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The Impact of Renewing Long-Lasting Insecticide-Treated Nets in the Event of Malaria Resurgence: Lessons from 10 Years of Net Use in Dielmo, Senegal

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Abstract. The occurrence of malaria resurgences could threaten progress toward elimination of the disease. This study investigated the impact of repeated renewal of long-lasting insecticide-treated net (LLIN) universal coverage on malaria resurgence over a period of 10 years of net implementation in Dielmo (Senegal). A longitudinal study was carried out in Dielmo between August 2007 and July 2018. In July 2008, LLINs were offered to all villagers through universal campaign distribution which was renewed in July 2011, August 2014, and May 2016. Malaria cases were treated with artemisinin-based combination therapy. Two resurgences of malaria occurred during the 10 years in which LLINs have been in use. Since the third renewal of the nets, malaria decreased significantly compared with the first year the nets were implemented (adjusted incidence rate ratio) (95% CI) = 0.35 (0.15–0.85), during the ninth year after net implementation). During the tenth year of net implementation, no cases of malaria were observed among the study population. The use of nets increased significantly after the third time the nets were renewed when compared with the year after the first and the second times the nets were renewed ($P < 0.001$). The third renewal of nets, which took place after 2 years instead of 3 years together with a higher use of LLINs especially among the young, probably prevented the occurrence of a third malaria upsurge in this village.

INTRODUCTION

The estimated global malaria death and incidence rates declined by 62% and 41% between 2000 and 2015, respectively.¹ This dramatic decrease in the disease burden encouraged hopes for eliminating malaria.^{2,3} However, much effort and supplemental progress are still needed to achieve this goal,^{2,4,5} given that no significant progress in reducing global malaria cases was made between 2015 and 2017.⁶ In addition, the occurrence of malaria resurgences,^{7,8} the loss of immunity among exposed populations,^{9,10} *Anopheles* resistance to pyrethroid insecticides,¹¹ and *Plasmodium* resistance to artemisinin¹² pose serious threats to the future of malaria elimination efforts. Malaria resurgences have been observed in some endemic countries following a dramatic decrease in the disease through the large-scale use of long-lasting insecticide-treated nets (LLINs). Long-lasting insecticide-treated nets were noted by the WHO Pesticide Evaluation Scheme (WHOPES) to retain effective pyrethroid insecticidal activity under field conditions for at least 3 years.¹³ However, the incorrect use of LLINs could have an impact on the physical and biological efficacy of bed nets.^{14,15}

A strategy of LLIN universal coverage (UC) has been implemented in Dielmo, Senegal, West Africa, since 2008, and comprehensive renewal campaigns took place in 2011, 2014, and 2016. The UC strategy combined with the widespread use of artemisinin-based combination therapy (ACT) has significantly changed the epidemiology of malaria in Dielmo, from being holoendemic in 1990 to hypoendemic since 2010.¹⁶ However, two malaria resurgences have occurred during the

10-year period when Dielmo was under LLIN universal net coverage.¹⁷ Both outbreaks occurred during the third year of the 2008 and 2011 LLIN UC campaigns, respectively. To avoid a probable third malaria resurgence in the village, nets were renewed in May 2016, 2 years after the UC campaign in 2014, instead of 3 years, with the help and agreement of the Senegal National Malaria Control Program. The aim of this study was to investigate the evolution of malaria cases after 10 years of LLIN implementation and three net renewal campaigns between 2008 and 2018, and their association with the occurrence of malaria resurgences in Dielmo village.

METHODS

Setting: The village of Dielmo. The Dielmo research site has been described in detail elsewhere.¹⁸ In brief, the village is located in a Sudan Savannah region of central Senegal, 280 km southeast of Dakar, on the marshy banks of Nema, a small stream. Malaria transmission was continuous over the years from the beginning of the Dielmo research project in 1990 until 2009, when transmission became seasonal from July to October.¹⁶ The village comprised a population of 481 inhabitants in 2015 living in 42 households, with a median of eight persons per house.

Quarterly LLIN use surveys. In July 2008, LLIN (Permanet® 2.0, active ingredient: deltamethrin, Vestergaard Frandsen Group SA, Lausanne, Switzerland) UC was introduced for the first time in the village, and bed nets were offered to all villagers. Before distribution of the nets, all sleeping places in each household of the village were listed. A sleeping place was defined as the place where individuals in the household sleep. It could be occupied by a single individual or by several individuals. During the distribution campaigns, one net was allocated to every sleeping place. In July 2011, August 2014, and May 2016, the LLIN UC was renewed; that is, old LLINs were replaced by new LLINs. Before each new campaign, all nets

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from the previous campaign are removed from the study area. During these renewal campaigns, the criteria for net distribution were the same as those for the first UC in 2008. During the distribution campaign of 2008, 2011 and 2014, only Permanet 2.0 LLINs were given to the villagers. In the 2016 campaign, a mix of Permanet 2.0 and Olyset (active ingredient: permethrin) LLINs was distributed. Simultaneously, with the introduction of LLINs, repeat home-based surveys were carried out to assess their use. All households in the village which were included in the project (representing more than 98% of the village households) participated in the survey. Each participating household was visited quarterly in the morning by two technicians charged with recording whether the nets were hung above the bed the night before and administering a short questionnaire to household members about LLIN use. Individuals were asked if they had used nets the night preceding the visit and whether they never, always, or sometimes used nets. This allowed the creation of two groups according to the frequency of net use: those who always used nets and those who did not consistently use nets. This second category included individuals reporting to “never” use to “sometimes” use or to not own an LLIN during the corresponding quarter.

