

Lubombo Spatial Development Initiative

Maputo Province



Annual Report 2009

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1. Introduction

The Lubombo Spatial Development Initiative (LSDI) is a tri-lateral partnership between the governments of South Africa, Swaziland and Mozambique. The aim of this spatial development initiative is to foster economic growth in the area surrounding the Lubombo Mountains which can be broadly defined as Southern Mozambique, Eastern Swaziland and North-Eastern parts of South Africa. This region, although brimming with potential, is characterised by high levels of poverty, unemployment and a general lack of social well-being. The goal of the LSDI is to maximise investment into the development of tourism, agriculture and mining industries in the region with subsequent accelerated economic and social upliftment of the local residents. The LSDI aspire to develop the intrinsic economical potential and sustainable employment through the concentration of investment and progression of public-private partnerships (PPPs).

The protocol for the LSDI was signed in 1999 by President Mbeki, President Chissano and King Mswati III of South Africa, Mozambique and Swaziland respectively. The protocol provides a platform for regional co-operation and service delivery, and is aimed at developing the Lubombo region into an internationally competitive economic zone. This will establish a stable environment for cross-border collaboration and a framework for investment, economic growth, job creation and maximising the natural wealth of the region.

One of the most serious threats to the success of the initiative is Malaria. Large parts of the Lubombo region can be classified as malaria endemic or seasonal malaria areas. The prevalence of life threatening malaria caused by the *Plasmodium falciparum* parasite was a serious deterrent to the successful economic and social development of the region. Malaria is a serious febrile disease, and the morbidity and mortality associated with malaria result in a significant reduction in productivity in the agricultural and mining sectors. The fear of malaria under potential local and international tourists has a negative effect on the growth of this high potential industry. Coupled with the high costs associated with the control and treatment of the disease, it results in

widespread economic decline that promotes poverty. Malaria also impacts negatively on the social well being and level of education of communities in affected areas.

In the late 1990s it was realised that malaria was not a problem that could be viewed in a country-specific manner, and that there was a need for a regional, intra-country approach to the fight against malaria. An essential component for the success of the LSDI was the establishment of the Lubombo Malaria control programme in October 1999. The inauguration of the Malaria control programme constituted the formation of the Regional Malaria Control Commission (RMCC) which is comprised of scientist, control experts and health specialists from all three countries. The emphasis of the control programme is to establish cross-border collaboration towards strengthening malaria control.

With effective malaria control programmes established in both South Africa and Swaziland, the main focus of the LSDI malaria control programme is the extension of control to Southern Mozambique. This part of the LSDI region is generally considered to have the highest parasite count, and is a major point source for the re-introduction of malaria into neighbouring areas currently under control. This expansion is thus essential to ensure the success of the initiative in all three participating countries.

2. Control strategies

The primary interventions implemented towards effective malaria control is a two-pronged approach based on (1) vector control through indoor residual spraying (IRS) and (2) effective case management (definitive diagnosis and effective treatment). This is a strategic approach to reduce the transmission of the parasite from infected to uninfected individuals. To facilitate the implementation of interventions the Southern Mozambique region was divided into management zones (Figure 1).

Zone 1 reaches from the Kwa-Zulu Natal border to Maputo. Zone 1A is the area surrounding the MOZAL plant where malaria control was implemented as part of the company's social responsibility

campaign. Zone 2A comprised part of the Boane district, and Zones 2 and 3 extended north along the Kruger National Park border.

The vector control component in Mozambique has been implemented in a phased approach and started with Zone 1 in 2000 and followed by Zone 1A as the second phase in 2001. Phase three was initiated in 2002 and included implementation in Zones 2A, 2 and 3. In effect, the contiguous area under malaria control exceeds 100 000 Km².

