

Using Triangulation Methodology to Evaluate Reported Malaria Trends in the Urban Clinic of  
Maevatanana, Madagascar 2005-2010

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A thesis submitted in partial fulfillment of the  
requirements for the degree of

Master of Public Health

University of Washington

2012

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## Abbreviations

ACT	Artemisinin-based combination therapy
c-IMCI	Community-based Integrated Management of Childhood Illness (WHO and UNICEF Strategy)
CDC	Centers for Disease Control and Prevention
CHD	Centre hospitalier de l'district (District Hospital)
CSB	Centre de Santé de Base (Most basic health clinic)
CSBU	Centre de Santé de Base Urbaine (Urban, largest health clinic)
DHS	Demographic and Health Survey
DRS	Direction Regional de Santé (Regional Public Health Office)
EIR	Entomological Inoculation Rate
GFATM	Global Fund to Fight AIDS, TB, and Malaria
GMP	Global Malaria Programme
HMIS	Health Management Information System
IEC/BCC	Information, education, communication/behavior change communication
IPM/DULMN	<i>Institut Pasteur de Madagascar</i> (Pasteur Institute)/ Division of Emergency and Response against Disease
IPTp	Intermittent preventive treatment of pregnant women
IRS	Indoor residual spraying
LLIN	Long-lasting insecticide-treated net
MDG	Millennium Development Goal
MIS	Malaria Indicators Survey
NMCP	National Malaria Control Program
PMI	President's Malaria Initiative
PSI	Population Services International
RMA	Rapport Mensual de Activités de CSB (Monthly Report of Activities at CSBs)
RDT	Rapid diagnostic test
SP	Sulfadoxine-pyrimethamine
SPR	Slide positivity rate (#RDT+ cases / RDTs used)
SSD	Service de Sante de District (District-level Public Health Office)
SSS	Service des Statistiques Sanitaires (Annual Public Health Statistics Publication)
WHO	World Health Organization

## **Executive Summary**

The impact of malaria control programs has been widely investigated in recent years following the implementation of multifaceted control programs in many low-income countries. Some clinical studies show few signs of decreasing malaria incidence after the distribution of long-lasting insecticide treated nets (LLINs), the adoption of artemisinin-based combination therapy (ACT), and other malaria case-management strategies. In Madagascar, routine data collection has shown inconsistent results of malaria control interventions in some regions, such as the region of Betsiboka in northwest Madagascar, where different data sources show increasing and decreasing trends in malaria incidence less than two years after the first distribution of LLINs and the introduction of ACT and rapid diagnostic tests (RDTs).

In this study, hypotheses regarding the trends seen in the Health Management Information System (HMIS) and Sentinel Site data sources from a large clinic in the Betsiboka region, the CSBU in Maevatanana district, were evaluated using triangulation methodology. This study showed that the main reason for decreasing malaria trends seen in the HMIS data was the change in case definition for malaria after the introduction of RDTs. For the Sentinel Site data source, increases in the number of RDT+ malaria cases as well as the percentage of RDT+ malaria cases of all patient consults at the CSBU contradict what was expected after the implementation of malaria control interventions in 2007. The effects of malaria control interventions may be attenuated by changes in human behavior, such as increased fever consults at the CSBU and the improved capture ability of RDTs. However, increases in the proportion of malaria cases of all patient consults at the CSBU may suggest a true increase in malaria incidence. Furthermore, increases in reported malaria cases in the Sentinel Site data also corresponds to increases in ACT stock-out in Maevatanana, ambient temperature, as well as the presence of resistance to pyrethroids and quinolines. By collecting and comparing different data sources of different measurements, this study was able to make conclusions about the decreasing malaria trends in the HMIS data. However, the study showed inconclusive results regarding the increasing trends seen in the Sentinel Site data, and further investigation is needed.

## Introduction

The World Health Organization (WHO) estimates that about half of the world's population is at risk of malaria infection, with 90% of infections occurring in Africa (WHO, 2012). Roll Back Malaria's (RBM) goals of reducing malaria morbidity by 75% and eliminating malaria mortality by 2015 remain elusive for many African countries, even with increased funding from programs such as the Global Fund to Fight AIDS, TB, and Malaria (GFATM) and the President's Malaria Initiative (PMI) (WHO, 2012). Control interventions, including the distribution of long-lasting insecticide-treated nets (LLINs), the use of rapid diagnostic tests (RDTs), the prescription of intermittent preventive treatment of pregnant women (IPTp), indoor residual spraying (IRS), and improved treatment such as artemisinin-based combination therapy (ACT), have been implemented throughout many malaria-endemic and epidemic-prone regions of the world as countries attempt to meet RBM's goals.

It was predicted that the incidence of malaria would decrease after the implementation of control interventions, but some countries have not seen clear decreases in malaria, such as in Madagascar. An estimated 90% of Madagascar is endemic to malaria and its entire population is at risk of malaria infection. All four species of malaria parasite are present in the country, though most malaria cases are caused by *P. falciparum* (PMI-Madagascar, 2011). Malaria is the number one cause of reported hospital deaths and the third leading cause of morbidity in children under 5 years of age at health facilities (Service de Statistiques Sanitaires, 2010). These disconcerting figures led the National Malaria Control Program (NMCP) of Madagascar to create a national strategy in 2005, which was consistent with RBM and Millennium Development Goals (MDGs) to reduce childhood mortality (PMI-Madagascar, 2011). Its strategy included many country-wide interventions between 2005 and 2010, including the distribution of LLINs, the

introduction of ACT and RDTs at district health facilities, IRS in epidemic-prone regions, as well as the improvement of the case-management of suspect malaria cases. While many regions of Madagascar have reported decreases in malaria morbidity and mortality between 2005 and 2010 in multiple data sources, some regions continue to have uncontrolled malaria incidence and possible increasing trends. One of these regions is the Betsiboka region in northwest Madagascar.

