

Malaria in São Tomé and Príncipe: On the Brink of Elimination after Three Years of Effective Antimalarial Measures

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Abstract. In 2005, São Tomé e Príncipe began an initiative aimed at reducing malaria-related mortality to zero. The program included mass coverage with two antivevector intervention methods (indoor residual spraying and long-lasting insecticidal nets), artemisinin-based combination therapy, and intermittent preventive therapy in pregnancy with sulfadoxine-pyrimethamine. At the end of 2007, three years after intensified interventions began, malaria-attributed outpatient consultations, hospitalizations, and deaths decreased by more than 85%, 80%, and 95%, respectively, in all age groups. Mean prevalence of parasitemia and splenomegaly were also significantly reduced to 2.1% ($P < 0.0001$) and 0.3% ($P < 0.0001$) after two rounds of spraying from baseline prevalences of 30.5% and 48.8%, respectively. The dramatic reduction in malaria morbidity and mortality now enable serious consideration of new goals and strategies aimed at completely interrupting malaria transmission on these islands. We report evidence of the program's impact and the feasibility of and potential strategies for eliminating malaria from São Tomé e Príncipe.

INTRODUCTION

Malaria has long been a problem in São Tomé e Príncipe, stressing its health systems and hampering the economic development of the country. Before the early 1980s, intervention efforts were localized and intermittent. After independence, a full-scale malaria eradication program was undertaken that combined bi-annual indoor residual spraying (IRS) with *dichloro-diphenyl-trichloroethane* (DDT) and weekly prophylaxis with chloroquine. This reduced malaria prevalence from 19.2% to 0.6% and malaria-attributed mortality to zero.¹ When control measures abruptly ceased because of financial constraints, resistance of the vector to DDT, reduced acceptance by the people, and insufficient political commitment, the incidence of malaria morbidity and mortality increased during a devastating epidemic in 1985–1986.^{1,2} Thereafter, case management using chloroquine had been the sole anti-malarial intervention used until recently, despite the high *Plasmodium falciparum* resistance to chloroquine discovered in the early 1990s.^{2–5}

The Centro Nacional de Endemias (CNE) drafted a national malaria control strategy in 2004 that entailed scaling-up preventive strategies including IRS, long-lasting insecticidal nets (LLINs), intermittent preventive therapy (IPT), and early diagnosis and prompt treatment with artemisinin-based combination therapy (ACT).⁶ It was designed to achieve millennium development goals for malaria, and promote social and economic development in the country.⁷ We review the impact of current anti-malarial interventions on diverse indicators. The practicality of eliminating malaria from São Tomé and Príncipe and methods for achieving this goal are examined.

MATERIALS AND METHODS

Description of the islands. The two main islands comprising the Democratic Republic of São Tomé and Príncipe are located along the equator in the Gulf of Guinea, 240 km west of Gabon. Most of the 150,000 residents live along the shore because the rugged, volcanic interior region is sparsely inhabited. The climate, with an average annual temperature $>25^{\circ}\text{C}$, and a rainy season that extends from September to May,¹ enables perennial malaria transmission. Although all four species of *Plasmodium* have been detected,^{1–5} *P. falciparum* predominates, with prevalence rates exceeding 70% in some districts before the recent intensification.⁸ *Anopheles gambiae* s.s. forest cytoform (type M) is the only malaria vector in the country.⁹ It is primarily anthropophilic with a tendency towards exophilic and exophagic behavior.¹⁰ Outdoor biting, when it occurs, involves considerable zoophagy.

Current malaria prevention and treatment strategies.
Treatment of Malaria Cases with ACT. In 2005, the national malaria control program introduced artemisinin plus amodiaquine and Coartem® (Novartis, Basel, Switzerland) (artemether-lumefantrine) as the first-line and second-line drugs for treatment of uncomplicated malaria with support from the Global Fund against AIDS, Tuberculosis and Malaria (GFATM). Artemisinin plus amodiaquine was highly efficacious against *P. falciparum* in assessments undertaken soon after introduction.¹¹ Health service facilities and community level care are now generally accessible to São Toméans, and most facilities are equipped for early diagnosis and treatment of malaria cases. All hospitals, health centers, and most health posts are equipped with microscopes for examination of blood smears, and some health posts not equipped with microscopic diagnostics are using rapid diagnostic tests for malaria diagnosis. As a result, more than 90% of patients less than five years of age received diagnosis and prompt and effective anti-malarial treatment in 2006.¹² Quinine remains effective and continues to be used to treat severe malaria.³