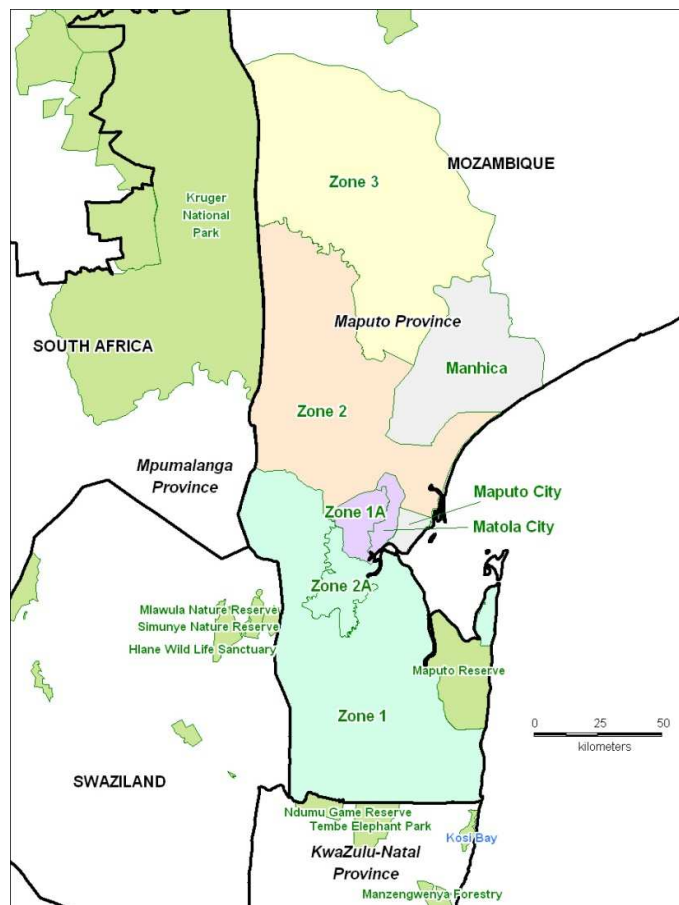


Figure 1: Map of the malaria control areas in the Lubombo spatial development initiative.

The most effective way of controlling malaria is to employ the synergetic advantage of combined vector control and effective malaria case management. It has been demonstrated that combination therapies that includes the compound Artemisinin not only improves cure rates, but also have the benefits of decreasing malaria transmission, and potentially inhibiting drug resistance. The RMCC included the use of artemisinin-based combination therapy (ACT) in their

two-pronged malaria control strategy. To optimise the success of ACTs, and to minimise costs, ACTs were introduced following the establishment of effective vector control.

3. Objectives

- 1.To reduce malaria incidence in the border areas of South Africa and Swaziland from 250/1000 to less than 20/1000. (*Achieved*)
- 2.To reduce malaria infections from 625/1000 to less than 200/1000 within three years after the start of IRS in Maputo Province (*Achieved*).
- 3.Provide updated tourist information booklets containing definitive malaria risk maps and prophylaxis guidelines. (*Achieved*).
- 4.Develop a regional malaria control programme. (*In place covering 200 000 km²*)
- 5.Develop a regional GIS base Medical Health Information Base (MHIS). (*In Place*).
- 6.To establish definitive diagnostics and effective treatment. (*RDTs and ACTs in place in all health facilities*)

4. Progress

The effectiveness of the malaria control programme is measured through the assessment of prevalence of malaria over time in Mozambique, as well as the incidence of malaria in neighbouring parts of South Africa and Swaziland. The effectiveness and success of the intervention methods are assessed using different markers including:

- (i) Progress: spraying and Artemisinin-based combination therapy coverage
- (ii) Biological: parasite prevalence rates, mosquito vector numbers and health facility patient numbers
- (iii) Tourism: bed occupancy, job creation and risk perceptions.

4.1. Reduction of Malaria Incidence

Initially parasite prevalence surveys were conducted in both South Africa and Swaziland, but with the significant reductions in prevalence in both countries, it was no longer useful to look at prevalence, and the shift was made towards monitoring malaria incidence in these countries.

The LSDI project reaches into South Africa at the border areas of Komatipoort in Mpumalanga and Ingwavuma in KwaZulu. Since the inception of the malaria control programme, malaria incidence rates in these areas have reduced by more than 99% (Figure 2).