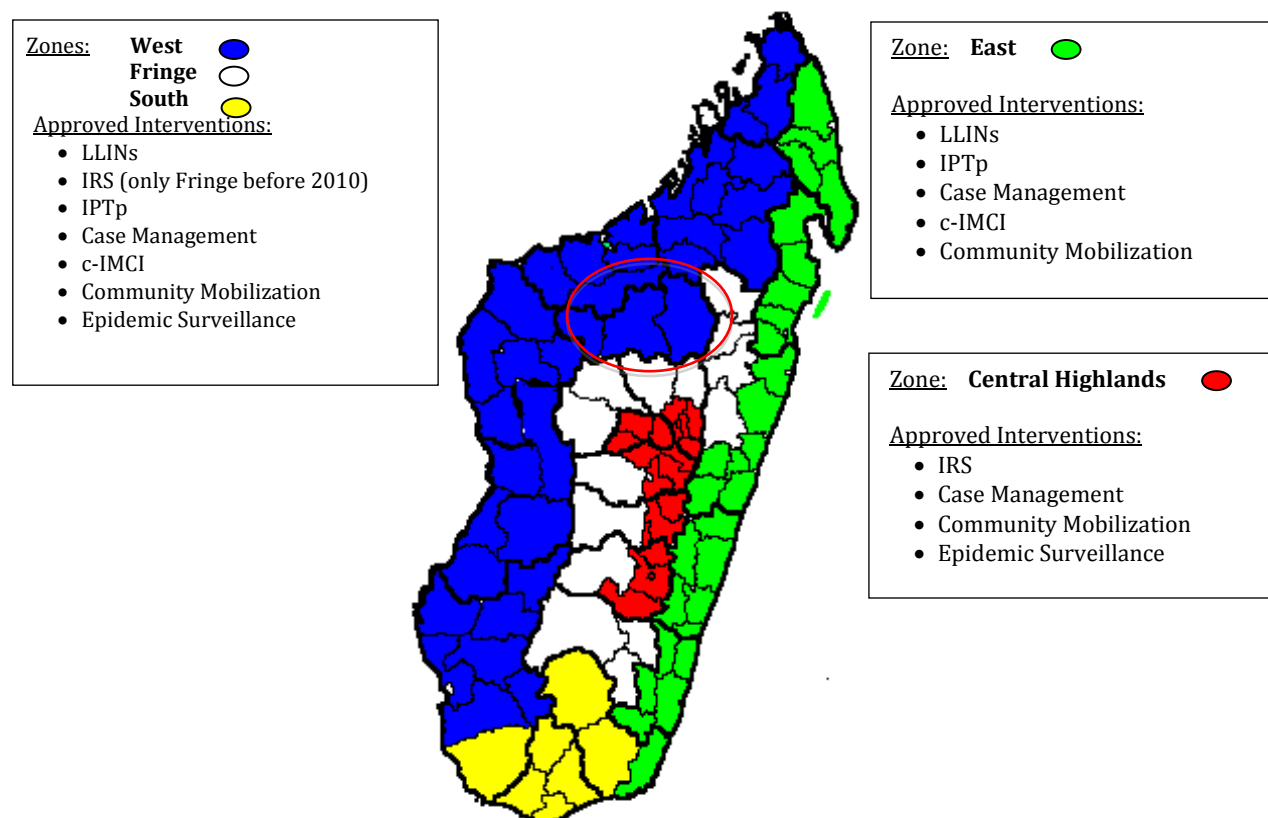


Figure 1: Map of the malaria epidemiological zones in Madagascar and approved control interventions for each zone. The red circle indicates the location of Betsiboka (PMI-Madagascar, 2011).

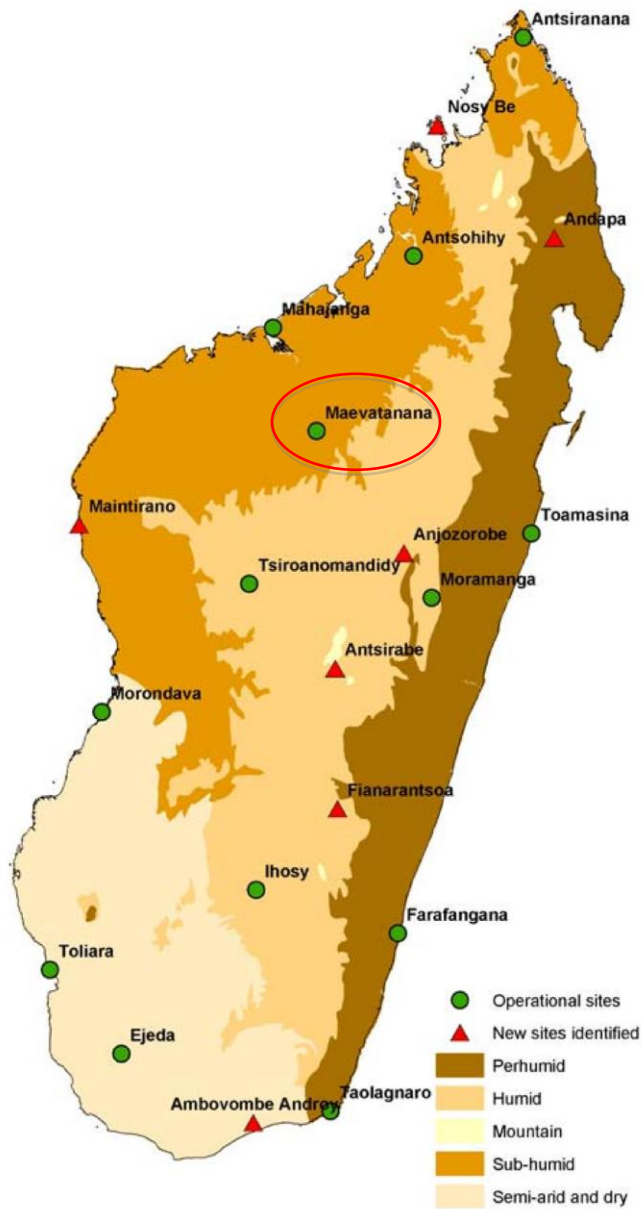
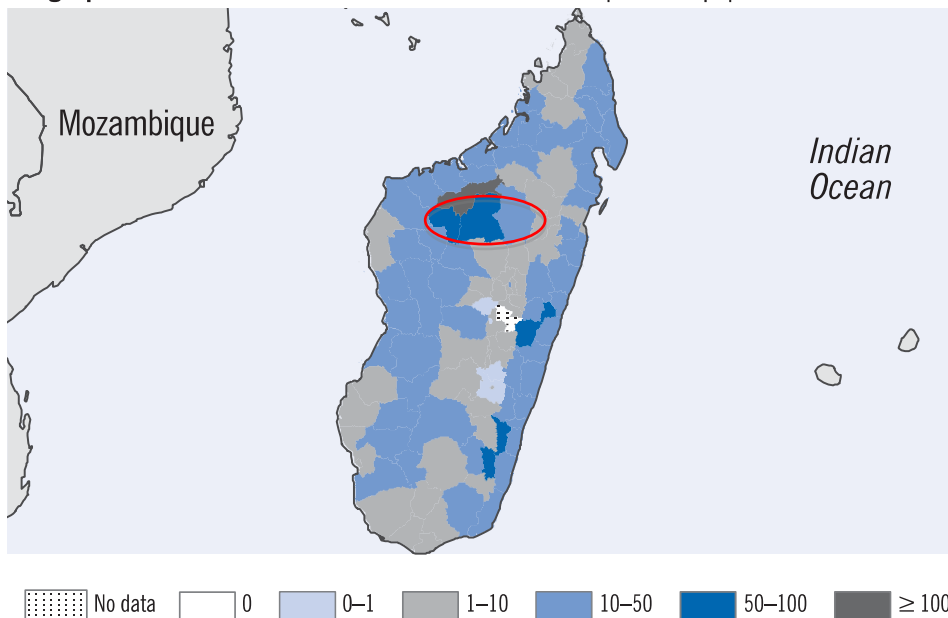


Figure 2: Map of the 13 Sentinel Sites established in early 2007 located within different climatic zones in Madagascar. CSBU Maevatanana is circled in red (Randrianasolo, 2010).

**Geographical distribution of confirmed malaria cases (per 1000 population)**



**Figure 3: Geographic distribution of malaria cases per 1000 population in Madagascar. Betsiboka region has some of the highest malaria rates per 1000 population in Madagascar and is circled in red (WHO, 2010).**

Betsiboka is part of the malaria epidemiologic zone of the west coast of Madagascar, in which malaria transmission is seasonal and greater than 6 months (PMI-Madagascar, 2011). There, malaria has been a major cause of morbidity in children and adults, comprising a reported 15-40% of childhood morbidity consults and 10-25% of adult morbidity consults between 2005 and 2010. Betsiboka also has one of the highest rates of malaria per 1000 population in Madagascar as shown in Figure 3 (Service de Statistique Sanitaires, 2010; WHO, 2010). Betsiboka was part of the countrywide LLIN distribution in late 2007 and the facilities there also began using RDTs and ACTs in mid-2007. Malaria incidence was expected to decrease after 2007 and remain low, with a subsequent LLIN distribution and IRS intervention in late 2010. However, contrary to expectation, some data sources from Betsiboka showed unabated malaria incidence and even increasing trends beginning as early as 2008.