Intermittent preventive therapy. Sulfadoxine-pyrimethamine is used solely for IPT in pregnancy, although, an *in vivo* study conducted in 2000 indicated approximately 20%

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clinical failures.¹¹ Another study showed high frequencies of resistance-associated mutations.¹³ The rate of IPT use by pregnant women reached 66.7% in 2005 and 75.9% in 2007.¹²

Interventions against malaria vectors. Current anti-vector interventions on São Tomé and Príncipe target adult mosquito vectors using IRS and LLINs. The CNE, in partnership with the Taiwan International Cooperation and Development Fund, apply alpha-cypermethrin at a dosage of 50 mg/m² to the interiors of all homes across São Tomé and Príncipe.¹⁴ A susceptibility study of *An. gambiae* to alpha-cypermethrin showed 100% sensitivity in 2004 and 94–100% sensitivity in 2005 one year after implementation.¹⁵ The program began with a limited pilot phase from July 2003 through July 2004, which resulted in a 25–50% reduction in prevalence of parasitemia.¹⁶ The program was extended to the entire country in December 2004, with 87% acceptance rate of IRS for dwellings and outhouses, and population coverage exceeded 90% in each of the three rounds completed thus far.¹⁴

In 2005, with funding from GFATM, the government began distributing free LLINs throughout the country with particular emphases on children less than five years of age and pregnant women. In three years, more than 50,000 LLINs were distributed using all levels of the health system, and at the end of 2007, 78.3% of households owned at least one bed net. The percentage of children sleeping under bed nets has increased from 1% in 1996 to 40% in 2004 and 57.9% in 2005.⁶

Data and estimation of malaria impact indicators. Multiple malaria program indicators selected from the list of the Roll Back Malaria Impact Indicators,¹⁷ were assessed using data from health information systems (HIS), malariometric surveys, and community death registers. Laboratory-confirmed (microscopy and rapid diagnostic tests) malaria and all-cause case data from hospitals, health centers, and health posts from 1995 through 2007 were obtained from the HIS records of CNE. The data, including outpatient consultations, hospital admissions, and deaths, were compiled on a yearly basis by age (< 5 and ≥ 5 years). Numbers of malaria-attributed and all-cause deaths were determined from HIS and community death registers. Data for 1995–1999 was consolidated nationally, and data for 2000–2007 were available by district. Mean monthly precipitation and temperature were obtained from the International Research Institute for Climate and Society (IRI) at the Earth Institute (IRI FD ECHAM4p5 History MONTHLY surface dataset for coordinates 5.625E 1.395307N).

Trends were determined for absolute number of malaria-related outpatient consultations, hospitalizations, and deaths by year. To assess the relative burden of malaria, malaria-attributed outpatient consultations, hospitalizations, and deaths were estimated. The attributable risk of burden is the proportion of all-cause burden that are attributable to malaria (%). To evaluate the quality of case management for severe and complicated malaria, malaria-case fatality rates in health facilities were determined. Each indicator was estimated for both age groups. In addition, two-slope linear spline models were fitted to these indicators for children less than five years of age to estimate two regression lines (slopes) for the pre- and post-intervention periods.

To determine mean malaria prevalence over time, we reviewed diverse malariometric surveys that recorded prevalence of parasitemia and splenomegaly among children 2–9 years of age and were conducted by CNE from 2003 through 2006.¹⁸