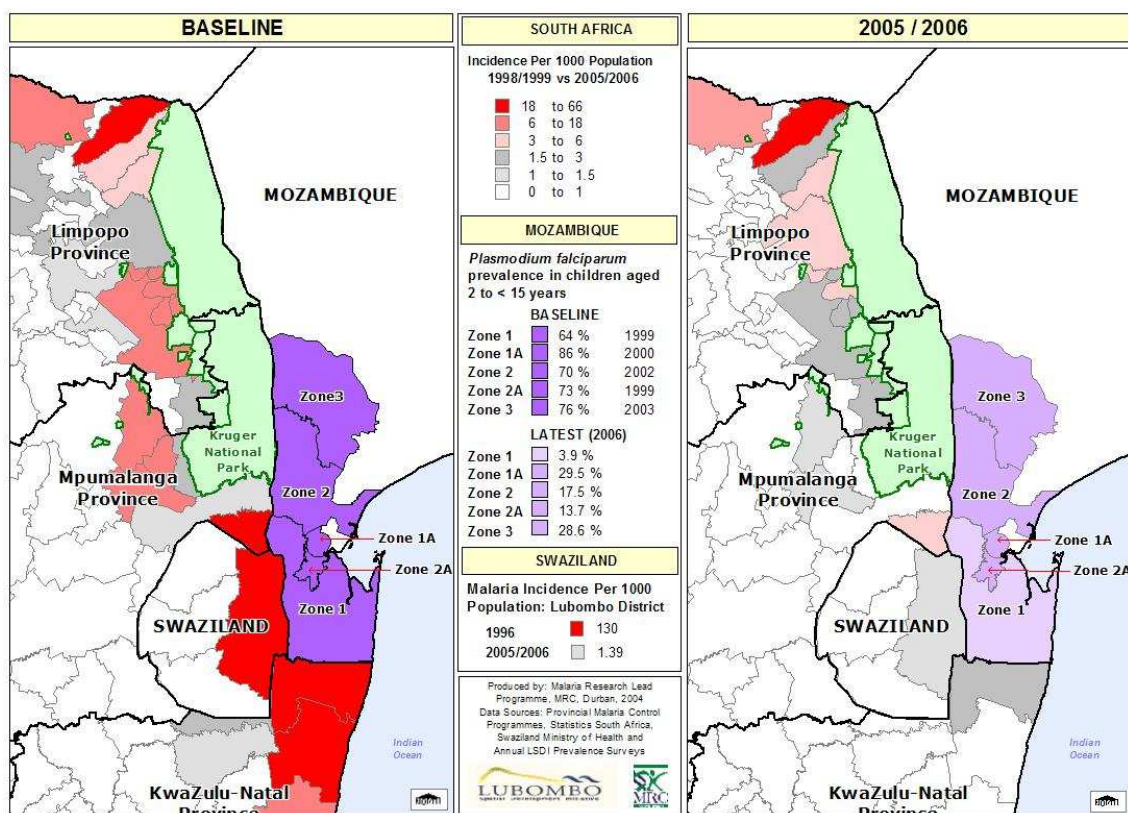


Figure 2: Map illustrating reductions in the incidence of Plasmodium falciparum parasites in South Africa and Swaziland and prevalence in Mozambique between the baseline in 1999 and latest survey in 2006.

Although the scale of the disease differs in the two areas, the trends are very similar, showing significant reductions after implementation of control measures at adjacent areas in Mozambique. The number of cases has been reduced significantly, and has remained low since 2002.

The incidence data for Swaziland is similar to that of South Africa with a 90% reduction in incidence rate since the implementation of the control programmes, and incidence rates remaining at low levels

4.2. Reduction of Parasite Prevalence in Mozambique

Annual surveys of parasite prevalence are conducted at 28 sentinel sites in Maputo (Figure 3).

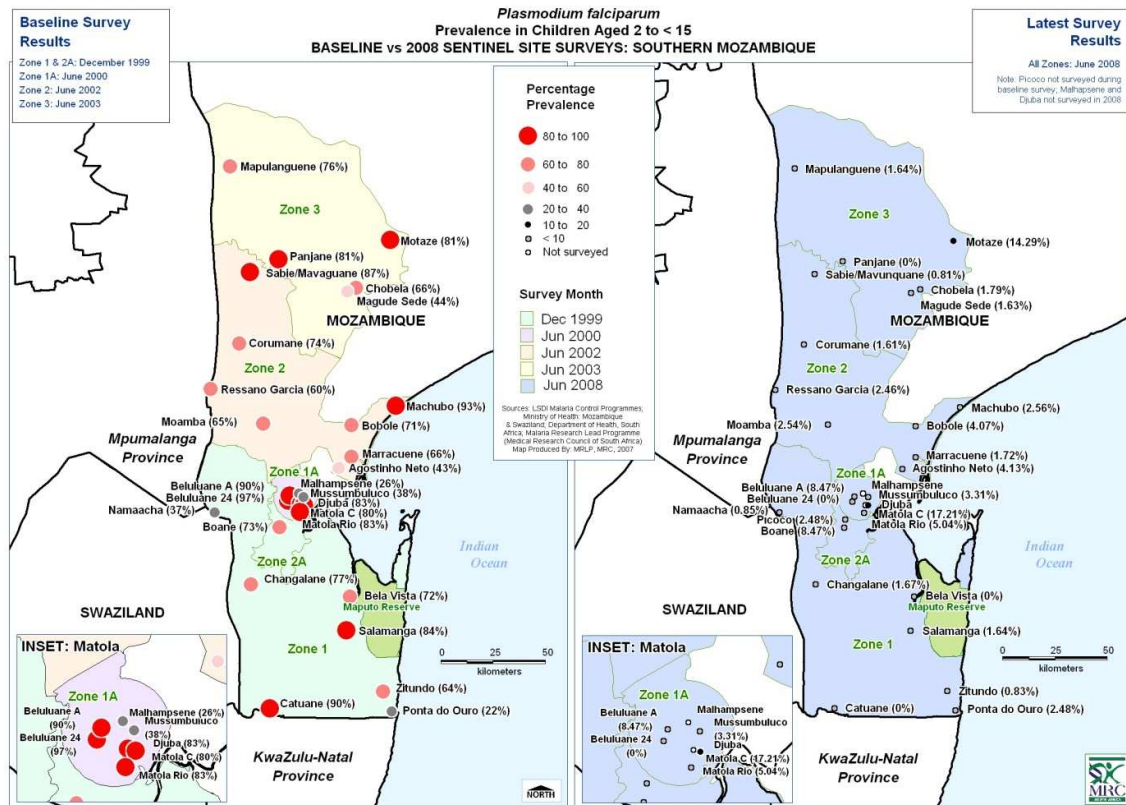


Figure 3: Maps indicating reductions in *Plasmodium falciparum* parasite prevalence at the sentinel sites in the different zones of Maputo province between the baseline surveys and 2008 survey

In Zone 1 and 2A, baseline studies were conducted in 1999 and 2000 before the commencement of spraying, and the results were combined to form a 2 year baseline for comparison of annual post spraying survey results. Baseline studies in Zone 1A was conducted during 2000, in Zone 2 during 2002 and in Zone 3 during 2003. Figure three clearly demonstrates the reduction of prevalence as monitored at the various sentinel sites.

