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Spatial Targeted Vector Control Is Able to Reduce Malaria Prevalence in the Highlands of Burundi

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Abstract. In a highland province of Burundi, indoor residual spraying and long-lasting insecticidal net distribution were targeted in the valley, aiming also to protect the population living on the hilltops. The impact on malaria indicators was assessed, and the potential additional effect of nets evaluated. After the intervention—and compared with the control valleys—children 1–9 years old in the treated valleys had lower risks of malaria infection (odds ratio, OR: 0.55), high parasite density (OR: 0.48), and clinical malaria (OR: 0.57). The impact on malaria prevalence was even higher in infants (OR: 0.14). Using nets did not confer an additional protective effect to spraying. Targeted vector control had a major impact on malaria in the high-risk valleys but not in the less-exposed hilltops. Investment in targeted and regular control measures associated with effective case management should be able to control malaria in the highlands.

INTRODUCTION

Malaria outbreaks have been frequently reported in the African highlands.[1–3] Their occurrence has been attributed to several factors, including climatic anomaly,[2,4] land-use changes,[5] drug resistance,[3,6] population migration,[7] and breakdown of both the local health system and vector control activities.[8] Different authors have shown that *Anopheles* density, malaria transmission, and corresponding human infections were higher and clustered around the breeding sites,[9,10] particularly in the lowly endemic[11] and epidemic-prone areas.[12] Highlands' hilly slopes[13] and cold nights[14] limit upward dispersal of adult mosquitoes from the valleys, accentuating their clustering.

During the last decade, malaria transmission in the Burundian highlands steadily increased and resulted in a major epidemic in 2000. Within a few months (December 2000 to March 2001), 2.9 million malaria cases were reported for a population of 6.7 million. After this epidemic, prevention became an absolute priority for the Burundi Ministry of Health (MoH). However, because of political unrest, most vector control activities (indoor residual spraying and insecticide-treated nets) implemented in the lowlands[15,16] and aimed at controlling malaria have been stopped since 1992. Nevertheless, vector control activities were shown to be feasible in the highlands and in the context of a complex emergency situation.[17] Therefore, a 4-year vector control program was set up in Karuzi, one of the highland provinces most affected by the 2000 malaria epidemic. This was targeted in time and in space, run between 2002 and 2005, and consisted of an annual round of indoor residual spraying (IRS) only at the bottom of the valleys and 1 distribution in 2002 of long-lasting insecticidal nets (LNs). Reductions of the vector population and the malaria transmission have already been reported.[18] We present here the impact of these targeted vector control activities on the prevalence of malaria infection.

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METHODS

Study area and population. Karuzi is located in the central plateau of Burundi at an altitude of 1450–2000 m. It is a hilly province with a surface of 1457 km^2 and an estimated population of 302,062 inhabitants (EPISTAT: Epidemiology and Statistics Cell Burundi, 2002).[19] The annual average temperature is 19°C with the coolest season recorded in June–July and the hottest in September–October. There are 2 rainy seasons, from September to December and from January to May, with an average annual rainfall of 1160 mm. According to the MoH, malaria in the high plateau is hypo- to meso-endemic and prone to epidemics. An increase of malaria cases is usually observed at the end of the 2 rainy seasons, and recent epidemics occurred after the second one (EPISTAT database).[19] In 2002, malaria was responsible for ~60% of the total outpatient attendances in Karuzi (MSF-B database, 2002).[20] *Anopheles gambiae* sensu stricto (s.s.) and *Anopheles funestus* are the main vectors.[18]

Study design. Vector control activities were described in a previous study.[18] Briefly, 4 zones were identified in this study: (1) intervention-treated valleys (population of 67,187 and area of 264 km^2), (2) corresponding intervention-nontreated hilltops (51,161 inhabitants; 201 km^2), (3) unsprayed control valleys (11,744 inhabitants; 50 km^2), and (4) control hilltops (10,709 inhabitants; 55 km^2). In treated valleys, 1 annual IRS round was performed in June–July using deltamethrin 5WP (in 2002–2004) or alphacypermethrin 5WP (in 2005) at a concentration of 25 mg of active ingredient/m^2. IRS coverage exceeded 90%, except in 2002 (86%). LNs (PermaNet® 1.0) were distributed in 2002, before the first IRS round on the basis of 2 LNs per sprayed house. Intervention areas correspond to large valleys with many irrigation fields and high population density. The control areas were smaller and were selected to enable the evaluation of the vector control intervention. In both intervention and control areas, people had access to antimalarial treatment. Nine cross-sectional studies were performed. The first was carried out before the start of the vector control activities to provide baseline data. Then, 2 yearly surveys were carried out, 3 and 9 months after each annual IRS round. The study was designed to have by survey 80% power to detect 20% difference in malaria prevalence