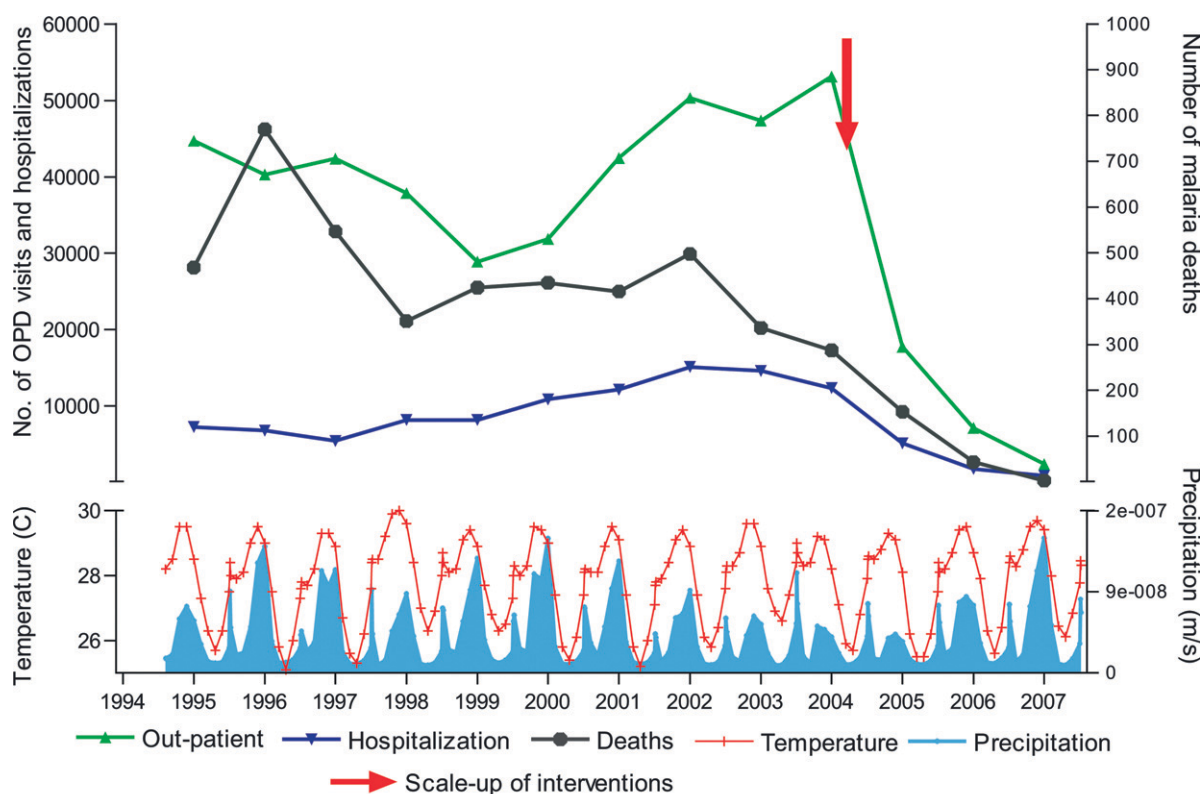
These surveys were conducted before and after the initiation of IRS operations in various districts of São Tomé and Príncipe. A total of 36 malariometric surveys were undertaken: 17 before the initiation of the IRS program, 13 after the first round of IRS, and 6 after the second round of IRS. Mean prevalence of parasitemia and splenomegaly were estimated for each of the three periods.

RESULTS

Malaria morbidity and mortality have decreased substantially since 2005. Reported malaria cases (outpatient and inpatient) and deaths from 1995 through 2007 in relation to precipitation and temperature are shown in Figure 1. Prior to the recent initiatives, malaria had been the dominant public health problem in the country. The annual number of outpatient consultations had exceeded 40,000, with more than 10,000 hospitalizations and more than 400 deaths attributed to malaria. By 2007, the malaria burden had been reduced highly significantly, with only 2,371 outpatient consultations, 834 hospitalizations, and 3 malaria related deaths (Figure 1). Rainfall and temperature remained similar before and after the scale-up of interventions. Time-series analysis, controlling for seasonal change, indicated a non-significant trend for rainfall ($P = 0.87$) and temperature ($P = 0.55$), which suggested that changes in burden could not be attributed to climatic anomalies.

Before the scale-up of control efforts (2000–2003), on average malaria accounted for 50% of outpatient consultations in both age groups, 70% of admissions and 50% of deaths in children < 5 years of age and 60% of admissions and 20% of deaths in persons ≥ 5 years of age (Figure 2). As is typical where malaria transmission is intense, malaria-attributed hospitalizations and deaths were higher in children < 5 years of age than in persons ≥ 5 years of age, and the risk of uncomplicated malaria (outpatient) was similar in both age groups. The malaria-attributed outpatient consultations, which exceeded 50% in both age groups prior to the scale-up of control efforts, decreased by 92.6% and 87.2% in 2007 in children < 5 years of age and in persons ≥ 5 years of age, respectively (Figure 2A). During the same period, the malaria-attributed hospitalizations (Figure 2B) decreased by 87.5% and 82.3% in children < 5 years of age and in persons ≥ 5 years of age, respectively. Similarly, the malaria-attributed deaths (Figure 2C) showed a reduction by more than 95% in both age groups. However, the malaria case-fatality rate remained unchanged over time in both age groups (Figure 2D). Interestingly, much of the difference in the risk of severe malaria (hospitalization) and malaria-related death between the two age groups disappeared after scale-up of interventions, which indicated a control effect in all age groups. These gains extended to all districts. Data for outpatient department visits and hospitalizations are shown in Table 1. Results of spline regression models for four indicators in children less than five years of age are shown in Table 2 and reaffirm the reduction of malaria burden. Malaria-attributed outpatient visits, hospitalizations, and deaths showed an accelerated and highly significant decrease post-intervention, and the slope for malaria case-fatality showed a decrease that was not significant.

