS program spraying all houses initially with the synthetic pyrethroid Deltamethrin (Bayer Crop Science, Isando, South Africa) and from January 2005 twice yearly with the carbamate insecticide Ficam (Bayer), assuming a residual effect of ~6 months.[15,22] By mid-2008, a total of eight rounds of insecticide had been sprayed. ACT, consisting of oral artesunate with sulfadoxine-pyrimethamine (SP), was introduced free of charge to children < 15 years and pregnant women as the first-line treatment in March 2005, in association with routine definitive diagnosis, the training of doctors and nurses in case management according to the national treatment policy, and Intermittent Preventative Treatment of pregnant women (IPTp) with two doses of SP, at least 30 days apart. In October 2007, vector control was intensified through a universal door to door campaign to distribute and hang long-lasting insecticide-treated nets (LLINs) to cover all sleeping areas, free of charge to the user. Adherence to all components of the intervention was promoted through information, education, and communications (IEC) campaigns.

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Monitoring and evaluation. Surveillance was based on a system of sentinel areas surrounding the sites shown in Figure 1,[14,16] which include 86% of all houses in Bioko according to a recent census carried out by BIMCP. The 2004 mortality survey did not include three sites (Moca, Santa Maria, and Punta Europa), representing ~9.5% of households; data from these three sites were excluded from all comparisons of the 2004 and 2008 mortality data.

Surveys were carried out on random cross-sections of households in each of the sentinel areas in February to April of each year from 2004 to 2008 using a survey instrument adapted from the malaria indicator survey developed by the Roll Back Malaria Monitoring and Evaluation Reference Group.[23] Houses were sampled systematically from hand-drawn maps in 2004 and 2005 and sampled randomly from lists constructed at each sentinel site by enumerating all households using personal digital assistants (PDAs) equipped with global positioning systems (GPSs) in 2006 and 2007. In 2008, households were randomly sampled from census lists in each sentinel site. Subject to informed written consent from a responsible person, children 2 to < 15 years of age had their hemoglobin measured (HemoCue, Ängelholm, Sweden) and were tested for *P. falciparum* using ICT malaria rapid tests (R&R, Cape Town, South Africa). Children testing positive for parasitemia, with hemoglobin < 11 g/dL, or who were febrile were referred to a local field clinic for appropriate treatment (anti-malarial, antipyretic, or iron supplementation).

In 2004 and 2008, women of reproductive age from survey households were asked about history of their previous live births using the standard child mortality module of the Demographic and Health Surveys questionnaire.[24] On a subsample of households, extensive information on household wealth, income, and expenditure was collected in 2004. Principal source of lighting, acting as a proxy indicator of household wealth, was collected from the sub-sample of households in 2004, and from all sampled houses in 2008.

FIGURE 1. Location of sentinel sites used to monitor the Bioko Island malaria control intervention, 2004 to 2008.

Window traps were fitted to bedrooms of ~100 houses to monitor mosquito vector species, relative abundance, sporozoite prevalence, and molecular markers of insecticide resistance, as described in more detail elsewhere.[15] We report here on changes in sporozoite prevalence in malaria vector mosquitoes, which was measured using polymerase chain reaction (PCR) techniques.[25,26] Mean prevalence of sporozoites was calculated for specimens grouped by date of spraying at the locality of capture, resulting in a pre-spray period, and periods separated by the timing of Rounds 2, 4, and 6. Sporozoite-positive *Anopheles melas* were found in one site only (Riaba); we have therefore restricted the data for this species to this site.

The timing of the main intervention and monitoring activities is shown in Figure 2.

Total monthly rainfall was available from the weather station at Malabo airport, Bioko, from January 2000 and aggregated into 12-month periods from March 2000 to coincide with survey reporting intervals.