PMI/CDC and NMCP program managers have focused attention on Betsiboka, particularly Maevatanana district located in the center of the region, because of the possibility of increasing malaria incidence after the implementation of control interventions, indicating a possible malaria resurgence, insecticide resistance, or other malaria control issues. The Ministry of Health's Health Management Information System (HMIS) data from the largest clinic in Maevatanana district, the Centre de Santé de Base Urbaine (CSBU) showed a decrease in reported malaria after the 2007 implementation of control interventions; however, Institute Pasteur de Madagascar's (IPM/DULMN) Sentinel Site surveillance data from the CSBU, which started collecting data regularly in 2008, showed increases in RDT+ malaria cases and the proportion of RDT+ malaria cases of all consults from 2008 to 2010. Because all districts involved in the NMCP in Madagascar received the same interventions, it is of interest to investigate the contrasting trends seen in the HMIS and Sentinel Site data at the CSBU.

The contrasting data sources from the CSBU steered this study towards investigating hypotheses regarding trends in malaria incidence and suggesting aims for future research as well as improvements in data collection for monitoring malaria control programs. This study focuses on the CSBU because it houses two data sources: the HMIS data as well as the Sentinel Site surveillance data, and data collected from this clinic have historically been more complete than data from other health facilities in Betsiboka. Moreover, the CSBU receives about 30% of total patient consults in Maevatanana district, therefore allowing for more generalized conclusions about the region.

In order to evaluate the trends seen in the HMIS data and Sentinel Site surveillance data from the CSBU, triangulation methodology was used to collect and compare different data sources documenting malaria trends at the CSBU as well as the rest of the Betsiboka region. The

methodology allowed for the generation of hypotheses about the main determinants of the two trends documented at the CSBU. Through the iterative process of triangulation, the research aims regarding malaria trends at the CSBU were narrowed to the following:

## **Aims and Hypotheses**

Specific Aim 1: To evaluate whether the decrease in reported malaria cases per month in the HMIS data from the CSBU in Maevatanana, Madagascar is due to changes in the case definition of malaria or to a true decrease in malaria cases.

Hypothesis 1: The reported decrease in malaria cases in the HMIS data from the CSBU is likely due to the change in the case definition of malaria and the elimination of suspect malaria cases from the monthly reports.

Specific Aim 2: To assess the extent to which trends in reported RDT+ malaria cases from the Sentinel Site data from the CSBU document a true increase in malaria incidence between 2008 and 2010.

Hypothesis 2: The reported increase in RDT+ malaria cases and the percent of RDT+ malaria cases of all patient consults is not consistent with expected outcomes of the NMCP interventions, and the reported trend is corroborated by other data sources.

## Literature Review

With increased funding for malaria control interventions from GFATM and PMI programs, many large-scale interventions have been implemented in Africa in the last decade. Malaria incidence was expected to decrease after the implementation of multiple control interventions, but some countries have seen little evidence indicating this trend (Yeka, 2007). These unabated trends in malaria cases could result for many reasons, including changes in case definitions, the development of insecticide and quinoline-resistant parasites, problems in pharmacy management, climate change, and more.

Malaria control programs in Africa are generally monitored by data collected by the Ministry of Health of a specific country (denoted HMIS data), and the following indicators are used to assess malaria trends over time: reported malaria cases (per 1000 population) and reported malaria deaths (per 100,000 population) (WHO, 2012). HMIS data are routinely collected and are useful for tracking disease incidence overtime in multiple locations, but the quality and completeness of HMIS data are a common problem. Malaria monitoring mechanisms have historically depended on the clinical diagnosis of malaria before RDTs were introduced. This practice led to an overestimation of reported malaria cases and an over-prescription of anti-malarial drugs (Masanja, 2010). On the other hand, a new study has shown that malaria may be drastically underestimated worldwide, and that morbidity may be shifting to other age groups (Murray, 2012). These issues call for better metrics and evaluation strategies when implementing malaria control interventions. Since the introduction of RDTs, their efficacy in differentiating between suspect and confirmed malaria cases has been demonstrated in numerous studies (Ochola, 2006; Jensen, 2009). But the use of RDTs may have an impact on monitoring systems, such as

through the transitioning of the case definition in HMIS data sources. For example, the use of RDTs to capture malaria cases has changed the case definition of malaria in Madagascar's HMIS data, complicating the interpretation of reported trends. In Madagascar, Sentinel Site surveillance data source has used the case definition of RDT-confirmed malaria to more accurately depict malaria incidence and identify potential epidemics (Randrianasolo, 2010; Sserwanga, 2011). Because of its reliance on RDT-confirmed malaria instead of clinical diagnosis, the Sentinel Site surveillance data source in Madagascar have been more reliable for reporting malaria cases after the implementation of control interventions.

While control interventions have impacted routine monitoring of malaria, they also cause other problems that could potentially hinder malaria control. Potential increases in malaria incidence after control interventions are not unique to Madagascar. Currently, there are many studies throughout Africa that do not demonstrate a decrease in malaria incidence after multiple population-wide interventions, and there are many hypotheses for the persistent malaria incidence. For example, studies have suggested that resurging malaria incidence corresponds to resistance to insecticides used in LLINs and the transfer of malaria burden to older populations (Trape, 2011; Talisuna, 2011; Mathanga, 2012). Other research in Africa has shown that combination therapies such as ACT may not protect treated patients in the short-term against malaria infection, allowing for re-infection and a subsequent higher number of patient visits at health facilities during seasons of high transmission (Bukirwa, 2006). Furthermore, with climate change, researchers have looked at the impact of changing climates on malaria transmission and distribution in order to strengthen current programs (Krefis, 2011; Ye, 2007). The

continuing escalation of malaria control programs require systematic monitoring and evaluation, which can be challenging in resource-poor countries.

In order to investigate the determinants of trends seen in data sources from the CSBU in Maevatanana, triangulation methodology was used to collect data that focused on different populations, different measurements, and different methodologies, and gave a more comprehensive picture of trends of malaria incidence (Rutherford, 2010).

Triangulation methodology has been frequently used in investigating HIV trends in Africa, and it is now being developed as a tool for monitoring malaria trends in countries with active control programs (Rutherford, 2010; Miles 2012). This methodology uses available data to answer pressing program questions when time and funds are limited.

## **Methods**

Triangulation methodology was used to gather data and assess trends in data sources, and through an iterative process, define specific hypotheses and research questions regarding trends in malaria incidence at the CSBU in Maevatanana district. This methodology was selected because it utilized existing data in a comparative manner, and allowed for a clearer understanding of trends in malaria incidence without requiring additional primary data collection. This process involved the collation, synthesis, and qualitative analysis of data from multiple existing sources to investigate research aims (HIV Triangulation Resource Guide, 2009). Also, stakeholder meetings were conducted in order to refine research aims as well as generate hypotheses, ensuring collaboration and interest in the results.