Implementation of a nationwide IRS program was associated with an overall reduction in the prevalence of parasitemia and splenomegaly throughout the country. The mean



Source for temperature and precipitation: IRI FD ECHAM4p5 History MONTHLY surface dataset, 5.625E 1.395307N

FIGURE 1. Scale-up of malaria interventions, yearly reported laboratory confirmed malaria out-patient consultations, hospitalizations and deaths, and mean monthly precipitation and temperature in São Tomé and Príncipe, 1995–2007.

prevalence of parasitemia and splenomegaly and 95% confidence intervals for surveys undertaken before and after the first and second rounds of the IRS program among children 2–9 years of age are shown in Figure 3. Mean prevalence of parasitemia, which was 30.5% before the initiation of IRS, decreased to 8.3% and 2.1% ($P < 0.0001$) after the first round and second round of IRS, respectively. Similarly, the mean prevalence of splenomegaly decreased to 27.1% and 0.3% ($P < 0.0001$), respectively, after the first and second rounds of IRS from a pre-intervention prevalence of 48.8%. The reduction in prevalence of parasitemia was particularly remarkable when compared with the reduction in prevalence of splenomegaly after the first round of IRS.

DISCUSSION

The reduction in malaria burden achieved in the wake of the recently intensified anti-malarial efforts in São Tomé and Príncipe is comparable with the effect of the full-scale eradication program carried out during the early 1980s.¹ This time, however, the prospects of sustaining these efforts and successes appear much more favorable because of the strong external financial and technical support.¹⁷

Although climatic conditions favorable to malaria transmission remained the same, malaria morbidity and mortality showed a marked reduction within three years after the recent scale-up began. This can only be explained by the combined effect the integrated package of preventive measures and universal access to effective ACTs. Although the relative influence of each control measure cannot be

determined precisely, the use of IRS has probably contributed most because gains began to accrue even before LLINs had been widely distributed. The IRS pilot, which was implemented from July 2003 through July 2004, resulted in a 25–50% reduction in prevalence of parasitemia.¹⁹ Parasitologic assessment of the IRS program among children less than nine years of age before the IRS campaign and 12 months after the first spraying round showed a dramatic reduction of prevalence of malaria parasitemia.¹⁴ This finding is consistent with prior reports of the impact of IRS on malaria incidence.²⁰

The rapid therapeutic response to ACTs, combined with its probable anti-gametocidal properties,^{21,22} would also contribute substantially to the reduction of malaria transmission.²³ Deployment of ACTs in Zanzibar may have contributed to reduction of malaria-associated morbidity and mortality within two years.²⁴

With coverage increasing dramatically over the last three years, the contribution of LLINs should also not be underestimated. The personal as well as community protective effects of nets have likely played a major role in reducing the malaria burden.²⁵ The use of insecticide-treated bed nets has been shown to reduce deaths in children less than five years of age by up to 20% in Africa,²⁶ and a study in São Tomé and Príncipe has also shown a significant reduction in the prevalence of malaria among bed net than in nonusers.⁹ Because of the potential synergies involved, these reductions may not have been achieved as quickly if the integrated measures had not been introduced simultaneously.²⁷