In Zone1, baseline prevalence of infection was at 62% in 1999/200 and was reduced to 2.15% in 2007 and to 1.08% by June 2008. (Figure 4) In Zone 1A, baseline prevalence was 87.27% at 2000, and was reduced to 13.24% in 2007 and to 6.82% in 2008. In Zone 2A, baseline prevalence was 76% during 1999/2000 and was reduced to 0.44% in 2007, but raised to 5.44% in 2008. In Zone 2 baseline prevalence

was 69.42% in 2002 and was reduced to 4.18% in 2007 and to 2.49 in 2008. In Zone 3 baseline prevalence was 69.53% in 2003 and was reduced to 14.21% in 2007 and 3.89% in 2008.

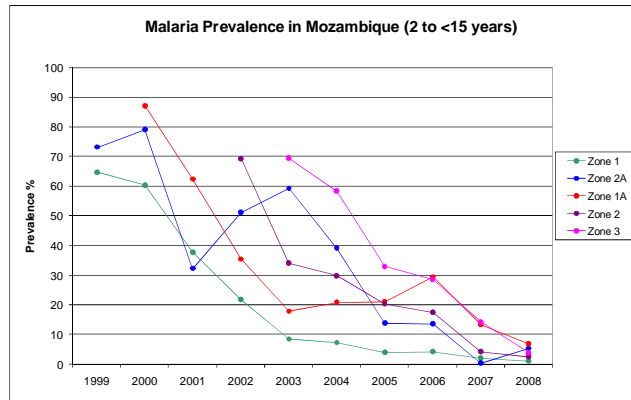


Figure 4: Malaria prevalence in children of 2 to <15 years of age from Maputo Province of Mozambique

These results clearly indicate that the LSDI malaria control programme is having a positive impact on the prevalence of malaria throughout Maputo province, and that the goals are being met. In all zones the prevalence have decreased significantly below the baseline values, and the reductions in prevalence between 2007 and 2008 shows that the programme is continually improving the malaria situation in the province.

4.3. Malaria risk maps and Prophylaxis guide.

The tourism component of the project has been successfully completed, and all goals have been met through the development of risk maps, and the development and subsequent revisions of prophylaxis advice booklets. Copies of these booklets have been distributed to tourist facilities. The significant reduction in malaria incidence in the LSDI area contributed to a reduction of malaria risk to visitors at tourism facilities in the area. This has already contributed to development initiatives of local and international extent within the greater St Lucia Wetland Park where a range of tourist facilities will be developed.

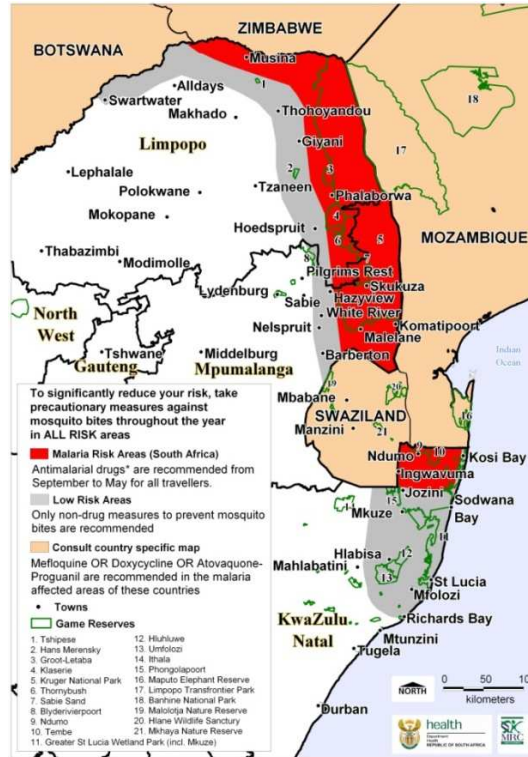


Figure 5: Malaria risk map for the LSDI regions in South Africa

The positive malaria control results are increasingly influencing tourism policy, and South African Tourism is using the “malaria free” campaign to enhance its international marketing approach.

4.4. Establishment of the Regional Malaria Control Programme

4.4.1. Regional Management

With the inauguration of the malaria control programme in October 1999, the Regional Malaria Control Commission (RMCC) comprised of scientists, control experts and health specialists from the three countries were constituted. The RMCC meets quarterly with the venue being rotated between countries. Decision making on matters relating to the project is supported by evidence and input from the experience and expertise of its members. Decisions are based on consensus amongst members with all members having equal input. The RMCC reviews the progress of the project in the respective countries, finding solutions to problems that may occur, and presents its findings and recommendations to governments, funders and the Regional Co-ordinating Mechanism (RCM). The RCM was introduced as per requirement of the Global Fund to fight Aids, Tuberculosis and Malaria (GFATM) to effectively manage financial allocations by the Global Fund.