Sample size considerations. The sample size for under-5 mortality was based on a requirement to have 80% power for all sites combined to show a reduction in under-5 mortality by at least one third from 200 per 1,000 at baseline to 134 per 1,000 in 2008, assuming a design effect of 2.5 caused by between-site variation of responses, and a 5% significance level. Using the log-rank test for survival probabilities,[27] data on 420 deaths would have to be observed in ~12,500 under-5 child-years. It was estimated that ~2,500 women had to be interviewed in the 2004 and 2008 surveys combined, assuming the average number of eligible child-years reported per respondent to be 5. Under-5 follow-up was reported at baseline for the period March 1999 to February 2004, whereas post-intervention follow-up, reported in 2008, extended from March 2004 to the survey date in 2008.

Statistical analysis. Under-5 child mortality was estimated by deriving Kaplan-Meier survival probabilities to age 5 years for reported live births for each of the comparison periods, excluding twins. Pre-intervention birth histories reported in the 2004 survey were used to calculate pre-intervention child mortality, left censoring child years before March 1999 (5 years before the start of malaria control activities), and right censoring child years by the nominal start date of the malaria control project on March 1, 2004, the child's fifth birthday, or the date of death if deceased, whichever came first. Similarly, birth histories reported in the 2008 survey were used to calculate the post-intervention child mortality rate, this time left censoring child-years follow-up on March 1, 2004 and right censoring by the 2008 survey date, the child's fifth birthday, or date of death, whichever came first.

Kaplan-Meier survival for each individual year from March 1999 to February 2008 was calculated to obtain year-specific child mortality rates.

A consumption-based measure of household per capita annual income was derived from information on household expenditure (including annualized consumption values of durables and estimated values of home produced consumption goods), savings, and net lending obtained from a subsample of households from the 2004 survey.[28–30] The relationship between estimated household per capita income and access to electricity for lighting at baseline was investigated using a simple regression model.

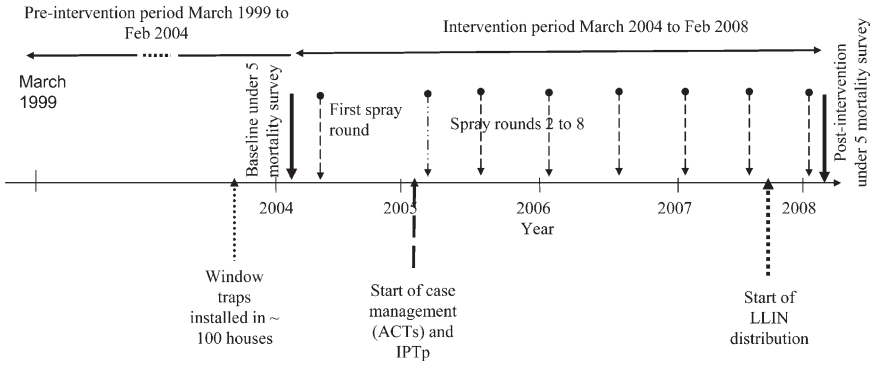

FIGURE 2. Timing of intervention activities and under five mortality surveys, Bioko, 2004 to 2008.

Using proportional hazards (Cox) regression analysis, hazard ratios (HRs) for under-5 mortality for the intervention period relative to pre-intervention were calculated. Birth year, as a marker of time period, was used to test whether there was a secular trend in mortality in the intervention and pre-intervention periods, respectively. Access to electricity as the principal source of lighting was included in the Cox model to determine whether under-5 mortality was independently associated with intervention period, by controlling for this proxy measure of household wealth. For a subsample corresponding to years for which annual rainfall data were available, the Cox model was used to investigate whether changes in under-5 mortality could be explained by variation in rainfall in the preceding 12-month periods.

Possession and use of ITNs, IRS coverage, and uptake of IPTp by pregnant women were calculated from survey responses. Annual ACT consumption for all government health facilities combined was derived from an automated procurement and supplies management system.