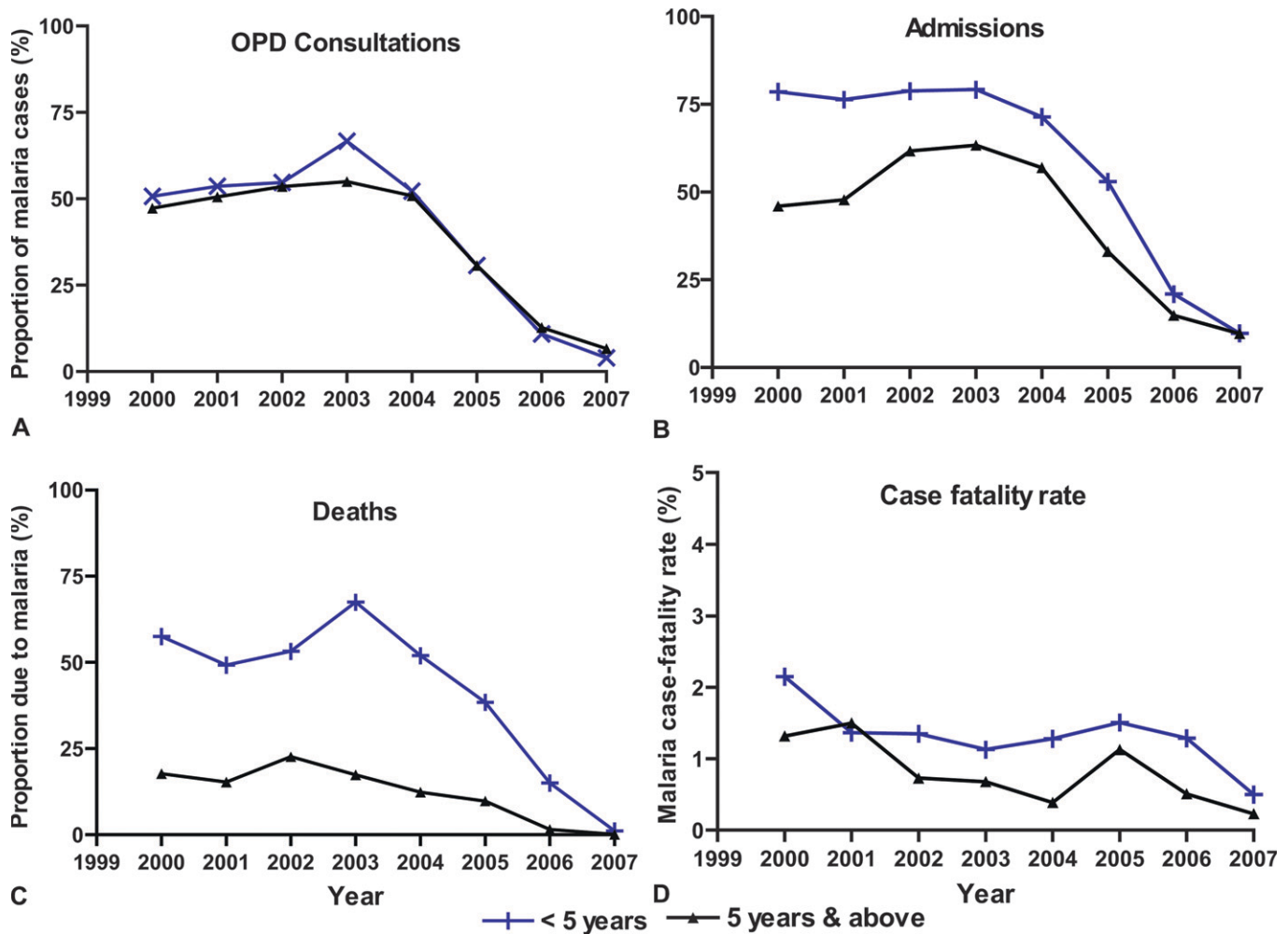


FIGURE 2. Malaria-attributed (proportion of all-cause attributable to malaria) out-patient consultations (A), admissions (B), and deaths (C), and case-fatality rates (D) by age group in São Tomé and Príncipe, 2000–2007.

The malaria case-fatality rate remained unchanged over time in both age groups, an indication that the quality of severe malaria case management has not yet improved. The reduction in the absolute number of severe malaria cases caused by the rapid therapeutic response to ACTs may result in hospitalization of only the sickest patients, which may increase malaria-specific mortality if not accompanied by improved case management. Thus, further efforts are still needed to improve health outcomes beyond what has been accomplished by reducing transmission.

Health service coverage, completeness of reporting over time, and health-seeking behaviors are the major limitations of HIS data. However, persons in general enjoy comparatively good access to health service facilities and community level care. Thus, the information obtained captures most cases in the country. No major changes in the HIS occurred during this period. Thus, the malaria cases and deaths recorded reliably indicate the time trend in malaria incidence. Moreover, to demonstrate a consistent finding, we have included malaria-attributed outpatient visits, admissions, and deaths to control any change in access and use of health services and completeness of reporting over time.

These findings suggest that complete elimination of transmission can now be seriously considered. Elimination will

require new goals and strategies adapted to the current malaria situation. New intervention approaches may be necessary to attack vector populations refractory to current approaches and to consolidate the reductions in burdens already achieved by the current integrated approach.