Participants and procedures. In this study, we focused on person-trimester observations covering the period before and after LLIN implementation, from August 2007 to July 2018. All inhabitants of Dielmo who were enrolled in the project during this period and who had spent at least 30 days in the quarter in Dielmo were included in the study. The presence or absence in the village of each enrolled household member was monitored, and the location of the absent member was reported daily. Since June 2006, clinical malaria attacks have been treated with the combination artesunate + amodiaquine. In case of fever, patients were referred to the project health center to be examined by a nurse. Thick smears stained with Giemsa were performed to determine the presence of the malaria parasite. Episodes of fever were attributable to *Plasmodium falciparum* clinical malaria attacks when parasite density was higher than an age-dependent threshold.¹⁹ From 2011 onward, the diagnostic and treatment policies were modified to maximize efforts to limit malaria transmission, as the level of anti-*Plasmodium* antibodies among Dielmo inhabitants has declined.⁹ The rapid diagnosis test (RDT) and polymerase chain reaction were then combined with the thick smear to improve disease diagnosis. Artesunate plus amodiaquine was systematically given to all patients with fever associated with malaria parasites detected by at least one of these diagnostic tools.

To assess asymptomatic carriage and malaria prevalence each year, cross-sectional surveys were conducted quarterly, with two surveys during the dry season and two in the rainy season. Thick smears and RDT (since May 2011) were performed on all individuals enrolled in the Dielmo project who were present in the village during the survey.

Entomological studies. Every month, two households were used to trap mosquitoes over three consecutive nights. These two households, 200 m apart, have been mosquito collection sites since the beginning of the Dielmo project in 1990 and remained unchanged throughout the course of the study.^{20,21} In each collection site, the human landing catch method was performed inside and outside the houses to assess malaria transmission. The Dielmo health center provided medical surveillance for all collectors, as for the other members of the community. Entomological inoculation rates (EIRs)

per number of infective bites/person/night were then assessed from the monthly values for human bite rates (i.e., the number of landing mosquitoes per person) and the proportion of infected mosquitoes.²² Rainfall was also measured each month of the study period. Rainfall was defined by the cumulative number of millimeters of rainfall during the previous month at the beginning of the given period, to estimate the time interval between the occurrence of rainfall and the occurrence of malaria cases.

Outcome and definition of independent variables. The study period was 11 years, including a 10-year follow-up of bed net use from August 2008 to July 2018 and a 1-year control period from August 2007 to July 2008. Clinical malaria attacks occurring among our study population were grouped together into 44 quarters over 11 years (August–October, November–January, February–April, and May–July of each year, defined in advance). Our analysis was thus based on person-trimester observations. The outcome variable was the number of malaria attacks per person per quarter.

The following variables were analyzed: 1) age-group (classified in six groups as follows: < 5, 5–9, 10–14, 15–29, 30–44, and ≥ 45 years), 2) rainfall, 3) gender, 4) the year of LLIN use (defined as the observation of 1 year of net use, starting from August of the preceding year to the following July), and 5) the EIR. Each variable was analyzed separately using bivariate analysis to assess the association with malaria risk. Random-effect negative binomial regression models were used to analyze clinical malaria episodes, taking into account the interdependence of successive observations in the same individuals. Variables that were $P < 0.2$ in bivariate analyses were integrated in multivariate analyzes.²³ Stepwise elimination of variables was performed based on the Akaike information criterion in the model. The days of monitoring for each person per quarter were controlled as the exposure variable in the multivariate model. In addition, the final model was adjusted for rainfall to control its effect. The significance level was fixed at $P = 0.05$ in the final model.

Malaria morbidity was assessed by estimating the incidence rate. For each year of study, the clinical malaria attack incidence rate was calculated as the ratio of the number of clinical malaria attacks recorded divided by the number of person-days of follow-up during a given period. The mean yearly incidence rates were derived from the daily incidence rates based on 365.25 days per year. The χ^2 test for incidence rates was used to compare the incidence rate for each year.

Analyses were performed using Stata Software, version 11.0 (College Station, TX).

RESULTS

A total of 17,304 person-trimester observations, corresponding to 631 individuals aged from 1 month to 103 years, with a mean age of 24 years and a proportion of 51% females were analyzed. Among these observations, 502 clinical malaria attacks were noted, of which 466 (2.7% of 17,304 persons) related to individuals who had at least one malaria attack per quarter during the study period, and 16,838 (97.3%) observations were related to villagers who had no malaria attacks. The number of clinical malaria attacks varied from 1 to 3 attacks per person per quarter. A total of 1,693 person-trimester observations concerned the tenth year of net implementation, in which no cases of malaria were observed.