For each year, prevalence of infection with *P. falciparum*, moderate-severe anemia (Hb < 8 g/dL), and reported fever in the last 4 weeks in children 2–5 years, and odds ratios (ORs) relative to 2004, were calculated.

Prevalence and ORs, relative to pre-IRS baseline, were calculated by spray round intervals for sporozoite status for each malaria vector species.

Variance estimation took account of clustering of responses within sentinel areas, using the method by Rao and Scott[31] for complex sample surveys as implemented in the statistical package Stata.[32]

Approval. Ethics approval for the study was granted by the Equatorial Guinea Ministry of Health and Social Welfare.

RESULTS

Intervention coverage. According to survey responses, IRS coverage declined slightly from 87% (95% CI = 80–91) after the first year of IRS to 79% (95% CI = 75–82) in 2008 (Table 1). ITN use, monitored from 2006 onward, increased sharply rising from 12% in 2006 to 73% in 2008. Dual vector control of IRS and ITN use resulted in > 80% of children

TABLE 1
Coverage of program interventions, Bioko, pre-2004 to 2008

Intervention	Pre-intervention coverage	Post-intervention coverage* (% [95% CI]; *N*)		
		2005	2006	2008
IRS†:				
Proportion sprayed, all houses[1]	Not known, assumed nil	87 [80–91]; 1274	77 [74–80]; 2142	79 [75–82]; 2795
ITN‡/Bednet§ ownership; houses owning at least one of:				
Any mosquito net	Not known	Not measured	45 [37–54]; 2297	95 [93–96]; 2923
ITN			26 [21–31]; 1699	94 [92–95]; 2478
ITN/bednet use; sleeping the previous night under:				
Any mosquito net, all ages	Not known		29 [23–37]; 12011	77 [72–81]; 12472
Any mosquito net, 2 to < 5 years	29%¶	Not measured	30 [24–36]; 1822	76 [70–81]; 1407
ITN, all ages	Not known		12 [10–14]; 9612	73 [68–78]; 10725
ITN, 2 to < 5 years	4%¶		12 [10–15]; 1453	72 [66–78]; 1209
ITN or IRS protection:				
Proportion 2- to < 5-year-old children living in an IRS-treated house or sleeping under an ITN	Assumed 4%	85** [80–91]; 1274	83 [78–86]; 1650	95 [92–96]; 1328
IPTp††: Proportion of women who had a live birth during the previous year, who during their pregnancy:				
Took any SP/Fansidar	Not known	Not measured	Not measured	31 [27–35]; 503
Took at least two doses of SP/Fansidar				19 [16–24]; 503

Data from household surveys as indicated.
* BIMCP household surveys.
† Indoor residual spraying.
‡ Insecticide-treated net.
§ Bednet means any net whether treated with insecticide or not.
¶ Multiple Indicator Cluster Survey (MICS), 2000, unpublished.
** Assuming IRS protection only.
†† Intermittent preventive treatment of pregnant women.

under 5 being protected by at least one of the two methods throughout the intervention period, the proportion rising to 95% (95% CI = 92–96) in 2008 (Table 1).

IPTp resulted in 31% (95% CI = 27–35) of women reporting that they had taken at least one dose of SP during their last pregnancy, whereas 19% (95% CI = 16–24) reported that they had taken two doses at least 30 days apart, based on 2008 survey responses (Table 1).

In the first year after the introduction of ACTs in 2005, the number of doses consumed at public health facilities was 28,425; this declined to 10,775 doses in 2008. Self-reported malaria episodes, derived from illness history questions in annual household surveys, declined from 66% of all reported illnesses in 2005 to 16% of all reported illness episodes in 2008 (data not tabulated).