4.4.2. Southern Mozambique spray programme

Vector control in Southern Mozambique rest on twice annual Indoor Residual Spraying (IRS) rounds on houses and structures. IRS was introduced in Zone 1 in 2000 and was incrementally extended to other zones within the province (Table 1) to cover a total area of 20617 km² over seven districts.

Table 1: Stepped wedge design of indoor residual spraying intervention in Maputo Province, Mozambique.

Year	2000	2001	2002	2003	2004	2005	2006	2007	Area (km ²)
Zone	Cumulative Spray Rounds								
1	2	4	6	8	10	11	12	13	7591
1A		2	4	6	8	9 / 10	11	12	407
2			2	4	6	7 / 8	9	10	5723
3					2	4	6	7	6893

Spraying is conducted by trained spraying personnel using Hudson expert pumps with appropriate nozzles and is overseen by managers. Training is provided before each spray round, and includes appropriate techniques, safety measures and personal protection for working with the relevant insecticides.

4.4.3. Knowledge Aptitude and Practices (KAP) Surveys

KAP surveys were conducted at community level in Swaziland and Maputo Province during 2007 to identify knowledge gaps. This information is applied in the design of strategies towards development of focussed malaria education programmes.

4.4.4. Prevalence of antimalarial resistance markers

The development and spread of resistance to both chloroquine (CQ) and sulfadoxine-pyrimethamine (SP) in the *Plasmodium falciparum* malaria parasite is a major contributor to the continued burden of Malaria. The use of artemisinin combination therapy (ACT) has been widely introduced to counter or mitigate the development and spread of drug resistance. Recent work has however shown that the use of an ineffective partner drug or combinations thereof in association with the artemisinin derivative severely compromises the efficacy of the ACT.

Chloroquine used to be the antimalarial of choice in Mozambique, but was replaced with the ACT artesunate plus SP from 2004. The ACT was implemented in phases from 2004, and by 2006 all districts in Maputo province were using this ACT.

Prevalence of the mutations essential for SP resistance was studied by the Malaria Research Lead Programme of South Africa before the implementation of the ACT. The findings showed that the prevalence of two of the five mutations essential for resistance to SP were at baseline levels, which supported the implementation of artesunate plus SP in Maputo. Continuing surveillance of the resistance markers have however shown an increase in the prevalence of DHPS markers following ACT introduction, and by 2007 prevalence of all 5 mutations exceeded 30% which is an early warning of imminent therapeutic failure and reduced efficacy of the ACT.

Since 2007 there was an alarmingly sharp increase in dhps double prevalence in 3 of the 5 zones (Figure 6).

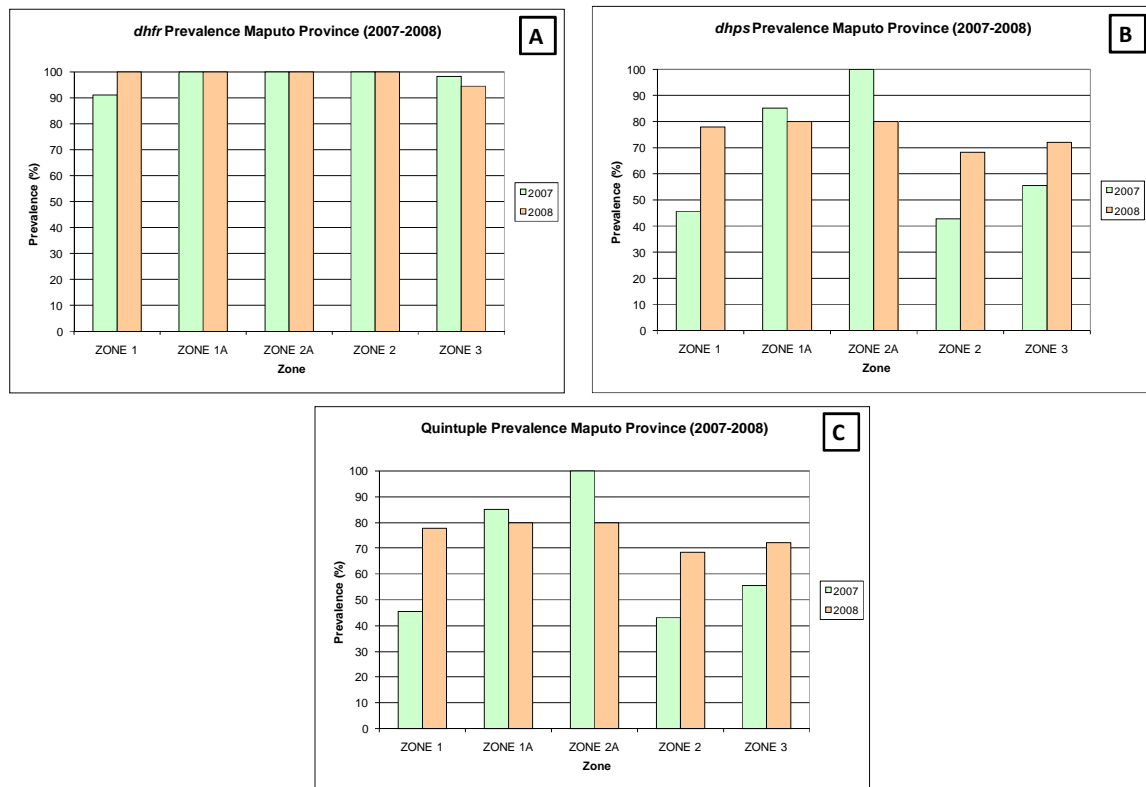


Figure 6: Prevalence of the dhfr triple mutation (A), dhps double mutation (B) and the quintuple mutation (C) by zone and year in Maputo province.