TABLE 1

Sociodemographic and other characteristics of the entire population and according to the absence or presence of malaria attacks ($n = 15,611$)

Characteristic	Subcategory	Number of observations ($n = 15,611$), n (%)	Malaria cases	
			No ($n = 15,145$), n (%)	Yes ($n = 466$), n (%)
Year of use of LLINs	First year of use of LLINs	1,470 (8.50)	1,454 (9.60)	16 (3.43)
	Year before LLIN implementation	1,404 (8.11)	1,242 (8.20)	162 (34.76)
	Second year of use of LLINs	1,549 (8.95)	1,535 (10.14)	14 (3.00)
	Third year of use of LLINs	1,551 (8.96)	1,455 (9.61)	96 (20.60)
	Fourth year of use of LLINs	1,514 (8.75)	1,494 (9.86)	20 (4.29)
	Fifth year of use of LLINs	1,567 (9.06)	1,548 (10.22)	19 (4.08)
	Sixth year of use of LLINs	1,600 (9.25)	1,501 (9.91)	99 (21.24)
	Seventh year of use of LLINs	1,572 (9.08)	1,543 (10.19)	29 (6.22)
	Eighth year of use of LLINs	1,626 (9.40)	1,622 (10.71)	4 (0.86)
Age-group (years)	Ninth year of use of LLINs	1,758 (10.16)	1,751 (11.56)	7 (1.50)
	< 5	2,544 (16.30)	2,456 (96.54)	88 (3.46)
	5–9	2,520 (16.14)	2,407 (95.52)	113 (4.48)
	10–14	2,111 (13.52)	2,016 (95.50)	95 (4.50)
	15–29	3,386 (21.69)	3,287 (97.07)	99 (2.92)
	30–44	2,230 (14.28)	2,194 (98.39)	36 (1.61)
Gender	≥ 45	2,820 (18.06)	2,785 (98.76)	35 (1.24)
	Male (ref)	7,629 (48.87)	7,369 (48.66)	260 (55.79)
	Female	7,982 (51.13)	7,776 (51.34)	206 (44.21)

LLIN = long-lasting insecticide-treated net.

These observations (1,693) were not considered for the analysis; 15,611 observations were then analyzed (Table 1).

Incidence of clinical malaria attacks over the study period. Figure 1 describes the evolution of malaria incidence over the entire study period among adults and children. Overall, malaria declined significantly, from 0.58 attacks per person per year before implementation of LLINs to 0.05 and 0.04 attacks per person per year during the first and the second years of net use, respectively ($P < 0.001$). An upsurge of malaria was observed during the third year of net use, and the incidence of malaria increased to 0.30 attacks per person per year ($P < 0.001$). In response to the increase in malaria, the LLIN UC was renewed for the first time in July 2011 by replacing all nets from the first UC campaign in 2008 with new ones. Following that, malaria consequently decreased during

the first and the second years after the nets were renewed (a mean of 0.05 attacks per person per year during these 2 years; $P < 0.001$). Again, an upsurge occurred during the third year after the first renewal of the LLINs, and the incidence of malaria increased to 0.26 attacks per person per year ($P < 0.001$). Following that, a new UC campaign took place in August 2014 corresponding to the second time nets were renewed, and malaria decreased from 0.26 to 0.08 and 0.01 attacks per person per year in the first and the second years after the nets were renewed for the second time ($P < 0.001$). This third net UC campaign lasted only 2 years instead of 3 years to avoid the upsurge of malaria observed each time in the third year of the two previous UC. Thus, a fourth net UC campaign was conducted in May 2016, before the beginning of the rainy season.

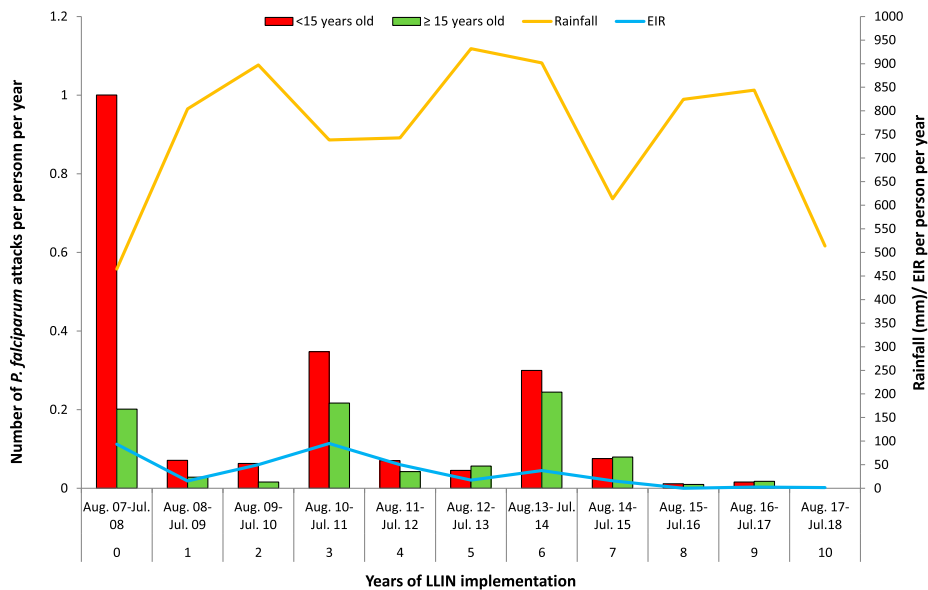


FIGURE 1. *Plasmodium falciparum* malaria attack incidence according to the year of long-lasting insecticide-treated net use among the population of Dielmo. This figure appears in color at www.ajtmh.org.