between intervention and control areas, with 95% confidence, assuming a design effect of 2 and a prevalence of 40% in the control group. A random cluster-sample design was used for every survey. The selection of houses was detailed in a previous paper.[18] Totals of 450 houses in Survey 1, 600 houses in Survey 2, and 800 houses for Surveys 3–9 were selected. All members of the household were enumerated, and 2 individuals—one between ages 1 and 9 and one over age 9—were chosen at random, irrespective of any clinical symptoms. When a selected person was not present on the survey day, another appointment was made. Entomological evaluations were carried out in the same houses, and results have been presented elsewhere.[18]

Thick and thin blood smears were collected and stained with Giemsa (5% for 20 minutes). Parasite density was determined on the basis of the number of parasites per 200 white blood cells (WBC), assuming a total WBC count of 8000/μL. Thin blood films were used to confirm species identification. Quality control was done on 10% of the slides of each survey. When the discrepancy was more than 5%, all slides were re-read. A rapid diagnostic test (RDT; Paracheck-Pf®) was also used. Individuals found to be positive by the RDT were treated according to MoH guidelines [in 2003, 30 mg oral quinine per kg body weight over 7 days; from 2004 onward, artesunate (5 mg/kg/day) and amodiaquine (10 mg/kg/day) for 3 days]. The axillary temperature was measured. A short questionnaire to collect data on age, sex, net use, malaria attacks, and treatment history during the past 2 months was administered.

To estimate malaria incidence after 3 IRS rounds, infants 1–11 months old were included in Survey 6. In this study, all infants were recruited in the selected houses to reach a number of 8. When the number of infants was not sufficient, additional closest houses were sampled to reach the required number of infants.

Statistical analysis. The following malariometric indices were evaluated: (1) history of malaria-like illness and (2) malaria treatment during the past 2 months, (3) prevalence of malaria infection (proportion of positive blood smears for malaria parasites, both sexual and asexual forms), (4) prevalence of high-density parasitemias (proportion of blood smears with more than 5000 parasites/μL among the total number of slides examined), and (5) prevalence of clinical malaria defined as malaria infection and fever (axillary temperature $\geq 37.5°C$).

The data were analyzed using the survey logistic regression in Stata 9.2 (Stata Corp., College Station, TX), taking into account the study design. A cluster is a group of 4–8 houses, according to surveys and areas. Malaria indicators were analyzed by age group (1–9 and > 9 years) for valleys and hilltops. The malaria indices were first compared between untreated valleys and hilltops (Table 1). Baseline data on population characteristics and malaria indicators in the 4 zones were summarized with proportions or means (Table 2). The prevalence of infection was analyzed using the following independent variables: survey identification, intervention versus control, and their interaction terms (Table 3). A multivariate regression logistic was used to assess the effect of using a net and living in a sprayed valley on prevalence, clinical malaria, and high-density parasitemias (Table 4). Finally, analyses of malaria infection in 1- to 11-month-old infants were done in valleys and control areas with intervention versus control as the main independent variables. This bivariate model included also age as a potential confounder.

Ethics. The Ethics Committee of the Institute of Tropical Medicine, Antwerp, approved the study. At the time of the implementation of the program and surveys, the Institutional Ethical Committee was not functional in Burundi. However, the Ministry of Health signed an agreement for the vector control program and the study design and the National Malaria Control Program (LMTC) offered close collaboration. Informed consent was obtained for the individuals or their parents included in the survey. In case of refusal, other houses were selected.