The triangulation methodology for this study included the following steps (Rutherford, 2010):

1. Identify questions

2. Identify existing data sources and background information: All data sources reporting on malaria cases were collected for Maevatanana district, including HMIS data, Sentinel Site data, Demographic and Health Survey (DHS) and Malaria Indicators Survey (MIS) reports, Global Malaria Programme (GMP) data, and information from published research on the Betsiboka region.
3. Hold stakeholder meetings to discuss research aims, methods, and data sources: For this study, weekly meetings were conducted with the NMCP program manager in Betsiboka and the director of the CSBU between August 2009-August 2011 in order to discuss hypotheses and evaluate trends in data sources. Monthly meetings were also conducted with a stakeholder and research partner from PMI/CDC in order to refine research aims, collect and assess the quality of data sources, and generate hypotheses. The primary researcher presented the initial findings and the triangulation methodology to all regional NMCP program managers on March 8, 2011 in Antananarivo, Madagascar for a quarterly NMCP meeting.
4. Refine research aims: The first four steps were part of the iterative and collaborative process of defining actionable research aims that addressed the needs of the Maevatanana community, NMCP program managers, and other stakeholders. Original aims regarding trends in malaria incidence in Betsiboka were refined to investigate malaria trends from two data sources reporting on the CSBU in Maevatanana district.
5. Gather data sources: Data sources were provided by the regional NMCP program manager from Betsiboka, national NMCP data managers, IPM/DULMN data managers, and the PMI/CDC program manager and partner.

6. Assess data quality and make observations from each data set: This step included gathering information about data quality (i.e. completeness) and describing the malaria case definition applied and the indicators used in each source. The data sources are further described in the data matrix in Appendix I.
7. Identify and analyze trends in data sets and hypothesize: Time-series line graphs were developed for each data set, evaluating the number of reported malaria cases per month, the percentage of reported malaria cases of all patient consults per month, and the percent of slide positivity rate (SPL) from the HMIS and Sentinel Site data sources for the CSBU. The direction and strength of the trend was qualitatively assessed through application of a loess curve, which is a line fitted to the data through the application of least-squares calculations to subsets of the data. The process smoothed the data without applying a specific function (Cleveland, 1988).
8. Check (corroborate, refute, modify) hypotheses.
9. If necessary, identify additional data and analyze.
10. Summarize findings and draw conclusions.
11. Communicate results and recommendations to stakeholders.
12. Outline next steps for action: The results of this study will be submitted for publication and will be available as a tool for NMCP program managers to use when investigating malaria trends in Madagascar.

### **Estimate of baseline malaria prevalence for the CSBU in Maevatanana**

Studies of malaria incidence and trends in Madagascar before control interventions were implemented are lacking. One study before malaria control interventions occurred was conducted in Maevatanana district in 2007, and found that about 20% of school children surveyed tested positive for the presence of *P. falciparum* anti-MSP1 antibodies (Rzakandrainibe, 2009). This study was community-based and focused on symptomatic and asymptomatic participants, and therefore, may not represent an accurate baseline for malaria incidence at the CSBU before control interventions. Percentage of RDT+ malaria cases of all patient consults reported in the Sentinel Site data reach this community level-percentage in early 2010 (see Figure 8), but again, these measurements may not be comparable because of the difference in populations being surveyed (i.e. symptomatic vs. asymptomatic persons, different age groups, different health-seeking behaviors, etc.).

# Results

## Results: Aim 1

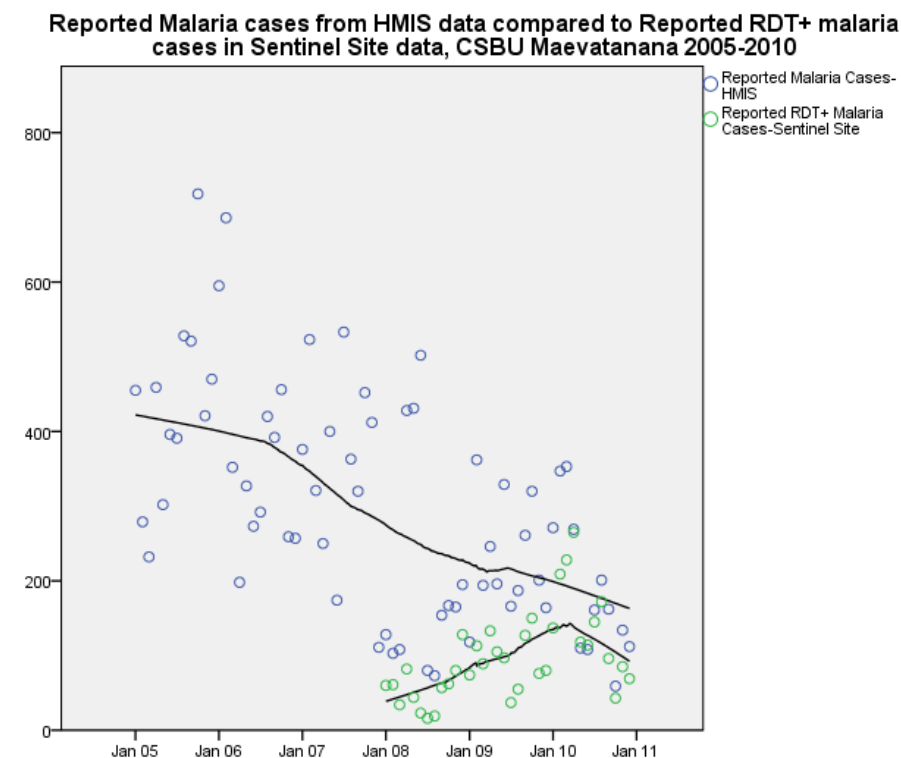
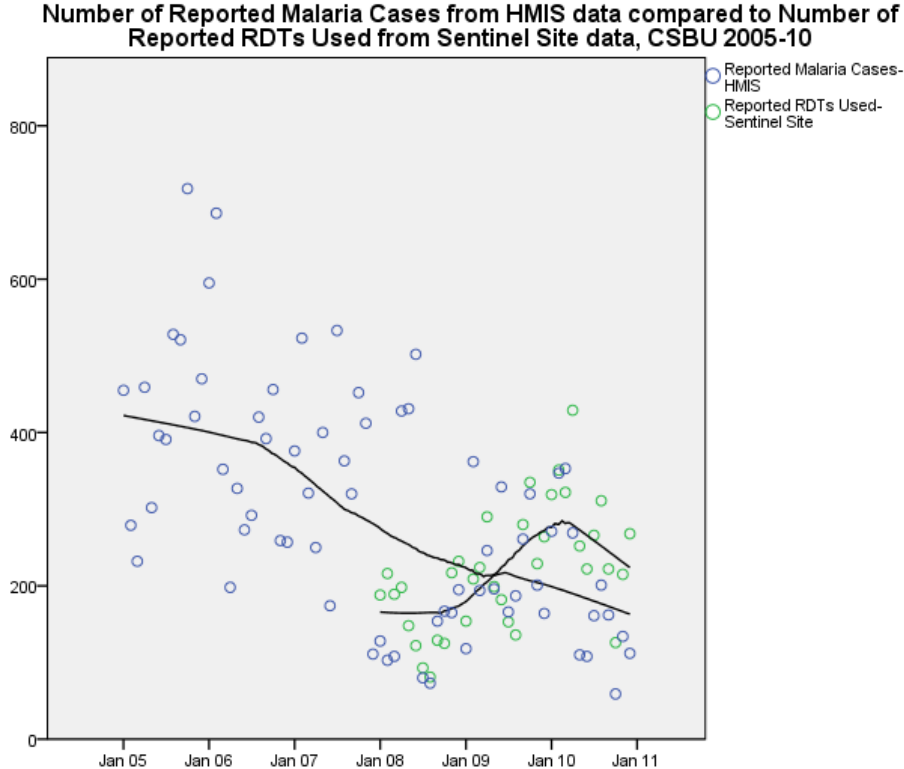


Figure 4: Monthly reported malaria cases from HMIS data (2005-10) compared to monthly reported RDT+ malaria cases from Sentinel Site data, CSBU (2008-10).