Indicators of malaria transmission intensity. Between March 2004 and March 2008, mean prevalence of infection with *P. falciparum* in children 2 to < 5 years in Bioko fell from 42% pre-intervention to 18% in 2008 (OR = 0.31; 95% CI = 0.2–0.46; $P < 0.001$; Table 2). Over the same period, prevalence of moderate-severe anemia in the same age group declined from 15% to 2% (OR = 0.11; 95% CI = 0.07–0.18; $P < 0.001$). The proportion of children under 5 reported to have had a fever in the past 4 weeks decreased from 14.2% in 2004 to 6.3% in 2008 (OR = 0.41; 95% CI = 0.22–0.76; $P = 0.008$).

There was a sharp decline in the presence of *P. falciparum* sporozoites in *Anopheles gambiae* s.s. from 6.8% before IRS spraying to 0.6% in 2007/2008 (OR = 0.10; 95% CI = 0.02–0.56; $P = 0.009$), with most of the reduction occurring after the first spray round, and in *A. melas* from 9.9% to 0% after the first spray round (Table 3). As has been previously reported,[15] abundance of *An. gambiae* s.l. dropped by > 90% in the period between baseline and the third spray round. The third malaria vector in Bioko, *Anopheles funestus*, all but disappeared, with no specimens having been found after the third spray round.[15]

Under-5 mortality. Valid reported birth histories for the pre-intervention period from March 1999 to February 2004 and the intervention period from March 2004 to the survey date in 2008 were obtained from 1,041 and 1,326 women, respectively, from the 2004 and 2008 household surveys. One hundred ninety-seven and 61 child deaths and 5,643 and 4,558 child-years under age 5 were recorded in the two surveys, respectively (Table 4).

All-cause under-5 mortality fell from 152 per 1,000 births (95% CI = 122–186), estimated from 2,338 reported birth histories before the introduction of malaria control measures, to 55 per 1,000 (95% CI = 38–77), estimated from 2,132 reported births during the first 4 years of the malaria control intervention period (unadjusted HR = 0.34; 95% CI = 0.23–0.49; $P < 0.001$). Mortality rates for individual years from March 1999 to February 2008, based on reported follow-up and deaths, were subject to large sampling error caused by small numbers but showed that the reduction in under-5 mortality risk coincided with the start of malaria control activities from 2004 onward, relative to the pre-intervention period before February 2004 (Table 4).

There was no evidence of a secular trend in under-5 deaths through association with year of birth of the child either in the pre-intervention period (HR = 0.95/yr; 95% CI = 0.84–1.07; $P = 0.37$) or in the intervention period (HR = 1.05/yr; 95% CI = 0.85–1.30; $P = 0.61$). In a regression model using intervention and pre-intervention data, and including year of birth as a trend variable and post-February 2004 as a binary categorical variable, the adjusted HR for intervention period versus pre-intervention was 0.40 (95% CI = 0.20–0.77; $P = 0.009$), and the adjusted HR for trend was 0.97 (95% CI = 0.87–1.08; $P = 0.51$).

In the subsample for which household wealth data had been collected in 2004, household per capita income in houses with electricity was estimated to be US$286 (22%) higher than in houses without ($P = 0.057$ after allowing for cluster effects). Access to electricity for lighting, which was available in both surveys, was therefore used as an approximate proxy for household wealth. The proportion of households having electricity as their principle source of lighting increased from 40% in 2004 to 69% in 2008. In the subsample, the unadjusted mortality HR for intervention period was 0.30 (95% CI = 0.16–0.54; $P = 0.001$), whereas the unadjusted mortality HR for households having electric lights was 0.53 (95% CI = 0.35–0.80; $P = 0.005$; Table 5). From the model containing intervention period and electric lights, the adjusted HR for intervention period was 0.33 (95% CI = 0.17–0.63; $P = 0.002$), and the adjusted HR for electric lights was 0.69 (95% CI = 0.42–1.13; $P = 0.13$).