The primary challenge to sustain the current efforts and new intervention approaches will be the availability of funding. Thus, more work will be needed to secure sustained internal and external funding. The successful elimination of malaria in Taiwan was as a result of government initiative and commitment, development of basic health structures and community support, careful planning and organization, and strong assistance of international organizations.²⁸ Thus, it will be essential for the health service to show the political will to sustain high expenditures on malaria control even when it ceases to be a dominant proportion of the overall burden of disease. Failure to sustain the effort under these conditions seems to have been the main cause of the resurgence of malaria in India in the 1970s and 1980s, after achieving a 99.8% reduction in malaria incidence in the 1950s and 60s.²⁹

The unique physical situation of São Tomé and Príncipe provides additional reasons for optimism. The relatively small land surface of the islands, the accessibility of transmission zones, the small population, and the distance from the African

TABLE 1
Number of reported outpatient consultations and hospital admissions caused by malaria and malaria-attributed (proportion of all cause attributable to malaria) out-patients and admissions by district and year, São Tomé and Príncipe, 2000–2007*

Year	Persons < 5 years of age													
	Cantagalo		Caué		Lemba		Lobata		Me Zochi		Regaio Automoma do Príncipe		Agua Grande	
	OPD malaria visits	Malaria admission	OPD malaria visits	Malaria admission	OPD malaria visits	Malaria admission	OPD malaria visits	Malaria admission	OPD malaria visits	Malaria admission	OPD malaria visits	Malaria admission	OPD malaria visits	Malaria admission
2000	1,434 (0.55)	-	1,049 (0.64)	372 (0.84)	874 (0.55)	831 (0.88)	2,251 (0.56)	175 (0.87)	1,977 (0.53)	-	727 (0.45)	343 (0.69)	3,657 (0.43)	6,105 (0.78)
2001	1,644 (0.46)	-	1,552 (0.84)	522 (0.87)	2,847 (0.66)	698 (0.68)	2,753 (0.53)	228 (0.9)	2,740 (0.53)	-	763 (0.45)	323 (0.86)	5,800 (0.49)	7,069 (0.76)
2002	1,636 (0.46)	-	1,967 (0.81)	676 (0.88)	2,478 (0.64)	1,185 (0.85)	3,004 (0.58)	425 (0.9)	2,817 (0.51)	-	1,055 (0.47)	559 (0.87)	7,821 (0.52)	8,250 (0.76)
2003	1,912 (0.52)	-	953 (0.7)	488 (0.81)	4,442 (0.78)	1,021 (0.83)	4,114 (0.67)	640 (0.97)	2,383 (0.5)	-	874 (0.41)	444 (0.87)	4,415 (0.42)	7,304 (0.77)
2004	3,841 (0.56)	-	1,522 (0.63)	530 (0.72)	3,739 (0.68)	953 (0.79)	5,210 (0.6)	562 (0.86)	3,386 (0.54)	-	508 (0.37)	188 (0.76)	3,404 (0.33)	5,993 (0.69)
2005	1,327 (0.31)	-	828 (0.61)	152 (0.46)	1,140 (0.37)	206 (0.48)	1,043 (0.23)	228 (0.56)	1,842 (0.41)	-	304 (0.26)	120 (0.69)	1,805 (0.23)	2,279 (0.53)
2006	317 (0.11)	-	206 (0.27)	52 (0.19)	528 (0.19)	73 (0.23)	321 (0.08)	98 (0.33)	569 (0.14)	-	204 (0.14)	78 (0.48)	415 (0.06)	631 (0.19)
2007	118 (0.05)	-	151 (0.17)	43 (0.21)	102 (0.05)	17 (0.08)	73 (0.02)	70 (0.29)	100 (0.03)	-	18 (0.02)	9 (0.09)	115 (0.02)	261 (0.08)
Total	12,229 (0.41)	-	8,228 (0.66)	2,835 (0.71)	16,150 (0.56)	4,984 (0.74)	18,769 (0.46)	2,426 (0.76)	15,814 (0.42)	-	4,453 (0.36)	2,064 (0.76)	27,432 (0.36)	37,892 (0.66)
Persons ≥ 5 years of age														
2000	1,860 (0.55)	-	973 (0.56)	112 (0.49)	996 (0.45)	498 (0.71)	3,409 (0.56)	232 (0.83)	3,750 (0.54)	-	1,559 (0.47)	394 (0.62)	7,337 (0.40)	1,784 (0.38)
2001	1,912 (0.45)	-	1,538 (0.73)	166 (0.65)	2,913 (0.60)	407 (0.59)	3,555 (0.53)	212 (0.74)	4,660 (0.46)	-	1,798 (0.53)	410 (0.63)	8,990 (0.48)	2,082 (0.42)
2002	2,077 (0.48)	-	2,183 (0.73)	304 (0.75)	2,427 (0.57)	612 (0.72)	4,133 (0.61)	420 (0.85)	5,108 (0.51)	-	1,986 (0.50)	640 (0.69)	11,817 (0.51)	2,266 (0.54)
2003	2,350 (0.51)	-	1,377 (0.6)	236 (0.60)	4,834 (0.78)	633 (0.71)	5,369 (0.72)	541 (0.90)	4,859 (0.53)	-	1,652 (0.47)	499 (0.68)	7,813 (0.43)	2,764 (0.58)
2004	4,952 (0.56)	-	1,542 (0.61)	259 (0.63)	4,547 (0.65)	697 (0.81)	7,556 (0.63)	435 (0.80)	5,215 (0.56)	-	996 (0.40)	236 (0.46)	6,706 (0.34)	2,487 (0.51)
2005	2,329 (0.36)	-	1,393 (0.62)	106 (0.35)	1,508 (0.35)	236 (0.43)	1,702 (0.27)	258 (0.42)	2,711 (0.41)	-	638 (0.25)	130 (0.36)	3,346 (0.21)	1,394 (0.30)
2006	652 (0.15)	-	394 (0.35)	33 (0.09)	827 (0.21)	81 (0.24)	634 (0.11)	125 (0.27)	832 (0.14)	-	306 (0.12)	63 (0.20)	899 (0.07)	484 (0.13)
2007	291 (0.09)	-	281 (0.21)	28 (0.12)	194 (0.08)	20 (0.07)	189 (0.05)	82 (0.27)	264 (0.06)	-	88 (0.07)	23 (0.06)	390 (0.05)	281 (0.09)
Total	16,423 (0.41)	-	9,681 (0.59)	1,244 (0.48)	18,246 (0.52)	3,184 (0.62)	26,544 (0.48)	2,305 (0.64)	27,399 (0.43)	-	9,023 (0.39)	2,395 (0.53)	47,298 (0.35)	13,542 (0.38)