Between this third net renewal, corresponding to the fourth net UC campaign, and July 2018, no malaria upsurge was observed. In addition, malaria has decreased significantly when compared with the first year the nets were implemented. The incidence of malaria was only 0.02 and 0 attacks per person per year during the first and the second years after the third net renewal ($P < 0.001$), respectively. The first and the second years after the third net renewal corresponded to years 9 and 10 since nets were first introduced in the village of Dielmo.

Factors associated with the risk of clinical malaria attacks. Table 2 shows the results of the bivariate and multivariate analyses. We have excluded the observations concerning the tenth year of net use (corresponding to the second year after the third net renewal) from the statistical analyses because no malaria case was observed during this period. In the bivariate analysis, the third year and the sixth year after net implementation and the year before net implementation were significantly associated with an increase in malaria when compared with the first year of net implementation, whereas the eighth and the ninth years after the net implementation were significantly associated with a decrease in malaria risk. The other years were not significantly associated with an increased malaria risk when compared with the first year of net implementation (Table 2). With an incidence rate ratio (IRR) (95% CI) of 0.77 (0.60–0.98), being female was found to be a protective factor.

After adjusting for potential covariates such as age, gender, rainfall, EIR, and days of monitoring of each person per quarter, the control year (year before net implementation), and the third year and the sixth year after net implementation remained significantly associated with an increase in malaria, compared with the first year of net implementation (adjusted IRR [aIRR] [95% CI] = [7.90–22.64]; aIRR [95% CI] = 6.22 [3.63–10.68] 13.38; aIRR [95% CI] = 5.65 [3.36–9.49], respectively). The eighth and the ninth years of net implementation in this village were significantly associated with a decrease in malaria risk when compared with the first year of

net implementation (aIRR [95% CI] = 0.22 [0.07–0.66]; aIRR [95% CI] = 0.35 [0.15–0.85], respectively). Only adults aged 30 years and older were protected against malaria attacks, compared with children aged less than 5 years (aIRR [95% CI] = 0.40 [0.26–0.62]; aIRR [95% CI] = 0.31 [0.20–0.49] for the age-groups 30–44 years, and 45 years and older, respectively). Older children and adults aged between 15 and 29 years were at the same risk of having malaria compared with children aged less than 5 years (aIRR [95% CI] = 1.00 [0.76–1.33]; aIRR [95% CI] = 0.96 [0.70–1.33]; 0.84 [0.61–1.17], respectively, for the age-groups 5–9 years, 10–14 years, and 15–29 years). When considering the 10 years of net use only, children aged 5–14 years and adults aged 15–29 years were at a higher risk of having malaria, whereas adults aged 30 years and older were at the same risk of having malaria compared with the children aged less than 5 years (aIRR [95% CI] = 1.91 [1.23–2.98]; aIRR [95% CI] = 2.40 [1.52–3.80]; aIRR [95% CI] = 2.08 [1.33–3.24]; aIRR [95% CI] = 0.94 [0.54–1.65]; aIRR [95% CI] = 0.77 [0.45–1.33] for the age-groups 5–9 years, 10–14 years, 15–29 years, 30–44 years, and 45 years and older, respectively). Rainfall was significantly associated with a risk of having malaria (aIRR [95% CI] = 1.0007 [1.0003–1.001]).

Malaria prevalence. During the 10 years that nets have been implemented in Dielmo, the prevalence of malaria has decreased significantly, both in children and adults. The prevalence decreased from 26% in 2007 (the year before the implementation of nets) to 0.5% in 2014. During the upsurge periods, the prevalence did not increase, and was 2.4% and 0.2% in 2010 and 2013, respectively. Malaria prevalence reached its lowest level in 2015 with 0%, and until 2018, the prevalence was around 0.2% (Figure 2).

Rainfall and the EIR. Compared with the first year after net implementation, rainfall increased significantly during the second, fifth, and sixth years after net implementation ($P = 0.024$, 0.002, and 0.018, respectively), whereas it decreased significantly during the year before net implementation, and in the seventh and tenth years of net implementation ($P < 0.001$,

TABLE 2
Random-effect negative binomial regression models exploring factors associated with malaria clinical cases ($n = 15,611$)