There was weak evidence that mean annual rainfall recorded at Malabo airport was lower for the intervention period than for the pre-intervention period (Table 4; $P = 0.17$). Cox regression modeling showed that under-5 mortality was associated with annual rainfall over the 8-year period for which rainfall data were available (HR = 1.007/10 mm; 95% CI = 1.002–1.012; $P = 0.01$). However, a multiple variable model with rainfall and intervention effect as explanatory variables showed that the association of under-5 mortality with intervention effect persisted, even after adjusting for annual rainfall (HR = 0.26; 95% CI = 0.13–0.51; $P = 0.001$), whereas there was no evidence for an association with rainfall, after adjusting for the intervention period (HR = 1.000/10 mm; 95% CI = 0.995–1.005; $P = 0.967$).

TABLE 2

Malaria transmission indicators in children 2–5 years, Bioko, 2004 to 2008

	Study year	Prevalence [% (*N*)]	OR [95% CI] relative to 2004	*P*
Infection with *P. falciparum*				
	2004	42 (829)	1	
	2005	26 (974)	0.50 [0.35–0.72]	0.001
	2006	20 (1,761)	0.35 [0.23–0.53]	< 0.001
	2007	27 (1,254)	0.52 [0.37–0.73]	0.001
	2008	18 (1,220)	0.31 [0.20–0.46]	< 0.001
Anemia (< 8 g/dL)				
	2004	15 (829)	1	
	2005	9.8 (975)	0.60 [0.44–0.81]	0.001
	2006	7.5 (1,759)	0.44 [0.34–0.58]	< 0.001
	2007	6.6 (1,231)	0.39 [0.28–0.53]	< 0.001
	2008	2.0 (1,198)	0.11 [0.07–0.18]	< 0.001
Reported to have had fever in last month				
	2004	14.2 (323)	1	
	2005	7.0 (976)	0.45 [0.26–0.79]	0.008
	2006	7.6 (1,802)	0.50 [0.24–1.04]	0.062
	2007	5.2 (1,288)	0.33 [0.18–0.59]	0.001
	2008	6.3 (1,403)	0.41 [0.22–0.76]	0.008

DISCUSSION

Our results stem from a highly evaluated program effort, not a randomized controlled trial. We observed strong evidence of

TABLE 3

Change in prevalence of *P. falciparum* sporozoites in malaria vector mosquitoes, Bioko, 2003 to 2008

	Malaria vector					
	Anopheles gambiae s.s.		*Anopheles funestus*		*Anopheles melas**	
Spray round, time period	Sporozoite positive % (*N*)	OR [95% CI]	Sporozoite positive % (*N*)	OR [95% CI]	Sporozoite positive % (*N*)	OR [95% CI]
Pre-round 1, 2003/4	6.5 (581)	1 (reference)	4.0 (372)	1 (reference)	9.9 (101)	1 (reference)
Pre-round 2, 2004/5	1.5 (791)	0.23 [0.13–0.43, $P < 0.001$]	2.3 (215)	0.92 [0.34–2.49, $P = 0.86$]	0.0 (7)	Not estimable
Pre-round 4, 2005/6	0.7 (431)	0.14 [0.06–0.34, $P < 0.001$]	0.0 (1)†	Not estimable	0.0 (6)	Not estimable
Pre-round 6, 2006/7	1.6 (688)	0.27 [0.15–0.49, $P < 0.001$]			0.0 (9)	Not estimable
Post-round 6, 2007/8	0.6 (176)	0.10 [0.02–0.56, $P = 0.009$]			0.0 (4)	Not estimable

* Riaba site only.
† No specimens of *An. funestus* have been caught on Bioko since December 1, 2005.

changes in a set of linked indicators. The simultaneous sharp decline in child malaria infections, anemia, and fevers, and in sporozoites in malaria vector mosquitoes, all point to a major reduction in malaria transmission in response to high coverage of interventions. The large reduction in all-cause child mortality over the same period can plausibly be linked to these trends in malaria transmission indicators.[13]