However the results for Zone 2A must be viewed with care as in 2007 the result was based on a single sample and the decline in dhps double prevalence in Zone 1A is a non-significant one. Given the high prevalence of dhfr triple mutation, quintuple mutation prevalence was very similar to that of the

dhps double. The high prevalence of the quintuple mutation seems to imply that the therapeutic efficacy of SP within Maputo province is rather limited and supports the decision to shift to artemether plus lumefantrine for the treatment of uncomplicated malaria. The swift roll out of artemether plus lumefantrine is essential to prevent artesunate acting as a mono-therapy due to the reduced efficacy of SP.

4.4.5. Vector species and infection rates

Baseline entomological surveys identified *Anopheles funestus* and *An. arabiensis* as the main malaria vectors Southern Mozambique. Vector numbers as monitored by daily exit trap catches from window traps installed at households to monitor reductions after spraying

Numbers of *An. gambiae s.l.* decreased rapidly after the first spray round and have remained low. Of the sample of mosquitoes from the post spraying collections and subject to specific species identification, *An. arabiensis* numbers decreased proportionately, with an increased prevalence of *An. merus* and *An. quadriannulatus*.

Plasmodium sporozoite rates

Molecular analysis to determine sporozoites rates was carried out on all positively identified mosquitoes. Sporozoite rates varied widely between zones and between pre and post-spraying. The pre-spraying rate for *An. gambiae s.l.* ranged from 0.84% to 10.9% (n=784) and post-spraying rates ranged from 0-1.22% (n=471)

The pre-spray sporozoite rate for *An. funestus s.s.* ranged between 4.69% and 5.28% (n=763). Post-spray rates ranged between 0 and 2.7%. (n=339) No other *A. funestus* member species was found to be infected.

4.4.6. Capacity development

A successful malaria control programme cannot exist without adequately trained staff at every level. Training was therefore a fundamental requirement for the implementation of a control programme in Mozambique where skills and experience were lacking. In Maputo training was provided to spray operators (techniques and safety), supervisors (managing spraying), field entomologists (research

techniques), field staff (use of GPS equipment), office staff (use of information system) and insectary staff (insect husbandry and research). Extended training included intervention assessment through morphological identification of window-trap caught mosquitoes, and residual efficacy bio-assays. This has necessitated the maintenance of an insectary as well as susceptibility and biochemical resistance testing to be conducted, which is forming part of a postgraduate degree.

The basic training of spray operators and supervisors contained 85% practical and 15 % theoretical content. Supervisors received additional, in-depth, training on matters relating to environmental hazards, toxicity, first aid and safe handling/disposal of insecticides. The training programme is a continuous process that is taking place on a yearly basis.

Training has also been provided to healthcare providers, including community healthcare workers on the implementation, monitoring and evaluation of interventions like ACTs and rapid diagnostic tests (RDTs). Training includes drug management, effective malaria diagnosis (through RDTs and microscopy), assessment of disease severity, treatment guidelines, indications for referrals, record keeping and pharmacovigilance. Support is provided through supervisory visits and the provision of malaria treatment guidelines, drug management manuals, pharmacovigilance handbook and adverse drug reaction reporting forms. The number of healthcare workers participating in this programme far exceeds the target of 300 that was initially set.

When a knowledge or skill gap is identified by the RMCC, academic training is provided to core contributors to the LSDI. Academic training at Diploma, Masters and Ph.D. level is provided in the fields of public health, tourism, drug and insecticide resistance and drug safety.

4.5. Malaria Information Systems

A Malaria Information System (MIS) is a computerised system allowing the input, management and output of malaria case data used for management and research. It includes a spatial component using a geographical information system (GIS) and the spatial data collected includes administrative boundaries, population, health facility locations, towns and other relevant information. New sources of data is continuously sought to ensure that the appropriate scales are provided and that the data is current. The

MIS is continually customised to minimise end-user skill requirements and to optimise access to different data sets. Input screens mirror data collection forms and automatic-linking and drop-down lists minimise data errors

A MIS was developed and implemented for each of the three participating countries in the LSDI. Data collected during routine operations are entered into the MIS, and consists of both in- and out-patient data of confirmed and clinically diagnosed malaria cases. Information collected during routine spraying operations are collated and entered into the MIS and plays a key role in the monitoring and planning of spraying activities. The MIS provides managers with information on both health facility diagnosed malaria cases and information relating to vector control activities.