RESULTS

Malaria in Karuzi. In the untreated zones (all the selected zones except the intervention valley in Surveys 2–9), children 5–19 years old had the highest prevalence of malaria infection, while individuals over age 50 had the lowest (20.2%). Malaria prevalence was lower in the hilltops than in the valleys but followed a similar trend (Figure 1). *Plasmodium falciparum* was the predominant species (85.2%, 2891/3393), followed by *Plasmodium malariae* (6.7%, 228/3393) and *Plasmodium ovale* (0.5%, 15/3393), with the remaining 7.6% (259/3393) being mixed infections. This distribution was almost constant throughout the surveys.

The proportion of individuals to declare a history of malaria-like illness, to have used antimalarial treatment, to be

TABLE 1

Malaria indices and risk (odds ratio) in untreated valleys (NT-V, valleys of Survey 1 and control valleys of Surveys 2–9) compared with untreated hilltops (NT-H, intervention and control hilltops of all surveys)

	NT-V	NT-H	OR (95% CI)	*P* value
Age group ≤ 9 years				
% History of malaria-like illness (*N*)	62.3 (1123)	48.3 (2172)	1.8 (1.5–2.2)	< 0.001
% Used malaria treatment (*N*)	27.9 (1122)	22.7 (2172)	1.3 (1.1–1.6)	0.011
% Prevalence (*N*)	52.6 (1072)	27.3 (2090)	3.0 (2.4–3.7)	< 0.001
% High-density parasitemias (*N*)	11.0 (1061)	5.0 (2079)	2.4 (1.7–3.2)	< 0.001
% Clinical malaria (*N*)	14.0 (1068)	6.2 (2087)	2.4 (1.8–3.3)	< 0.001
Age group > 9 years				
% History of malaria-like illness (*N*)	68.3 (1620)	59.9 (3166)	1.4 (1.2–1.7)	< 0.001
% Used malaria treatment (*N*)	30.5 (1620)	26.3 (3165)	1.2 (1.0–1.5)	0.029
% Prevalence (*N*)	43.1 (1545)	26.0 (3025)	2.2 (1.8–2.6)	< 0.001
% High-density parasitemias (*N*)	4.9 (1533)	3.0 (3004)	1.7 (1.2–2.3)	0.003
% Clinical malaria (*N*)	12.6 (1544)	7.4 (3024)	1.8 (1.4–2.3)	< 0.001

All *P* values and 95% confidence intervals (CI) were determined taking clustering into account.

TABLE 2
Baseline demographic characteristics and malaria indices in the intervention and control areas (Survey 1)

	Valleys				Hilltops			
	Control		Intervention		Control		Intervention	
Population	11,744		67,187*		10,709		51,163	
Area (km^2)	50		264		55		201	
Age group ≤ 9 years	N = 64		N = 54		N = 57		N = 93	
Mean age in years	6.1	(5.4–6.7)	5.6	(4.8–6.4)	6.1	(5.4–6.8)	5.3	(4.7–5.8)
% Males	46.9	(34.5–59.2)	59.3	(44.3–74.2)	49.1	(34.6–63.7)	55.9	(43.9–67.9)
% Sleeping under a net	3.1	(0.0–9.1)	14.8	(0.0–30.8)	0	–	25.8	(10.6–41.0)
% History of malaria-like illness	89.1	(80.8–97.4)	81.5	(72.2–90.7)	82.5	(70.4–94.5)	62.4	(51.2–73.5)
% Used malaria treatment	59.4	(42.3–76.5)	46.3	(29.5–63.1)	43.9	(24.6–63.1)	37.6	(25.6–49.7)
% Prevalence	51.6	(37.9–65.2)	66.7	(55.8–77.5)	33.3	(16.9–49.8)	38.7	(23.5–54.0)
% Clinical malaria	9.5[1]	(1.5–17.6)	13.2[2]	(1.8–24.6)	10.5	(0.0–21.0)	12.9	(3.7–22.1)
% High-density parasitemias	3.2[3]	(0.0–7.5)	9.3	(1.3–17.2)	10.7[4]	(0.0–21.2)	12.2[5]	(4.0–20.5)
Age group > 9 years	N = 79		N = 84		N = 80		N = 136	
Mean age in years	32.9	(28.3–37.6)	36.3	(32.8–39.8)	36.3	(31.9–40.8)	32.8	(30.0–35.5)
% Males	43.0	(34.2–51.8)	26.2	(16.1–36.3)	43.8	(33.9–53.6)	39.7	(31.0–48.5)
% Sleeping under a net	2.5	(0.0–7.5)	16.7	(3.5–29.9)	0	–	21.3	(8.7–33.9)
% History of malaria-like illness	86.1	(76.9–95.2)	79.8	(69.5–90.0)	90.0	(84.1–95.9)	65.4	(54.7–76.2)
% Used malaria treatment	58.2	(44.5–72.0)	57.1	(45.1–69.2)	57.5	(44.1–70.9)	42.6	(33.1–52.2)
% Prevalence	48.1	(37.1–59.1)	35.7	(21.7–49.7)	32.5	(21.3–43.7)	30.9	(22.8–39.0)
% Clinical malaria	6.3	(1.0–11.7)	3.6	(0.0–7.4)	10.0	(3.1–16.9)	2.9	(0.0–5.6)
% High-density parasitemias	6.9[6]	(1.3–12.4)	3.6	(0.0–7.4)	7.6[7]	(1.0–14.2)	4.4[8]	(1.3–7.5)