Year	HMIS, CSBU			Sentinel Site, CSBU			Differences Between Two Data Sources		
	Total Reported Patient Consults	Total Reported Malaria Cases	Percent Reported Malaria Cases of All Patient Consults	Total Reported Patient Consults	Total Reported RDT+ Cases	Percent RDT+ Cases of all Patient Consults	Difference in Number of Patient Consults Between Sources	Difference in Reported Malaria Cases (HMIS) and RDT+ cases (SS): Proxy number of suspect cases	Percent Difference in Reported Malaria Cases from HMIS data and Sentinel Site data for CSBU
2005	14553	5172	35.5%						
2006	13663	4507	33.0%						
2007	12733	4235	33.3%						
2008	13733	2534	18.5%	13532	666	4.9%	201	1868	73.7%
2009	15357	2744	17.9%	15464	1136	7.3%	-107	1608	58.6%
2010	16370	2287	14.0%	16496	1681	10.2%	-126	606	26.5%

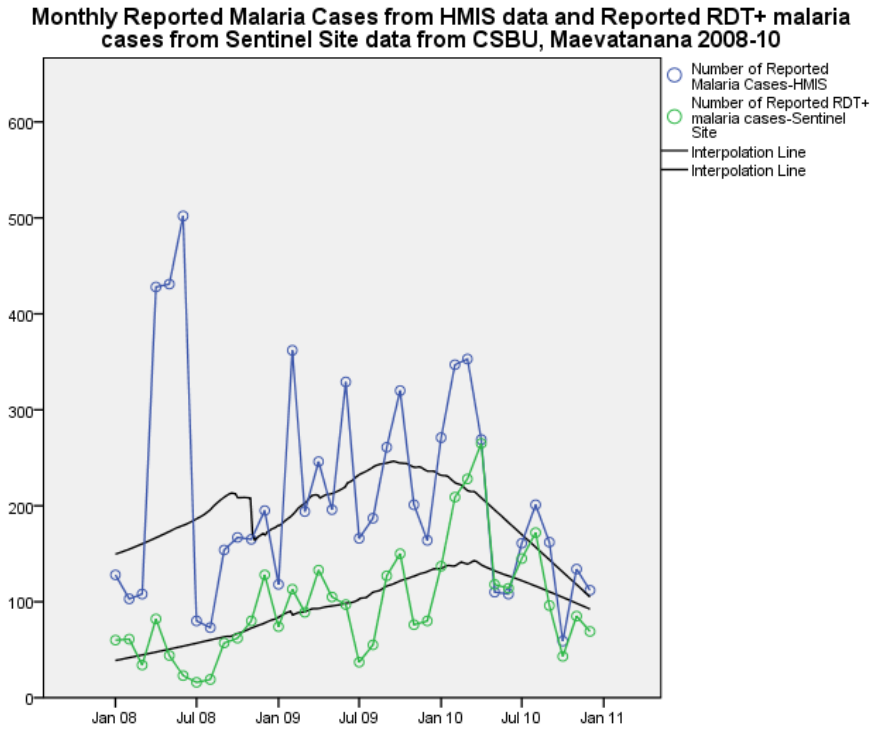
Table 1: Total reported malaria from the HMIS and Sentinel Site data sources for the CSBU (2005-10).



**Figure 5: HMIS reported malaria cases (2005-10) compared to the number of Sentinel Site reported RDTs used at the CSBU (2008-10).**

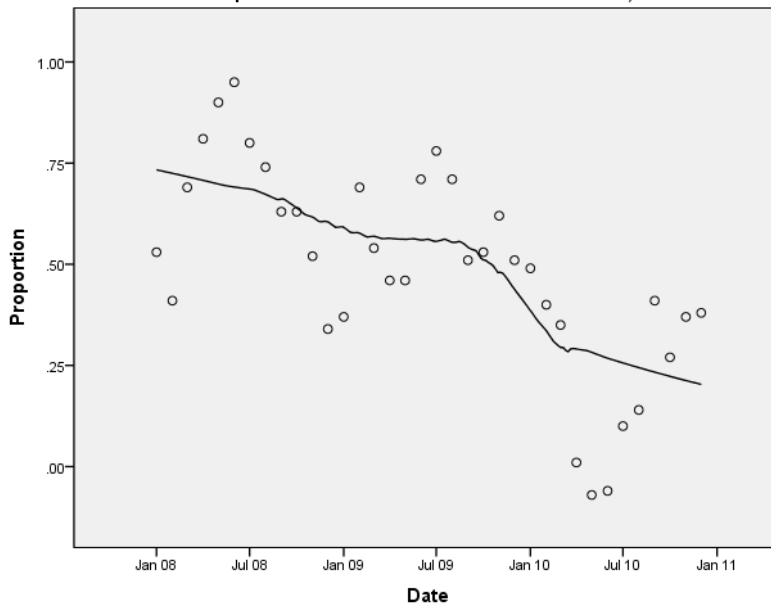
Between 2005 and 2010, reported malaria cases have decreased in HMIS data from the CSBU (Figure 4). The case definition for malaria in the HMIS data source was the clinical diagnosis of malaria, which included suspect cases as well as biologically confirmed cases when RDTs became available in mid-2007. As shown in Table 1, HMIS reports from the CSBU in Maevatanana showed a decrease in reported malaria cases by about 50% between 2005 and 2010, from 5172 cases in 2005 to 2287 cases in 2010 (a decrease from 35.5% to 14.0% reported malaria cases of all patient consults). The most dramatic decrease occurred between 2007 and 2008, from 4235 reported malaria cases to 2534, corresponding to the introduction of RDTs and ACTs in mid-2007, as well as the first distribution of LLINs in October 2007. As depicted in Figure 5, the decrease in reported malaria cases in the HMIS data corresponds to an increase in

the number of reported RDTs used from the Sentinel Site data source for the CSBU. This trend suggests that as RDT usage increased, the number of reported malaria cases in the HMIS data decreased as suspect malaria cases were increasingly eliminated from monthly HMIS reports.



**Figure 6: Monthly total reported malaria cases from HMIS and Sentinel Site data for CSBU (2008-10).**

**Proportion of Reported Malaria from HMIS data Attributable to Suspect Malaria Cases when compared with Sentinel Site data from CSBU, 2008-10**



**Figure 7: Estimated percent difference of reported malaria in the HMIS data and reported RDT+ malaria cases in the Sentinel Site data for the CSBU (2008-10).**

As shown in Figure 6, for the period in which both data sources are available from 2008 to 2010, the difference between the number of reported malaria cases from the HMIS data and the number of reported RDT+ malaria cases from the Sentinel Site data increasingly narrows. Moreover, as described in Table 1, the difference in the number of reported malaria cases between these two sources decreases from 1868 cases in 2008 to 606 cases in 2010. Furthermore, there is a decrease in the percent difference between HMIS data and the Sentinel Site data at the CSBU, from a difference of 73.7% in 2008 to 26.5% in 2010 (Figure 7). In general, the decrease in suspect malaria cases being reported by HMIS data for the CSBU likely accounts for the decrease in reported malaria in the HMIS data source, as the increase in RDTs used corresponds to a decrease in the difference between reported malaria cases from HMIS and the Sentinel Site data sources.