Reductions in overall child mortality that can be achieved through specific malaria control measures have been shown in a number of studies.[6,7,12,33] None have estimated effects as large as the one we have observed, but in some cases, protective efficacies exceeded 50%. Previous studies have estimated the total number of deaths linked to malaria to be as high as double the number of deaths directly caused by the disease, if mortality indirectly attributable to malaria is taken into account.[4,12] All-cause childhood mortality can therefore serve as an indicator of malaria-specific mortality, because of the high proportion of malaria-associated deaths in children under 5 in countries with stable malaria transmission in sub-Saharan Africa and because it reflects changes in the burden of both direct and indirect malaria mortality in children. In common with many less economically developed countries, reliable vital registration data are not available in Equatorial Guinea, and there are no data on hospital deaths for the pre-intervention period. However, all-cause under-5 mortality can be sufficiently reliably ascertained by birth history interviewing of women of reproductive age, sampled through representative household surveys.[24] Our estimate of under-5 mortality in the pre-intervention period of 152 per 1,000 was similar to a previous estimate of under-5 mortality for Equatorial Guinea of 156 per 1,000 for 2000[34] and broadly similar to the sub-Saharan average of 173 per 1,000 for 2003.[35]

Estimated under-5 mortality for individual years between March 1999 and February 2008 was predictably subject to large sampling variation on account of small numbers. The apparently immediate reduction in child mortality after the start of the intervention should, therefore, not be overinterpreted given the wide confidence limits for the annual rates. Nevertheless, the change in mortality rates coincides with the start of the intervention in 2004. This was confirmed by proportional hazards regression, which showed a reduction associated with the advent of the control measures, but no evidence of a secular trend in mortality, in either the pre-intervention period (HR = 0.95, $P = 0.37$) or the intervention period (HR = 1.05, $P = 0.61$). Sharp reductions in sporozoites in mosquitoes, reported fevers in children, and prevalence of infection with *P. falciparum* are all indicative of substantial reductions in transmission in response to the first round of IRS in 2004. Prevalence of anemia also dropped rapidly, reflecting the diminishing number of previous episodes of malaria that young children were exposed to in the period before each survey.

Before 2004, there was no concerted vector control intervention in Bioko, with neither house spraying nor large scale mosquito net distribution being implemented. According to BIMCP survey responses, the two vector control measures together, IRS and ITN use, achieved very high levels of

TABLE 4

Mortality by any cause in children under 5 years of age recorded in surveys conducted on Bioko in 2004 and 2008, respectively, and recorded annual rainfall, March 1999 to February 2008

			Under-5 mortality risk, deaths per 1000 births*		
Time period	Under-5 deaths	Follow-up, child-months	Estimate	95% CI	Total rainfall† (mm)
Pre-intervention					
March 1999–Feb. 2000	44	13,033	157	116–210	Not available
March 2000–Feb. 2001	52	13,551	189	134–257	1888
March 2001–Feb. 2002	36	13,933	137	91–197	1614
March 2002–Feb. 2003	26	13,827	111	77–158	2786
March 2003–Feb.2004	39	13,372	157	112–215	2361
March 1999–Feb. 2004	197	67,715	152	122–186	Mean 2162
Intervention					
March 2004–Feb. 2005	12	11,590	51	26–94	1771
March 2005–Feb. 2006	17	12,352	72	42–117	1356
March 2006–Feb. 2007	10	13,557	39	21–72	1696
March 2007–Feb. 2008	22	17,145	59	36–93	2018
March 2004–Feb. 2008	61	54,644	55	38–77	Mean 1710

* Estimated using Kaplan-Meier survival function.
† Malabo airport weather station.