Characteristic	Subcategory	Univariate analysis		Multivariate analysis	
		Incidence rate ratio (95% CI)	P-value	Adjusted IRR (95% CI)	P-value
Year of use of LLINs	First year of use of LLINs	1	–	1	–
	Year before LLIN implementation	11.70 (7.12–19.23)	< 0.001	13.38 (7.90–22.64)	< 0.001
	Second year of use of LLINs	0.78 (0.39–1.59)	0.50	0.79 (0.39–1.61)	0.518
	Third year of use of LLINs	5.67 (3.39–9.48)	< 0.001	6.22 (3.63–10.68)	< 0.001
	Fourth year of use of LLINs	1.13 (0.59–2.17)	0.70	1.19 (0.62–2.28)	0.600
	Fifth year of use of LLINs	1.05 (0.55–2.03)	0.88	1.05 (0.54–2.02)	0.893
	Sixth year of use of LLINs	5.57 (3.33–9.32)	< 0.001	5.65 (3.36–9.49)	< 0.001
	Seventh year of use of LLINs	1.61 (0.88–2.94)	0.12	1.71 (0.94–3.13)	0.080
	Eighth year of use of LLINs	0.22 (0.07–0.65)	0.006	0.22 (0.07–0.66)	0.007
Age-group (years)	Ninth year of use of LLINs	0.36 (0.15–0.86)	0.021	0.35 (0.15–0.85)	0.021
	< 5	1	–	1	–
	5–9	0.83 (0.60–1.14)	0.25	1.00 (0.76–1.33)	0.983
	10–14	0.65 (0.45–0.95)	0.024	0.96 (0.70–1.33)	0.826
	15–29	0.55 (0.38–0.80)	0.002	0.84 (0.61–1.17)	0.310
	30–44	0.31 (0.20–0.51)	< 0.001	0.40 (0.26–0.62)	< 0.001
Gender	≥ 45	0.23 (0.15–0.38)	< 0.001	0.31 (0.20–0.49)	< 0.001
	Male (ref)	1	–	–	–
Rainfall	Female	0.77 (0.60–0.98)	0.037	0.85 (0.68–1.08)	0.180
	–	1.0002 (0.9999–1.0005)	0.25	1.0007 (1.0003–1.001)	0.001
Entomological inoculation rate	–	1.03 (1.025–1.034)	< 0.001	0.997 (0.990–1.004)	0.473

LLIN = long-lasting insecticide-treated net.

respectively). During the third, fourth, eighth, and ninth years after net implementation, no significant difference in rainfall was observed when compared with the first year after net implementation. Rainfall increased significantly during the second malaria upsurge (sixth year of net implementation), whereas no difference in rainfall was observed during the first malaria upsurge (third year after net implementation) compared with the first year after net implementation (Figure 1).

The EIR decreased during the period of malaria decrease and increased during the malaria upsurges. The EIR decreased from 155.3 infective bites per person per year in 2008 to only 49.6 infective bites per person per year in 2009. However, it increased in 2010 and 2011 during the first upsurge period to 88.8 and 76.0 infective bites per person per year, respectively. In 2013 and 2014, during the second malaria upsurge, the EIR increased from 7.6 infective bites per person per year in 2012 to 43.1 and 18.2 infective bites per person per year, respectively. The EIR decreased from 18.2 in 2014 to only 2.8, 2.5, 1.7, and 0 infective bites per person per year in 2015, 2016, 2017, and mid-2018 (between January and July), respectively (Figure 2).

Net ownership and use. The ownership of a net in the village has evolved according to the period of the study (Figure 3). The ownership of nets was 88%, 84%, 90%, and 91%, the first year after net implementation and the first year after the first, second, and third nets' renewal, respectively. The ownership of nets reached its lowest level, with 70% and

72% of net ownership during the first and second malaria resurgence periods, respectively (Figure 3).

The rate of overall use of nets was highest among children aged less than 5 years and adults aged 30 years and older. It was significantly lower among older children aged 10–14 years and adults aged 15–29 years, especially during malaria upsurges, when their use of nets was only 47.8% and 43.2% during the first malaria upsurge and 39.8% and 31.9% during the second malaria upsurge, respectively. The use of LLINs was almost equal among children and adults during the ninth and the tenth years of net implementation, which corresponds to the first and the second years after the third net renewal (Figure 3). The level of LLIN use was high from the seventh to the tenth years of their implementation, with 71%, 77%, 82%, and 84% of the study population sleeping under nets, respectively, whereas less than 70% of the population used nets in other years (Figure 3). The use of nets reached its lowest level at 58% and 53% of net use during the first and the second malaria upsurges (corresponding to the third and the sixth years of net implementation in Dielmo), respectively. Net use increased significantly after the second and the third net renewal campaigns, from 53% to 71% ($\chi^2 = 78.45; P < 0.001$) and from 77% to 82% ($\chi^2 = 13.38; P < 0.001$), respectively. The use of nets increased significantly after the third net renewal campaign when compared with the year after the first and second time nets were renewed ($\chi^2 = 152.27; P < 0.001; \chi^2 = 43.60; P < 0.001$, respectively).