## Results: Aim 2

### Evidence: Increase in reported RDT+ malaria cases at the CSBU in Maevatanana from 2008 to 2010

Reported Number of RDT+ malaria cases and Percent RDT+ malaria cases of all Consults from Sentinel Site data CSBU, 2008-10

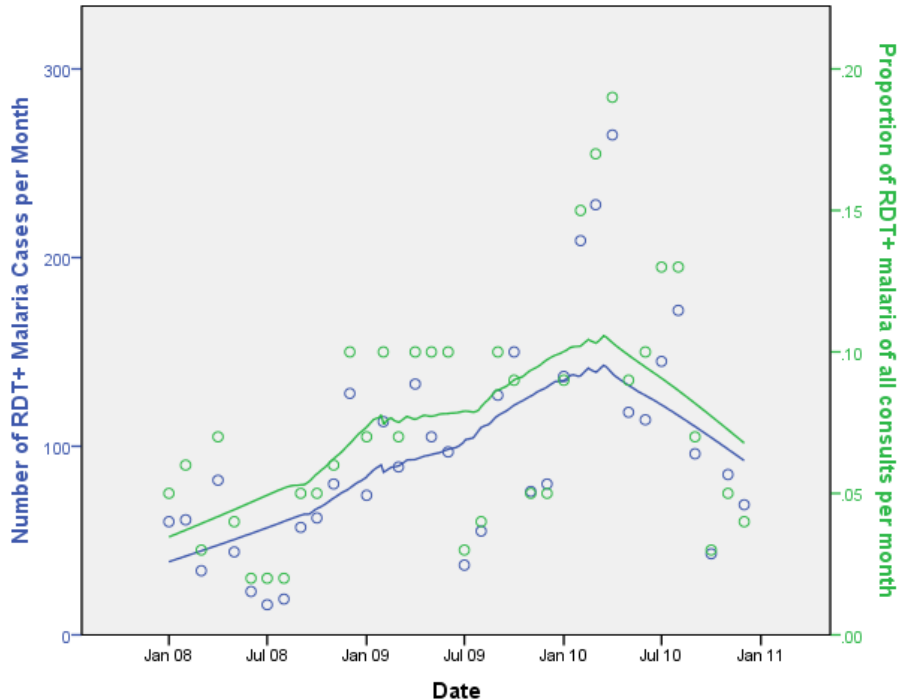
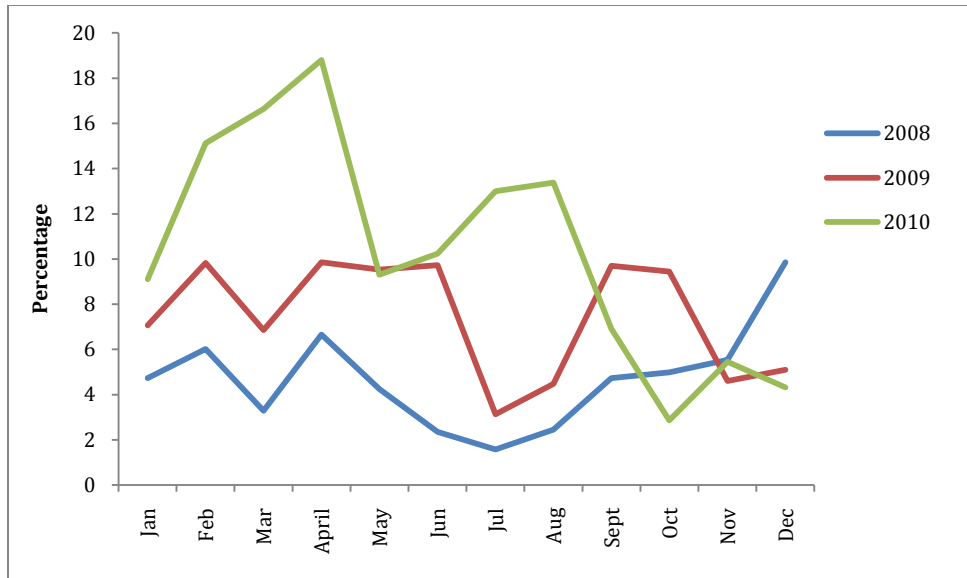


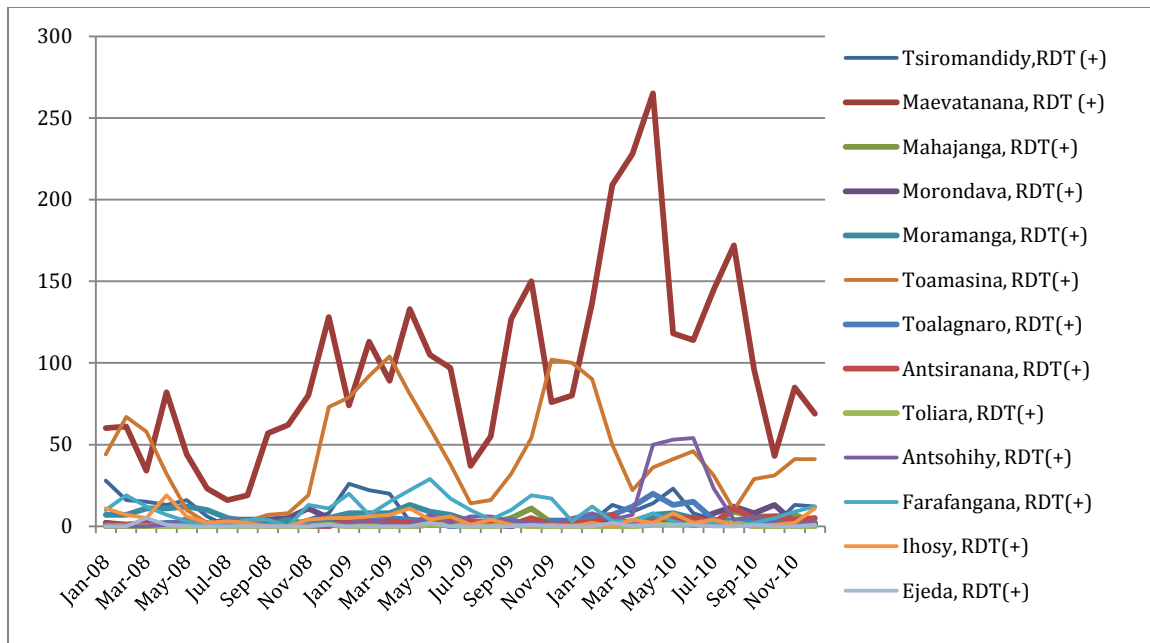
Figure 8: Total RDT+ malaria cases and percent of RDT+ malaria cases of all patient consults as reported in the Sentinel Site data source for the CSBU (2008-10).

Figure 8 shows that monthly reports from the Sentinel Site data for the CSBU demonstrate an increase in RDT+ malaria cases between 2008 and 2010 from 666 cases in 2008 to 1681 cases in 2010 (an increase in the percent of RDT+ malaria cases of patient visits at the CSBU from 4.9 to 10.2%) (Table 1). When looking specifically at the proportion of RDT+ cases of all patient consults at the CSBU for each year from the Sentinel Site data, the percentage remains the same for each successive year during the low transmission period between June and December. But during the higher transmission period from January to April, there is an increasing difference in monthly percentages between 2008 and 2010 (Figure 9).