TABLE 5

Effect of intervention period and electricity as main source of lighting on under-5 mortality: unadjusted and adjusted hazard ratios for under-5 mortality for a subsample for whom household amenity data were collected

	Under-5 deaths	Follow-up (child-months)	Unadjusted HR* [95% CI]	Adjusted HR [95% CI]†
Study period				
Pre-intervention period	51	15,168	1	1
Intervention period	60	53,056	0.30 [0.16–0.54; $P = 0.001$]	0.33 [0.17–0.63; $P = 0.002$]
Electricity as main source for lighting				
No	58	25,089	1	1
Yes	53	43,135	0.53 [0.35–0.80; $P = 0.005$]	0.69 [0.42–1.13; $P = 0.13$]

* HR = hazard ratio.
† HR for study period adjusted for electric light and *vice versa.*

coverage during the intervention period, with at least one of the two forms of vector control reaching all but a very small proportion of children in Bioko.

Malaria in pregnancy is generally associated with low birth weight babies and can therefore indirectly affect child survival. The introduction of IPTp did not result in a high uptake of this prevention measure, suggesting that IEC efforts in this area need to be strengthened. Its impact on child survival in this study is therefore likely to be modest.

ACT consumption at government health facilities was highest in 2005 when ACTs were introduced, declining by > 60% by 2008. There was a corresponding large decline in self-reported malaria episodes as a proportion of all illness episodes reported in household surveys. Although these data do not constitute proof of adequate access to effective treatment, they are an indication of declining demand for anti-malarial drugs that were widely available at health facilities.

To our knowledge, there were no other major concurrent child health interventions such as scaling up of vaccination programs, campaigns to increase use of oral rehydration salts to treat diarrhea, micronutrient distribution, or efforts to increase treatment of acute respiratory infections during the period on which we are reporting. Malaria transmission elsewhere in the region has remained high, with prevalence of infection in children under 5 estimated at 59% (95% CI = 51–67) in a large household survey in mainland Equatorial Guinea in 2007 as part of a baseline assessment by the Equatorial Guinea Malaria Control Initiative (unpublished data). HIV infection rates before the introduction of malaria control in Equatorial Guinea were thought to be low, with HIV-related attributable risk of child mortality estimated to be ~0.5%.[36] It is unlikely that changes in HIV-associated child mortality have confounded the impact of malaria control in the intervention period.

Our data allowed only a limited assessment of the effect of rainfall, which was lower in the intervention period than in the comparison period. Regression analysis confirmed the association between under-5 mortality and the intervention period after allowing for variation in annual rainfall.

One may expect to see a long-term decline in child mortality over time because of rapidly rising economic prosperity in Bioko. Adjusting the intervention effect for household access to electricity as an inexact proxy for household wealth showed that the intervention effect on mortality was little changed from the unadjusted value (adjusted HR = 0.33; 95% CI = 0.17–0.63; $P = 0.002$). We cannot claim that this proxy variable for household wealth adequately controls for changes in economic circumstances of households. Economic development and reduction in malaria transmission are related factors that would be expected to lead to improvements in child survival. The baseline survey on household consumption in Bioko showed that poor households spent a disproportionately large share of their income on anti-malarial drugs before the introduction of free treatment against malaria for children under 15 and for pregnant women by the BIMCP. It is very likely that the introduction of free treatment has been of considerable economic benefit to poor households. Similarly, there is likely to have been a reduction in foregone income because of adults having to care for sick children. Household wealth will therefore have increased not only as a result of oil-related economic development but also as a consequence of more effective malaria control. Disentangling the contributions that economic prosperity and malaria control have made toward the reduction in child mortality is therefore complex and perhaps a moot point when the overall reduction is as large as the one observed here. However, in the absence of targeted disease control interventions, the effect of oil- and mineral-related wealth on improvements of health in the general population may be only minor, as is shown by the example of Nigeria, where under-5 mortality declined only modestly from 230 per 1,000 to 191 per 1,000 between 1990 and 2006, despite high oil revenues.[37]

Our results show that, for Bioko, the United Nations MDG[1] of a two-thirds reduction in child mortality by 2015 has already been reached. This study showed how, even in settings of high transmission intensity, effective malaria control measures that achieve a high degree of coverage and that are sustained over time can bring about major improvements in health and thereby play a key part in the achievement of this critical MDG.

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