Mean and proportion are presented with their 95% confidence intervals (95% CI). All 95% CI were determined taking clustering into account.
* The population in the intervention valleys was collected during a census done before Survey 1; the other numbers were estimated from data given by the administration.
N = [1]63, [2]53; some parasite densities were missing.
N = [3]62, [4]56, [5]90, [6]73, [7]79, and [8]135; some temperatures were missing.

infected with high parasite density, and to have clinical malaria at the time of the survey was significantly higher in the valleys than in the hilltops (Table 1). These differences were seen in both age groups but were the highest in children under age 9.

Pre-intervention result. About 776 people were selected for Survey 1 (1–9 years old, 316; > 9 years old, 458), and among them 129 (16.6%) were absent. About half of the missing people (52.1%) were male in the age group 1–9 years, and this proportion is 36.7% in the older age group. For Surveys 2–9, the number of missing people was much lower, at 6.0% (611/10,127).

In the valleys, the demographic characteristics and the malariometric indices were similar in control and intervention areas (Table 2). In the hilltops, however, some differences were observed in terms of history of malaria-like illness and

TABLE 3
Prevalence of malaria infection in children ages 1–9 years and over 9 years, observed by surveys and by areas in the valleys, with risk (odds ratio) of infection in intervention relative to control valleys

	≤ 9 Years			> 9 Years		
	Prevalence (N)	OR (95% CI)	P value	Prevalence (N)	OR (95% CI)	P value
Survey 2						
Control	64.1% (39)	1	0.789	44.1% (59)	1	0.520
Intervention	61.1% (113)	0.88 (0.34–2.28)		38.2% (191)	0.79 (0.38–1.64)	
Survey 3						
Control	64.7% (119)	1	0.040	51.7% (178)	1	0.033
Intervention	44.2% (86)	0.43 (0.19–0.96)		35.8% (123)	0.52 (0.27–0.95)	
Survey 4						
Control	59.2% (130)	1	0.091	45.4% (196)	1	0.048
Intervention	42.5% (134)	0.51 (0.23–1.11)		32.3% (192)	0.57 (0.33–0.99)	
Survey 5						
Control	52.2% (136)	1	0.003	47.6% (185)	1	0.006
Intervention	28.5% (137)	0.36 (0.19–0.71)		26.9% (186)	0.41 (0.21–0.77)	
Survey 6						
Control	38.2% (136)	1	0.105	33.3% (204)	1	0.033
Intervention	26.0% (123)	0.57 (0.29–1.13)		20.8% (192)	0.53 (0.29–0.95)	
Survey 7						
Control	47.7% (128)	1	0.063	40.8% (184)	1	0.218
Intervention	31.7% (123)	0.51 (0.25–1.04)		31.7% (183)	0.67 (0.36–1.26)	
Survey 8						
Control	41.4% (133)	1	0.213	35.1% (185)	1	0.584
Intervention	30.6% (134)	0.63 (0.30–1.31)		31.9% (182)	0.86 (0.51–1.46)	
Survey 9						
Control	57.9% (133)	1	0.049	49.7% (191)	1	0.005
Intervention	39.4% (134)	0.47 (0.22–1.0)		33.5% (200)	0.51 (0.32–0.82)	

All P values and 95% confidence intervals (CI) were determined taking clustering into account. Odd survey numbers: April–May, 9 months after the annual IRS round. Even survey numbers: November–December, 3 months after the annual IRS round.