The effective and efficient functioning of the MIS requires local ongoing technical support which is provided by an Information Officer (IO) with the necessary skills to operate and develop the system. The IO must provide technical expertise relating to the data in the system, and must manage the information flow process before it reaches the MIS and thereafter.

4.6. Malaria Case management

Over the past five years, the LSDI has made a substantial contribution to improving malaria case management in Maputo province. Improvements in malaria case management have well exceeded targets set for the LSDI (Table 2)

Table 2: Summary of progress made, gauged against target indicators by year 5 of the LSDI.

Indicator	Targets	Actual Result	% of Target
Number of public healthcare facilities using ACT's as first line treatment of uncomplicated malaria	53	162	306%
Percentage of target public healthcare facilities with no reported stock-outs of either ACT's or RDT's	90%	100%	111%
Number of public healthcare facilities routinely using RDT's to confirm malaria diagnosis	53	163	308%
Proportion of definitively diagnosed cases appropriately treated with ACT	90%	123%	137%
Drug efficacy monitoring	2	2	100%
Number of districts with an established pharmacovigilance system	7	7	100%
ACT drug efficacy level	90%	98% / 100%	109% / 111%
Clinical personnel receiving in-service training	300	736	226%

The roaring success of malaria case management was made possible by:

- 1) The marked reduction in malaria case load following effective community based IRS and the widespread use of ACTs.
- 2) The limitation of treatment to only definitely diagnosed malaria cases.
- 3) Following the Ministry of Health directive to also distribute RDTs and ACTs to community health centres.

These factors allowed the large scale deployment of ACTs and RDTs to more healthcare facilities than planned, but within the defined budget, thereby far exceeding all targets. The efficient management of drug and RDT supplies and the use of extensive training and supervision has minimised stock-outs and wastage.

4.6.1. Significantly reducing Malaria Transmission

The most effective reduction of malaria transmission is accomplished through the considered combination of community based IRS with effective insecticides and the widespread use of ACTs as first-line treatment. The Artemisinin derivatives (artesunate and artemether) are known to reduce gametocyte carriage. Monitoring of gametocyte carriage has shown a significantly higher reduction in response to ACT treatment compared to SP monotherapy. The reduction was particularly evident in areas where ACTs was implemented as first line treatment in districts where IRS was well established.

The reduction of gametocyte carriage is equally important for reducing the spread of drug resistance. Increased post-treatment gametocyte carriage is an early indicator for increasing drug resistance, and precedes significant increases in treatment failure rates. Relatively higher gametocyte carriage in primary infections with the resistant genotypes following monotherapy fuels the spread of resistance, even before a significant rise in failure rates is observed.

4.6.2. Ensuring Effective Malaria Treatment

Starting with Namaacha in March 2004 and supported financially by the GFATM, the ACT artesunate plus SP was phased in on district level in all public sector health posts and health centres of the

LSDI region of Southern Mozambique. With the implementation of artesunate plus SP as the first line treatment nationally by the ministry of health in Mozambique (2006), health facilities in regions outside of the LSDI were also supplied with ACTs. The LSDI contributed to the optimal use of the ACTs by providing training and supervision. RDTs were provided in order to limit the use of ACTs to parasitaemic patients.

The LSDI have far exceeded all targets for the number of healthcare facilities routinely using RDTs and ACTs by extending the provision of ACTs, RDTs and relevant training to community healthcare workers. This contributes positively to the sustainability of future effective case management. The management systems implemented reduced stock-outs to the minimum and also reduced the duration of stock-outs where they occurred, effectively enabling all facilities to reach 100% of the stock-out targets.

The number of RDTs used and the proportion of clinically suspected malaria cases that are RDT positive vary by district (Figure 7)

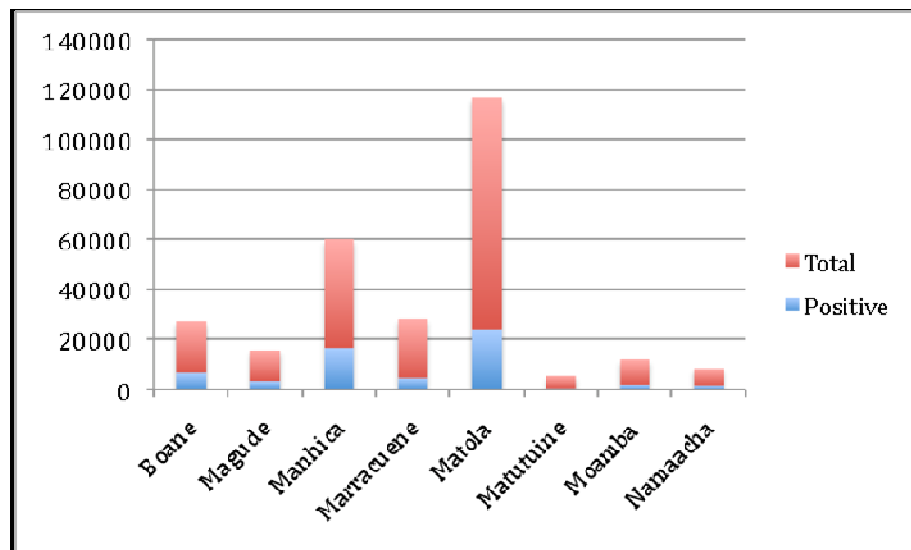


Figure 7: The number of suspected malaria cases tested and found positive using RDTs in 2008 by district in Maputo province.