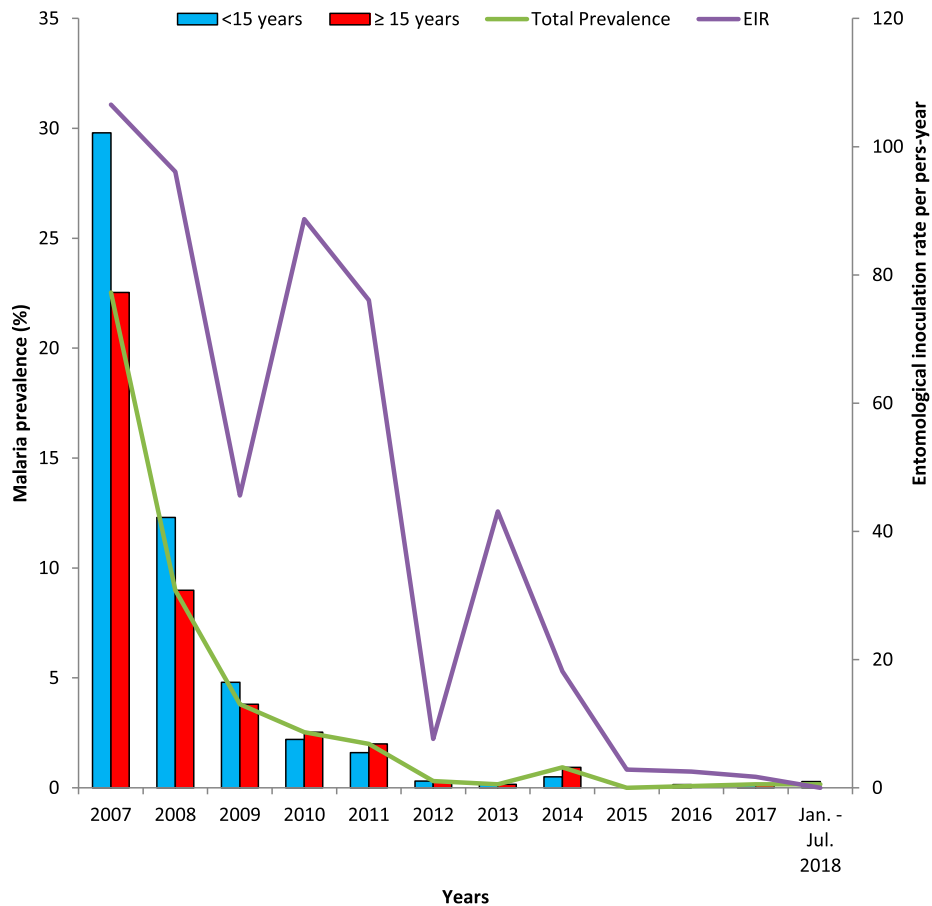


FIGURE 2. Malaria prevalence and entomological inoculation rate in Dielmo from 2007 to mid-2018. This figure appears in color at www.ajtmh.org.

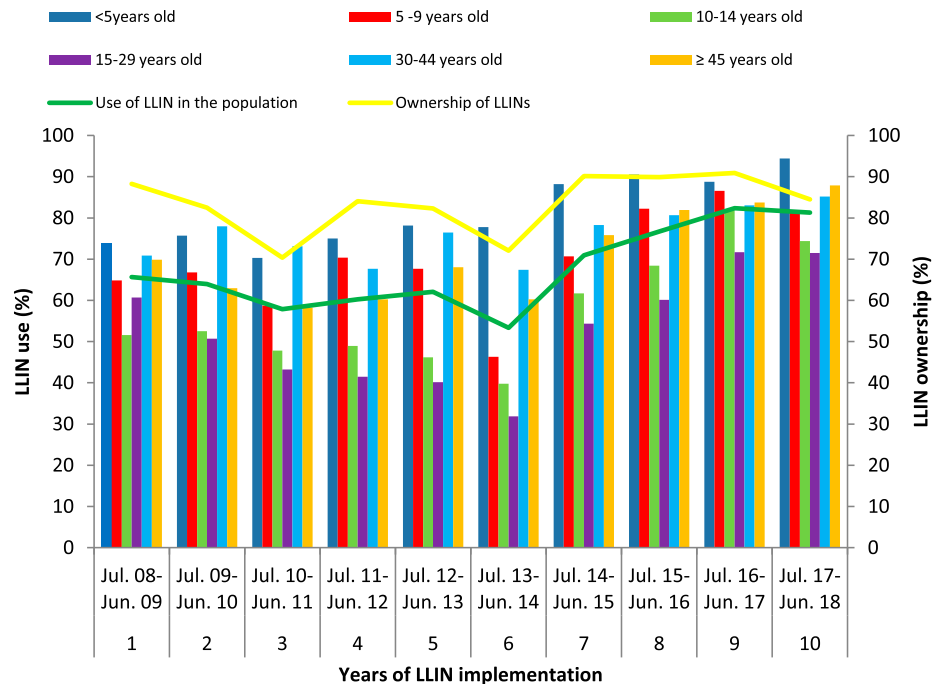


FIGURE 3. Long-lasting insecticide-treated net ownership and use according to the year of implementation among the Dielmo population by age-group. This figure appears in color at www.ajtmh.org.