TABLE 4

Impact of Indoor Residual Spraying and sleeping under a net on malaria prevalence, clinical malaria, and high-density parasitemias, 3 and 9 months after intervention in the valley (multivariate logistic regression used)

	Prevalence		Clinical malaria		High-density parasitemias	
	OR* (95% CI)	*P* value	OR* (95% CI)	*P* value	OR* (95% CI)	*P* value
3 months after intervention						
1–9 years						
Sleeping under net vs. not	1.21 (0.85–1.72)	0.298	1.10 (0.57–2.13)	0.766	1.09 (0.41–2.89)	0.862
House in sprayed valley vs. not	0.65 (0.42–0.99)	0.046	0.51 (0.26–0.98)	0.045	0.35 (0.16–0.79)	0.011
> 9 years						
Sleeping under net vs. not	1.0 (0.76–1.34)	0.977	0.82 (0.49–1.39)	0.468	1.19 (0.50–2.85)	0.688
House in sprayed valley vs. not	0.71 (0.52–0.97)	0.034	0.64 (0.37–1.10)	0.106	0.38 (0.18–0.78)	0.009
9 months after intervention						
1–9 years						
Sleeping under net vs. not	0.88 (0.60–1.31)	0.536	0.95 (0.57–1.57)	0.830	0.88 (0.48–1.62)	0.687
House in sprayed valley vs. not	0.45 (0.30–0.69)	< 0.001	0.63 (0.39–1.02)	0.059	0.61 (0.38–0.99)	0.045
> 9 years						
Sleeping under net vs. not	0.84 (0.61–1.15)	0.271	0.66 (0.41–1.07)	0.091	0.62 (0.31–1.27)	0.191
House in sprayed valley vs. not	0.55 (0.40–0.74)	< 0.001	0.74 (0.48–1.13)	0.156	1.03 (0.59–1.80)	0.916

* Odds ratio (OR) adjusted for IRS and sleeping under a net.

clinical malaria for the age group > 9 years. The proportion of people sleeping under a bed net was higher in the intervention areas. Most of the hills in the intervention areas were considered to be at high risk during the 2000 epidemic, and these households received LNs in 2001.[17] The overall parasite prevalence during Survey 1 was 40.2% (260/647): 17.9% (44/246; parasite counts were not done for 14 slides) had a high parasite density, and 19.7% (51/259; 1 body temperature data point was missing) had fever.

Post-intervention result. When intervention with control valleys were compared, children of age 1–9 years had a significantly lower risks of malaria infection [OR: 0.55, 95% confidence interval (CI): 0.42–0.72, $P < 0.001$], high-density parasitemias (OR: 0.48, 95% CI: 0.33–0.70, $P < 0.001$), and clinical malaria (OR: 0.57, 95% CI: 0.41–0.81, $P = 0.001$). Furthermore, histories of malaria illness (OR: 0.66, 95% CI: 0.52–0.83, $P < 0.001$) and antimalarial drug use (OR: 0.65, 95% CI: 0.49–0.85, $P = 0.002$) were lower in the intervention valleys compared with the control valleys. The impact of the intervention in the older age group was also significant but less pronounced for all of these outcomes. According to surveys, malaria prevalence was reduced in intervention valleys compared with control valleys by 12–64% in the ≤ 9 age group and by 14–59% in > 9 age group (Table 3). These differences were significant in children ≤ 9 years old for Surveys 3, 5, and 9 and in individuals > 9 years old for Surveys 3–6 and 9. No difference in malaria prevalence was observed between intervention hilltops and control hilltops (results not shown).