* Values are no. (%). OPD = outpatient department.

TABLE 2

Slopes for the relative change in malaria-attributable measures per year before and after current antimalarial efforts (indoor residual spraying) in children less than five years of age in São Tomé and Príncipe

Indicators	Pre-intervention	Post-intervention
Malaria-attributed out-patient consultations	-0.03 ($P = 0.8$)	-0.97 ($P < 0.0001$)
Malaria-attributed hospitalizations	-0.08 ($P = 0.35$)	-0.94 ($P < 0.0001$)
Malaria-attributed deaths	0.04 ($P = 0.77$)	-0.99 ($P = 0.001$)
Malaria-case fatality	-0.44 ($P = 0.29$)	-0.38 ($P = 0.36$)

mainland facilitate the distribution and impact of interventions. Antivector interventions are naturally assisted by the forces of island biogeography, which limit mosquito vectors to a single species and ensure that recolonization events will be relatively infrequent. Together, these characteristics make São Tomé and Príncipe uniquely suited for a strategy aiming to eliminate malaria from the islands.³⁰

The relative distance and isolation of São Tomé and Príncipe will also facilitate elimination by limiting imported human cases from the African mainland. Such has been the experience in other tropical islands such as Réunion, Mauritius, St. Helena, and the Seychelles.³¹ The presence of a single vector species with a propensity to feed on domestic animals provides a target with a lower vectorial capacity than a strictly anthropophilic vector, requiring less effort to reduce transmission potential to low levels.^{32,33}

Past malaria intervention efforts with IRS from 1980 through 1983 have also demonstrated the technical feasibility of eliminating malaria from islands where it remains endemic.¹ However, there is a need to continue the IRS program until gains in the interruption of malaria transmission have been further consolidated and the LLIN distribution program has had an opportunity to achieve universal coverage. Although, similar IRS operations dramatically reduced incidence of malaria cases,²⁰ transmission has never been completely eliminated,³⁴ and early interruption has led to the appearance of serious malaria epidemics.¹

Malaria elimination might be achieved in a staged manner, initially by significantly reducing the disease burden through conventional methods, followed by integration of diverse

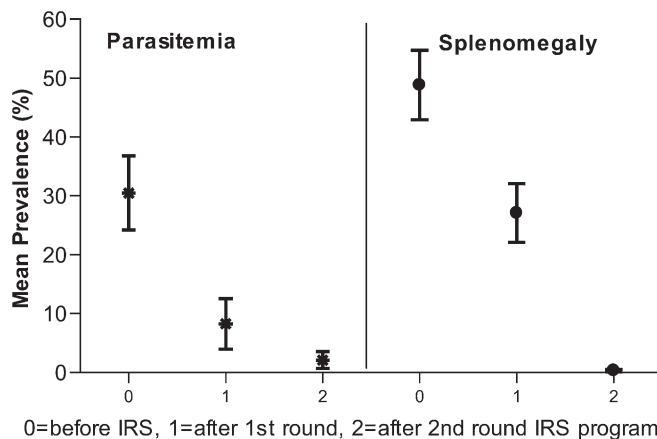


FIGURE 3. Prevalence of malaria parasitemia and splenomegaly among children 2-9 years of age before and after initiation of the first and second rounds of the indoor residual spraying program, São Tomé and Príncipe.