DISCUSSION

This study investigated the evolution of malaria morbidity after 10 years of net implementation and three successive net renewal campaigns in Dielmo, Senegal. The results of the study demonstrate the efficacy of using LLINs together with ACT to reduce malaria attacks in Dielmo, despite the occurrence of two malaria resurgences in this village, both occurring in the third year of the first and the second LLIN UC campaigns.^{17,24} Unlike the previous two net renewal campaigns that took place 3 years after their implementation and during the rainy season, the third renewal of nets in this village took place 2 years after their use and, for the first time, before the rainy season. The results of the study show that malaria decreased significantly during the first year of the third net renewal campaign when compared with the first year the nets were initially implemented in Dielmo. In addition, no cases of malaria were observed in the second year of the third net renewal campaign, and no malaria resurgence has been observed since this third net renewal. These results could be explained by the significant use of LLINs after the third net renewal campaign compared with the previous year of net use, especially among older children and young adults. Indeed, the use of nets increased significantly during the first and the second years after they had been replaced for the third time, when compared with the use of nets during the first year following the first and the second net renewal campaigns. This renewal of the nets after 2 years instead of 3 years, combined with the significant use of the nets, probably helped to avoid the occurrence of a new malaria resurgence in the village. This significant use of nets observed after the third net renewal could be due to an awareness campaign about LLIN use that takes place during the distribution of nets. The nonoccurrence of a likely third malaria resurgence in Dielmo cannot, however,

be explained only by replacing the LLINs 2 years after their introduction because this third net replacement program once again extended for 3 years, and no malaria upsurge was observed (data not shown). This observation shows that the resurgence of malaria in Dielmo appears to be independent of the length of the distribution replacement cycle of LLINs, as long as the LLINs are available and used regularly and an awareness campaign about LLIN use takes place beforehand. Long-lasting insecticide-treated nets were noted by the WHOPEs to retain effective pyrethroid insecticidal activity under field conditions for at least 3 years,¹³ although studies have demonstrated that the serviceable life of LLINs is closer to two rather than 3 years in Rwanda¹⁵ and that older insecticide-treated bed nets are associated with higher rates of *P. falciparum* in young children in Malawi.²⁵ Also, as demonstrated in some studies, 2 years appears to be a good timescale for the cycle of distribution replacement of LLINs, especially in areas where anopheles resistance to pyrethroids is more pronounced.^{14,15,26} The results of the study presented here support, however, 3 years of distribution replacement of LLINs in Dielmo because the question of efficient use of nets remains crucial. Even if no resurgence of malaria was observed when nets were replaced after 2 years instead of 3 years, the following renewal was performed 3 years after, and no malaria resurgence was observed (data not shown). The distribution replacement cycle of LLINs in this village could continue to be performed every 3 years, preferably before the rainy season to prevent parasite transmission occurring in the early rainy season. The good results obtained after the third renewal of nets in Dielmo could be explained by the greater use of nets, especially in older children and young adults, who were known in this village to not regularly use their net.^{27,28} This significant malaria decrease was probably reinforced by the overall

decrease in parasites in the community due to the vector control effect of LLINs over a prolonged period of time, as the prevalence of malaria is close to zero several years ago.

As seen in the Results, older children and young adults were at a higher risk of having malaria than children aged less than 5 years after implementation of nets in this village. This observation could be explained by the low use of nets by this sub-population due mainly to their strolls late at night, whereas children aged less than 5 years and their parents (mainly the mother) are sleeping together under the net.

It is worth noting that the decrease in rainfall certainly played a role in the significant decrease in malaria cases observed after the third net renewal campaign, although rainfall also fell significantly the year before nets were implemented in the village. The role of rainfall is debatable, however, as its increase was significantly associated only with the second malaria resurgence in Dielmo.

The control for rainfall, the EIR, and the days of monitoring of the villagers have reduced the impact of confounders in the context of the occurrence of malaria. However, the behavior of each villager could not be controlled, nor their bedtime, because previous surveys have demonstrated that the majority did not know their exact bedtime. One limitation of this study resides in the fact that the physical integrity of LLINs was not assessed 2 and 3 years after net replacement. Appropriate studies must be performed to measure the integrity of LLINs over time, to evaluate LLIN condition 2 and 3 years after their distribution in this village.

CONCLUSION

Net renewal combined with an awareness-raising campaign on the use of nets that contributed to a significant use of nets, especially among the young people, seems to be crucial in maximizing the protective effect of net use against malaria and avoiding malaria resurgences in Dielmo.