Use of LNs, based on individual declaration of sleeping the previous night under a LN, ranged between 70.2% (217/309) for Survey 2 to 18.5% (61/330) for Survey 9. LNs use was relatively high until Survey 6 (57.7%) and dropped below 36% afterward. When all survey results were combined, the relative impact of IRS and net use varied according to age group, season (9 months after IRS and 3 months after IRS), and malaria indicators (Table 4). Three months after the intervention, living in a sprayed valley significantly reduced prevalence, clinical malaria, and high-density parasitemias compared with houses located in control valley in all age groups, except for clinical malaria, in the > 9 age group. Sleeping under a net did not decrease any of the malaria indicators adjusted for spraying. Nine months after the intervention, when the residual effect of the insecticide used for IRS has ceased, prevalence was still lower in houses located in sprayed valleys for both age groups and also for high parasitemias in children 1–9 years old.

The prevalence of malaria infection among the infants examined during Survey 6 was 4.6% (33/711), with 24.2% (8/33) having fever and 33.3% (11/33) high-density parasitemias. Malaria prevalence was significantly lower in the intervention valleys than in the control valleys (OR: 0.14, 95% CI: 0.04–0.52, $P = 0.005$). No difference was observed between intervention hilltops and control hilltops (Table 5). Infants treated for malaria before the survey were significantly fewer in num-

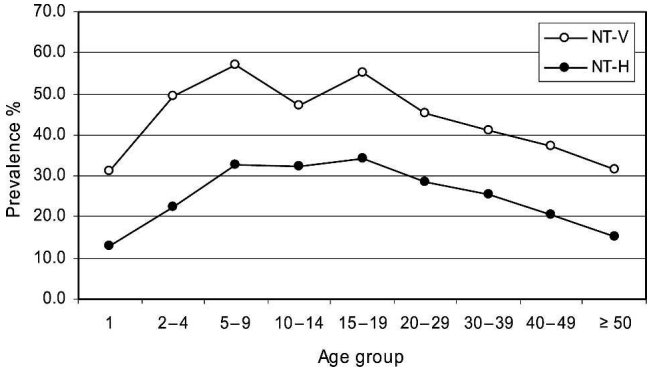

FIGURE 1. Age-specific malaria prevalence in untreated valleys (NT-V, valleys of Survey 1 and control valleys of Surveys 2–9) and hilltops (NT-H, intervention and control hilltops of all surveys).

TABLE 5

Malaria prevalence and risk of malaria infection in infants 1–11 months old by area (Survey 6)

	n/*N**	Prevalence	OR† (95% CI)	*P* value
Valley				
Control	17/161	10.6%	1	0.005
Intervention	3/189	1.6%	0.14 (0.04–0.52)	
Hilltop				
Control	6/182	3.9%	1	0.797
Intervention	7/179	3.3%	1.19 (0.30–4.74)	

* *n*/*N*, number of positive slide/number examined.
† OR adjusted for age; all *P* values and CI were determined taking clustering into account.

ber in the intervention valleys (3.7%, 7/189) than in control valleys (9.9%, 16/161; OR: 0.35, 95% CI: 0.13–0.91, $P = 0.039$).

DISCUSSION

In Africa, the spatial distributions of malaria have been extensively studied in low endemic and epidemic-prone areas, and focal vector control activities have been recommended.[10,11,14,21] In Karuzi, vector control activities was based on 1 distribution of LNs and a yearly round of IRS targeting the valleys, before the main transmission season. This was justified by the observation that 90% of malaria transmission occurred in the valleys.[18] Moreover, the baseline study showed that children are indeed 3 times more at risk for a malaria infection in the valleys compared with the hilltops.

Although control areas were similar to intervention areas in term of demographic characteristics and malaria indices, bednet use was higher in the intervention areas before the start of the operations. The choice of the intervention areas was made on the basis of the perceived risk for epidemic, i.e., the intervention valleys were considered to be more at risk than those selected as control areas. During the baseline study, malaria transmission was 15 times lower in the control compared with the intervention valleys.[18] Despite this difference and with a drop of infectious bites from 5.1 to < 0.5 per house per month after the first intervention round,[18] we were able to show a significant reduction of all malaria indices in the intervention valleys compared with control valleys. In a holoendemic area of Kenya, frequency of exposure to sporozoite-infected mosquitoes was correlated to malaria infection but even more to the high parasitemias.[22,23] It has been concluded that reduction in high parasite densities would reduce malaria morbidity and mortality.[22] These results are in agreement with our findings, where the most important impact was found on high parasitemias. The effect was even greater in children ≤ 9 years old, possibly because of their lower immunity. The impact of the intervention tended to decrease in the fourth year and could be linked to a relative increase of *An. gambiae* s.s. density in the intervention valleys, although not as high as in the control areas.[18]