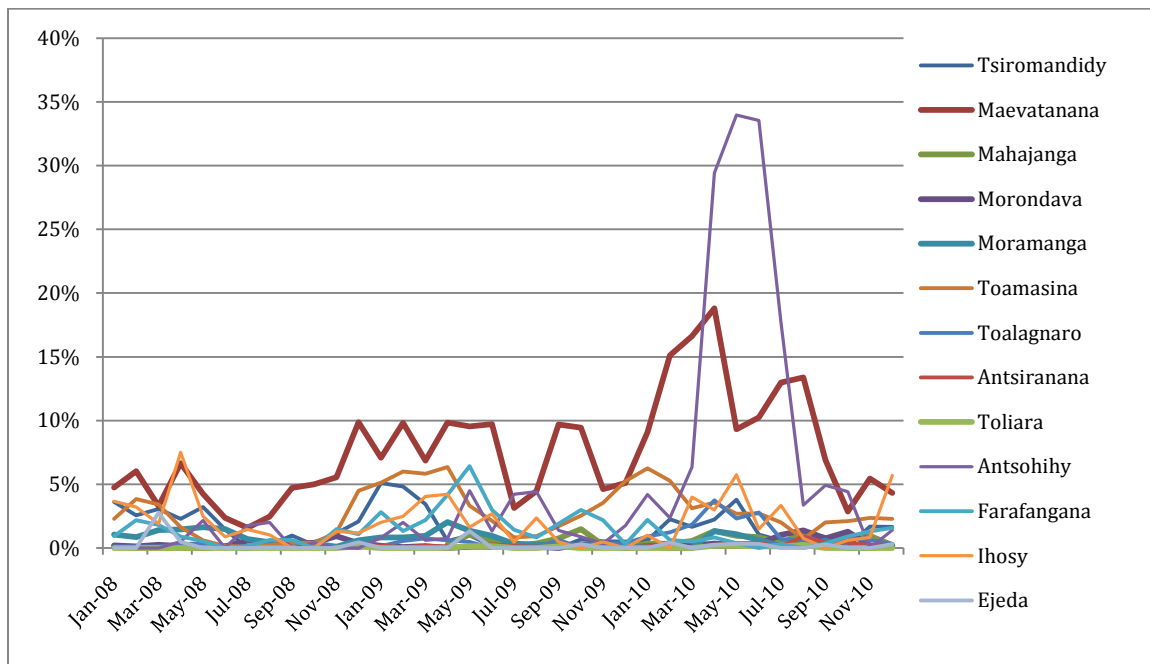


**Figure 9: Percent reported RDT+ malaria cases of all patient consults from Sentinel Site data for CSBU.**

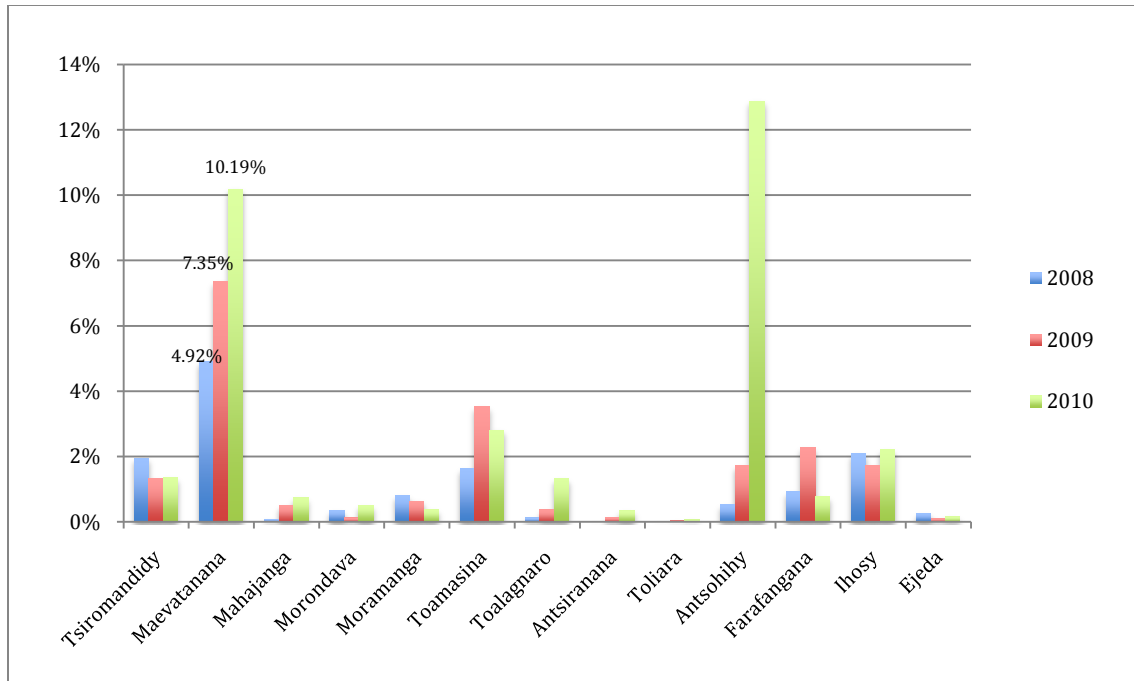
The trend in the Sentinel Site data has been concerning, given that it occurred soon after the 2007 distribution of LLINs as well as the introduction of ACTs and RDTs in mid-2007 in Maevatanana district. This trend is contradictory to what was expected after the implementation of control interventions, and it also contradicts what has been seen in most Sentinel Sites in Madagascar (see Figures 10 and 11). While most Sentinel Sites show a cyclical pattern of malaria incidence and very little if any increase (except for Antsohihy, also in western Madagascar), the Sentinel Site at the CSBU in Maevatanana shows increases in malaria incidence between 2008 and 2010. Furthermore, when looking at the yearly percent of reported RDT+ cases of all patient consults in Figure 12, Maevatanana and Antsohihy show the only large increases in yearly percentages between 2008 and 2010.



**Figure 10: Number of RDT+ malaria acases reported by 13 sentinel sites in Madagascar. The red line represents the number of RDT+ cases reported by the Sentinel Site at the CSBU, Maevatanana.**



**Figure 11: Percent of RDT+ malaria cases of all patient consults at Sentinel Sites in Madagascar from (2008-10). The Red Line represents the percentage reported by the CSBU, Maevatanana.**



**Figure 12: Percent RDT+ malaria cases of all patient consults by year for 13 Sentinel Sites in Madagascar (2008-2010).**

The SPR from the CSBU also increased between 2008 and early 2009 from 20% to 45% in the Sentinel Site data, then remains relatively stable at around 40-50% from mid-2009 to the end of 2010 (Figure 13). SPR has been used in other studies to estimate malaria incidence in the absence of longitudinal studies; however, the direct relationship between SPR and malaria incidence is not linear or exponential, making it difficult to interpret whether the increase in SPR between 2008 and 2009 corresponds to increases in true malaria incidence (Jensen, 2009). The SPR is also limited because of a lack of information about the incidence of non-malaria fevers presenting at the CSBU, which could impact the denominator when calculating the SPR.