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REFERENCES

1. WHO, 2016. *World Malaria Report 2016*. Geneva, Switzerland: World Health Organization.
2. Ghebreyesus TA, 2019. The malaria eradication challenge. *Lancet* 394: 990–991.
3. Roberts L, Enserink M, 2007. Malaria. Did they really say ... eradication? *Science* 318: 1544–1545.
4. Feachem RGA et al., 2019. Malaria eradication within a generation: ambitious, achievable, and necessary. *Lancet* 394: 1056–1112.
5. Mswati IK 3rd., 2019. An Africa free of malaria. *Lancet* 394: 988–989.
6. WHO, 2018. *World Malaria Report 2018*. Geneva, Switzerland: World Health Organization.
7. Hamel MJ, Adazu K, Obor D, Sewe M, Vulule J, Williamson JM, Slutsker L, Feikin DR, Laserson KF, 2011. A reversal in reductions of child mortality in western Kenya, 2003–2009. *Am J Trop Med Hyg* 85: 597–605.
8. Lee PW, Liu CT, do Rosario VE, de Sousa B, Rampao HS, Shaio MF, 2010. Potential threat of malaria epidemics in a low transmission area, as exemplified by Sao Tome and Principe. *Malar J* 9: 264.
9. Diop F, Richard V, Diouf B, Sokhna C, Diagne N, Trape JF, Faye MM, Tall A, Diop G, Balde AT, 2014. Dramatic declines in seropositivity as determined with crude extracts of *Plasmodium falciparum* schizonts between 2000 and 2010 in Dielmo and Ndiop, Senegal. *Malar J* 13: 83.
10. O'Meara WP, Mwangi TW, Williams TN, McKenzie FE, Snow RW, Marsh K, 2008. Relationship between exposure, clinical malaria, and age in an area of changing transmission intensity. *Am J Trop Med Hyg* 79: 185–191.
11. Ranson H, N'Guessan R, Lines J, Moiroux N, Nkuni Z, Corbel V, 2011. Pyrethroid resistance in African anopheline mosquitoes: what are the implications for malaria control? *Trends Parasitol* 27: 91–98.
12. Ashley EA et al.; Tracking Resistance to Artemisinin Collaboration, 2014. Spread of artemisinin resistance in *Plasmodium falciparum* malaria. *N Engl J Med* 371: 411–423.
13. WHO, 2005. *Guidelines for Laboratory and Field Testing of Long-Lasting-Insecticidal Mosquito Nets*. Geneva, Switzerland: World Health Organization.
14. Craig AS et al., 2015. Long-lasting insecticidal nets in Zambia: a cross-sectional analysis of net integrity and insecticide content. *Malar J* 14: 239.
15. Hakizimana E, Cyubahiro B, Rukundo A, Kabayiza A, Mutabazi A, Beach R, Patel R, Tongren JE, Karema C, 2014. Monitoring long-lasting insecticidal net (LLIN) durability to validate net serviceable life assumptions, in Rwanda. *Malar J* 13: 344.
16. Trape JF et al., 2014. The rise and fall of malaria in a west African rural community, Dielmo, Senegal, from 1990 to 2012: a 22 year longitudinal study. *Lancet Infect Dis* 14: 476–488.
17. Wotodjo AN, Doucoure S, Gaudart J, Diagne N, Diene Sarr F, Faye N, Tall A, Raoult D, Sokhna C, 2017. Malaria in Dielmo, a Senegal village: is its elimination possible after seven years of implementation of long-lasting insecticide-treated nets? *PLoS One* 12: e0179528.
18. Trape JF et al., 1994. The Dielmo project: a longitudinal study of natural malaria infection and the mechanisms of protective immunity in a community living in a holoendemic area of Senegal. *Am J Trop Med Hyg* 51: 123–137.
19. Roucher C, Rogier C, Dieye-Ba F, Sokhna C, Tall A, Trape JF, 2012. Changing malaria epidemiology and diagnostic criteria for *Plasmodium falciparum* clinical malaria. *PLoS One* 7: e46188.
20. Doucoure S, Thiaw O, Wotodjo AN, Bouganali C, Diagne N, Parola P, Sokhna C, 2020. *Anopheles arabiensis* and *Anopheles funestus* biting patterns in Dielmo, an area of low level exposure to malaria vectors. *Malar J* 19: 230.

21. Wotodjo AN et al., 2015. No difference in the incidence of malaria in human-landing mosquito catch collectors and non-collectors in a Senegalese village with endemic malaria. *PLoS One* 10: e0126187.
22. Fontenille D, Lochouart L, Diagne N, Sokhna C, Lemasson JJ, Diatta M, Konate L, Faye F, Rogier C, Trape JF, 1997. High annual and seasonal variations in malaria transmission by anophelines and vector species composition in Dielmo, a holoendemic area in Senegal. *Am J Trop Med Hyg* 56: 247–253.
23. Mickey RM, Greenland S, 1989. The impact of confounder selection criteria on effect estimation. *Am J Epidemiol* 129: 125–137.
24. Trape JF et al., 2011. Malaria morbidity and pyrethroid resistance after the introduction of insecticide-treated bednets and artemisinin-based combination therapies: a longitudinal study. *Lancet Infect Dis* 11: 925–932.
25. Andronescu LR et al., 2019. Net age, but not integrity, may be associated with decreased protection against *Plasmodium falciparum* infection in southern Malawi. *Malar J* 18: 329.
26. Gnanguenon V, Azondekon R, Oke-Agbo F, Beach R, Akogbeto M, 2014. Durability assessment results suggest a serviceable life of two, rather than three, years for the current long-lasting insecticidal (mosquito) net (LLIN) intervention in Benin. *BMC Infect Dis* 14: 69.
27. Wotodjo AN, Doucoure S, Diagne N, Sarr FD, Parola P, Gaudart J, Sokhna C, 2018. Another challenge in malaria elimination efforts: the increase of malaria among adults after the implementation of long-lasting insecticide-treated nets (LLINs) in Dielmo, Senegal. *Malar J* 17: 384.
28. Wotodjo AN et al., 2015. The implication of long-lasting insecticide-treated net use in the resurgence of malaria morbidity in a Senegal malaria endemic village in 2010–2011. *Parasit Vectors* 8: 267.