Through the use of RDTs, clinically suspected malaria cases can be tested, which will allow the targeted use of ACTs on patients carrying the malaria parasite. It is also beneficial for patients that test

negative for malaria, as their condition can then be re-assessed to find the actual cause of their illness more promptly.

The number of patients who are RDT positive compared to the number treated with ACT (Figure 8) is routinely monitored to determine ACT coverage rates among confirmed malaria cases, and monitor the overuse of ACT in patients who are aparasitaemic.

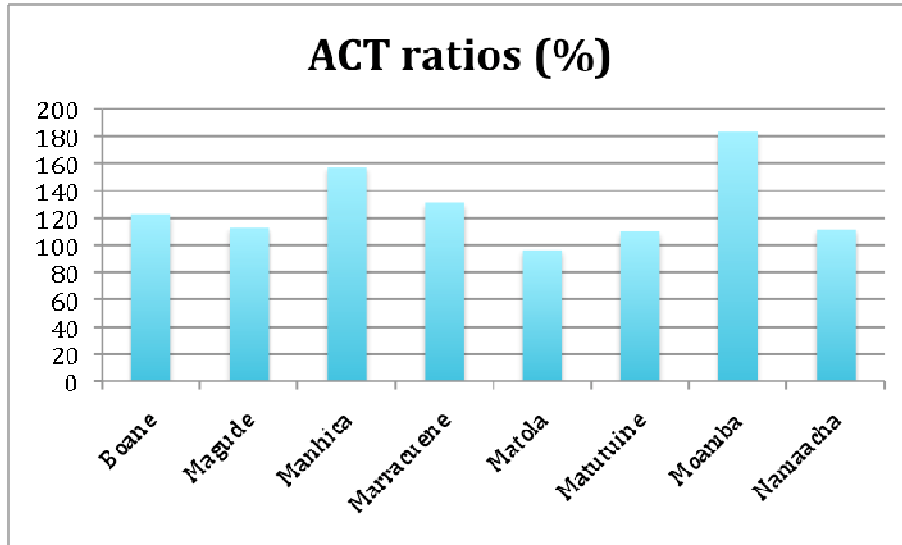


Figure 8: Proportion of RDT positive cases treated with ACTs at healthcare facilities in Maputo province.

The higher than expected proportion of RDT positive patients treated with ACTs at some facilities has been investigated. The healthcare facilities with the highest percentages are those with microscopy, so much of the apparent over-use of ACT is actually appropriate use in confirmed malaria cases. In this regard, healthcare worker training re-enforces the importance of limiting ACT use to confirmed malaria cases, although allowing the initial use of ACTs in severely ill patients.

Close monitoring of the efficacy within the LSDI have shown ACTs to be highly effective, and to be significantly more effective than monotherapy. Concern have been raised about the impact of age has on SP drug levels on individuals after it came to light that drug levels in pre-school children did not reach the same levels as in adults, although the internationally recommended dose was followed. This has raised the question of whether other vulnerable populations are similarly at risk of being treated with inefficient dosages. The LSDI has initiated two studies to assess antimalarial drug levels achieved in pregnant

women in Mozambique. The first study had to be terminated as only three pregnant women with malaria were enrolled throughout the study season, reflecting the marked improvements in Malaria control in Maputo. The second study on drug levels achieved in pregnant women given SP as intermittent preventative treatment (IPT) confirmed that pregnant woman achieve similar concentrations of sulfadoxine and slightly higher concentrations of pyrimethamine than non-pregnant women with uncomplicated malaria.

5. Monitoring an Evaluation

Each component of the LSDI Malaria Control Programme is comprehensively monitored as summarised in Table 3 below. This monitoring and evidence based policy is supported by the Geographic Malaria Information System.

Table 3: Monitoring and Evaluation of Malaria Case Management in the LSDI.

Activity	Progress
ACT In vivo therapeutic efficacy	Artemether-lumefantrine studied in KZN (2002), Mpumalanga and Limpopo (2007). Artesunate plus SP studied in Namaacha (2003), Catuane (2003), Boane (2004-2005), Magude (2004-5) and Matola (2006); SP monotherapy IPTp in Maputo /Gaza (2005-2007) Completed and manuscripts publishes / submitted / in preparation
Drug safety	Pharmacovigilance integrated into MOH Completed.
Economic evaluation	Kwa-Zulu Natal policy change: completed and published Maputo Province policy change: analysis ongoing Mpumalanga policy change: analysis completed
Drug Use Review	Data collection completed; data analysis completed. Thesis for MSc community Health submitted.
School-based IEC RCT	Research Completed. Thesis submitted led to graduation with MMed Clinical Pharmacology.

6. Publications

6.1. Scientific manuscripts.

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