methods not generally cost-effective in situations of high endemicity, including active case detection at the community level, mass presumptive treatment with ACTs, larviciding, and source reduction informed by intensive vector surveillance. With mass treatment of the populace living in active foci, the synergies associated with the gametocidal properties of ACTs should become highly evident at this point.

Transitions to a broader level of integration can be executed only after transmission has been subdued such that it becomes infrequent and highly focal, enabling additional intervention methods to be implemented without draining resources unsustainably. Current interventions including early diagnosis and treatment with ACTs, information education and communication, IRS, LLINs, and IPT in pregnancy would be sustained throughout this phase, and would only be relaxed once actual elimination is achieved. Inter-sectoral collaborations with entities such as the public works and agricultural and environmental sectors are also critical to broaden the involvement in malaria control, to include stakeholders with relevant capacities and expertise.

Elimination efforts will require robust and sensitive health-facility-based surveillance systems. As transmission decreases, foci of active transmission and imported cases must be identified and targeted for rapid response before they lead to outbreaks. Surveillance should continue even after malaria transmission has been eliminated, particularly near ports of entry of potentially infected travelers. Historical review of malaria control in Taiwan shows that vigorous malaria surveillance activities after the attack phase were responsible for eliminating all the remaining foci of transmission.³⁵

Malaria control programs linked to strong research activities are among the most successful.³⁶ Thus, to achieve malaria elimination, the malaria control strategies should be supported by a robust program of operational research including monitoring of drug sensitivity and insecticide resistance. In Sri Lanka, widespread insecticide resistance in the main *Anopheles* vectors might have been the main reason for the resurgence of malaria after many years of IRS program with the same insecticide.³⁷ Thus, monitoring of insecticide resistance, which is a constant threat, is critical in informing the program to take appropriate measures. The country should establish a link with experts and centers of excellence for the management of insecticide resistance. Monitoring of insecticide resistance on an annual basis is critical because the same pyrethroid is being used in multiple types of interventions.³⁸ Genetic profiling of vector populations to indicate that prevalence of knockdown resistance mutations are particularly valuable because of the early warning such sensitive indicators provide of potential control failures. Early warning provides an opportunity to switch to alternative insecticides before resistance can exert a measurable clinical impact.

Strengthening the general health services is critical to provide an institutional environment in which a program of intensified and diversified antimalarial activities designed to eliminate transmission can thrive. A health system that can diagnose and treat cases promptly and effectively will not only support monitoring efforts but may also reduce overall transmission by limiting the access of vectors to gametocytemic patients.

Further strengthening of the capacity to monitor and evaluate interventions through combination of epidemiologic and entomologic surveillance will be essential in supporting elimination efforts.³⁹ Effective monitoring and evaluation

can identify bottlenecks and obstacles early enough to enable them to be remedied before they adversely impact disease outcomes and stated goals. Malaria case incidence is a fundamental measure for monitoring the overall effect of all interventions on the population and for gauging how much additional effort, coverage, or efficiency is required to achieve elimination.

Elimination, when it occurs, would likely not be absolute given the regional context. In São Tomé and Príncipe, it would be defined as a stable endpoint in which transmission occurs infrequently and is not associated with particular locales. Any outbreaks that occur would be focal and associated more with re-introductions than with the intrinsic disease ecology. Reaching such an endpoint, although retaining the ability to detect and interdict outbreaks would prevent the type of explosive and calamitous resurgences of malaria that can occur when anti-malarial measures are interrupted. Thus, there is a need to actively prevent re-establishment and achieve a sustainable interruption of malaria transmission.

In conclusion, the evident vulnerability of malaria to intensive interventions on these islands, combined with improvements in access to anti-malarial measures, signal the possibility of eliminating malaria in São Tomé and Príncipe as a logical extension of the successes thus far achieved in reducing malaria transmission. Eliminating malaria from São Tomé and Príncipe will demonstrate the potential benefit of increased global funding in reducing the burdens of malaria in sub-Saharan Africa.

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