The impact of the vector control activities on malaria prevalence was particularly important in infants, with an 86% decrease in risk of malaria infection. This is a strong indication that malaria transmission was drastically reduced by the intervention, as these infants were born after its implementation. Prevalence of malaria infection in the whole population, and more particularly of asymptomatic carriers, was higher than expected for an area defined as low transmission and epidemic prone. The high prevalence of asymptomatic infections suggests a change to a higher level of endemicity. In such a changing situation, malaria prevalence among infants is than a more appropriate indicator of impact of ITN[23] or IRS.[24]

During the first 2 years of the intervention, the first-line treatment was sulfadoxine–pyrimethamine (SP), later replaced by an artemisinin-based combination therapy (ACT) because of high SP resistance,[26] ACT use should improve cure rates, decrease gametocyte carriage, and may reduce malaria transmission where this is unstable.[27,28] In the control areas of Karuzi, malaria transmission was higher after ACT implementation,[18] despite more than 20% of the study population having taken an antimalarial treatment. One reason could be the unreliability of the treatment history by the study population, i.e., antimalarial treatment would not be as frequent as estimated by the survey. However, another reason could be that asymptomatic individuals would maintain a sufficiently large gametocyte reservoir that was able to compensate for the potential reduction of transmissibility in the treated patients. In our study, the observed decrease of malaria indices in the intervention areas can be largely attributed to vector control activities as no influence of ACT on malaria transmission could be detected.

No additional protection by LNs use was observed on any of the malaria indicators 3 months after the intervention. The absence of impact on malaria morbidity of LNs when implementing IRS was also observed in Eritrea,[29] while a mutually additive effect has been reported in Equatorial Guinea.[30] However, in Equatorial Guinea the IRS coverage was only 77% compared with more than 90% obtained in Karuzi. When IRS coverage is high, the additional benefit of treated nets is limited, as shown by the entomological surveys where malaria transmission was already being reduced to an undetectable level after spraying.[18]

The upper altitude limit for malaria in the African highlands has risen in past decades, and formerly malaria-free areas have become epidemic prone.[2,4,31] The spread of the vectors' distribution in time and space expose the local populations to a longer transmission season, which results in an increased endemicity in the highlands.[7,32] In Burundi, at the beginning of the century the central plateaus were declared malaria-free, and then epidemics were reported.[5,33,34] In Karuzi, the high prevalence in children 2–9 years old (32.1–53.4% in control areas) and the high proportion of asymptomatic carriers show that malaria has become mesoendemic, with a more stable transmission. In epidemic-prone areas, emphasis has been put in malaria early warning systems and early detection systems,[35,36] and it was argued that regular vector control measures may be a waste of resources in these areas.[37] However, regarding the spread of malaria in most highland areas, regular vector control activities targeted to the high-risk areas could be more cost-effective than less-effective emergency interventions that often face delays in mobilization.[17]

The IRS activities in Karuzi were stopped at the end of the study, despite ongoing transmission. ACT use alone is unlikely to maintain the reduction in malaria incidence without being associated with preventive measures. In present study, targeted IRS was shown to be very effective to prevent highland malaria and this mainly because of the high coverage. In African highlands, IRS has the advantage of targeting the places of highest risk[38] (i.e., the valleys). However, effective implementation of IRS relies on highly professional vector control services, good planning and timing of the activities, and strict management and logistics support.[39,40] There is an urgent need to build up this capacity in many places. ITNs, especially if they are long-lasting, have the advantage of being less demanding to implement than IRS and of being able to be targeted at individuals most at risk.[41] As full coverage is essential to impact transmission, both methods can be combined if full coverage with IRS is difficult to achieve or sustain over time. Moreover, the combination of IRS and ITN could permit better management of insecticide resistance if unrelated insecticides are used.[42] Investment in targeted and regu-

lar vector control measures associated with effective case management could have a major impact on malaria morbidity in the African highlands.

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