Proportion of Reported RDT+ malaria cases of all RDTs used from Sentinel Site CSBU, Maevatanana 2008-10

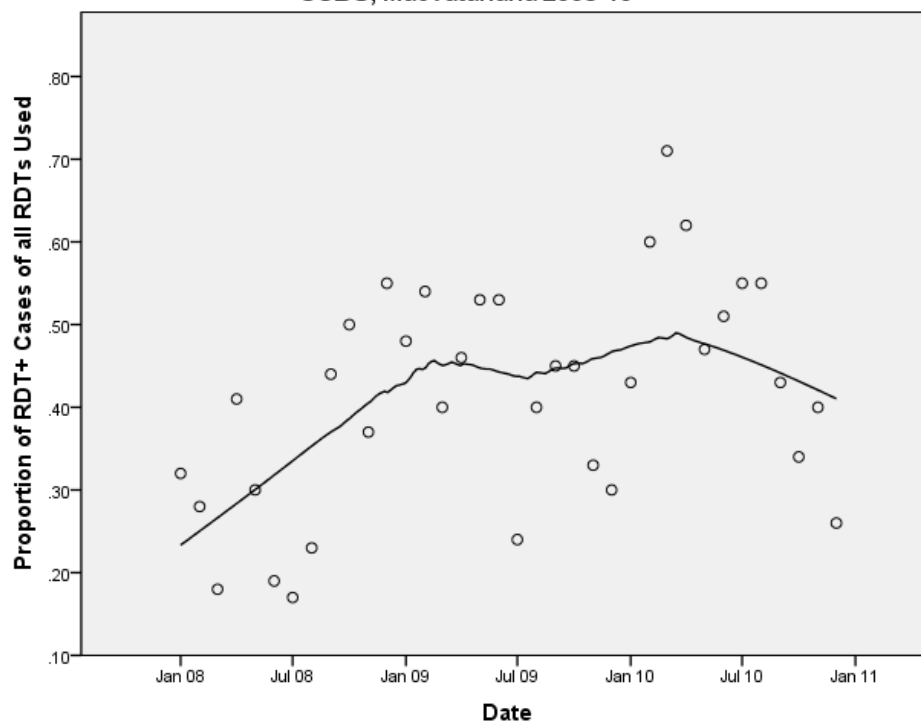
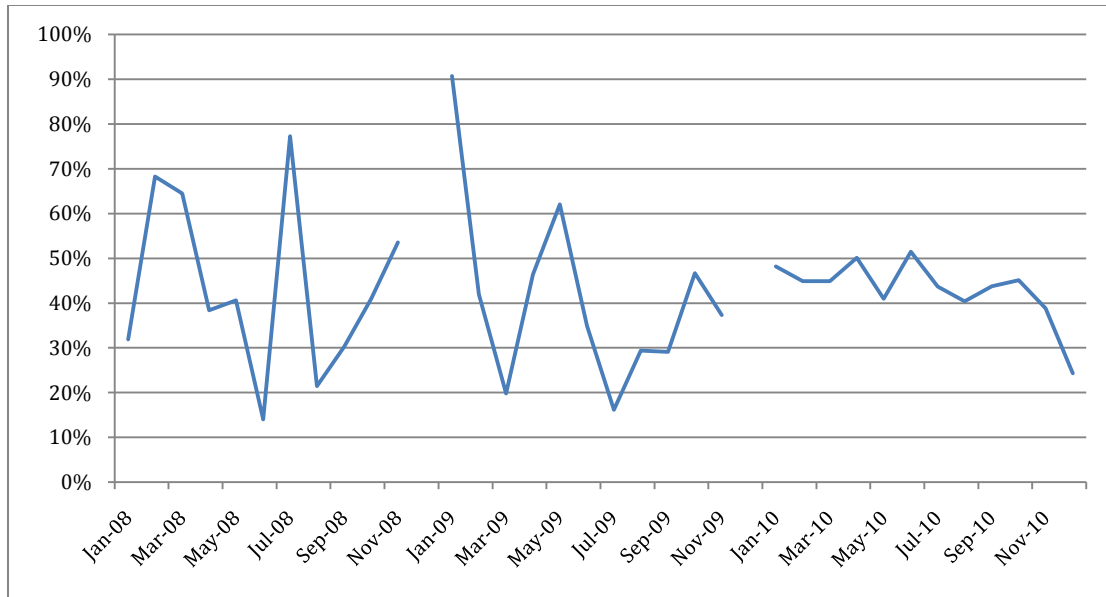
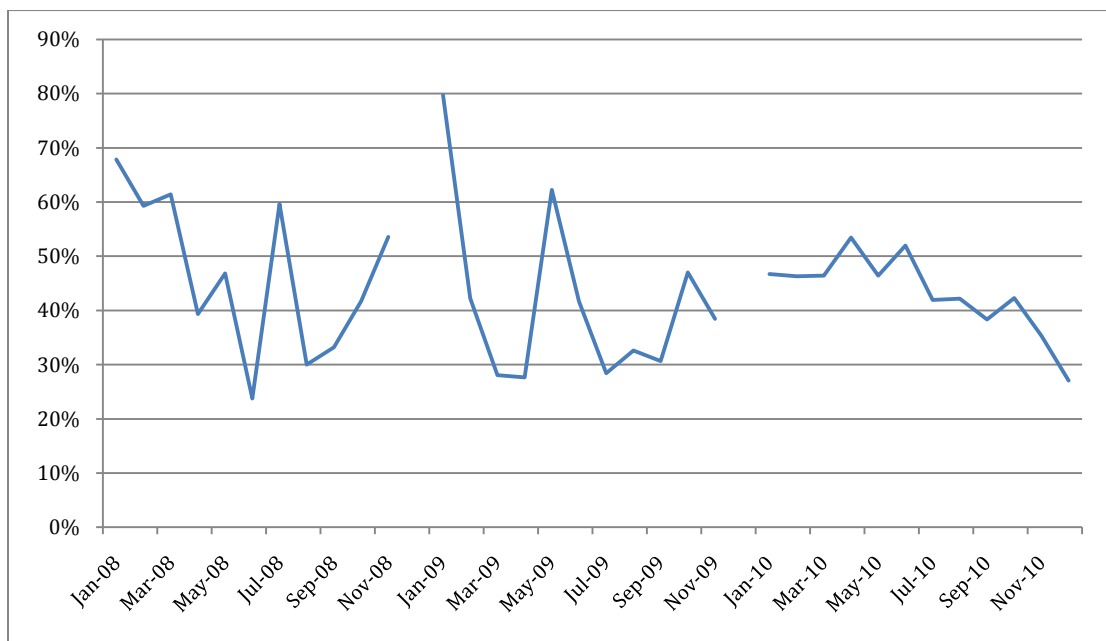


Figure 13: Monthly Slide Positivity Rate (SPR) from Sentinel Site data for the CSBU.

On the other hand, trends depicted in the GMP data for Maevatanana district and the Betsiboka region show similarities and differences to trends in the Sentinel Site data for the CSBU. GMP source collects data from all CSBS in a given district, while Sentinel Site data report on specific CSBs or hospitals in 13 different districts throughout Madagascar. GMP data for all the districts that have Sentinel Sites show a similar pattern to Sentinel Sites in regards to the proportion of RDT+ malaria cases of all patient consults. Trends in SPRs from the GMP data for Maevatanana district and Betsiboka region show large increases between 2008 and 2009 (between 20 and 90%) but not in 2010 (Figures 14 and 15). This data has similarities with the Sentinel Site data in terms of increasing malaria trends seen in 2008 to 2009; however, the stabilized trend in SPRs seen in 2010.



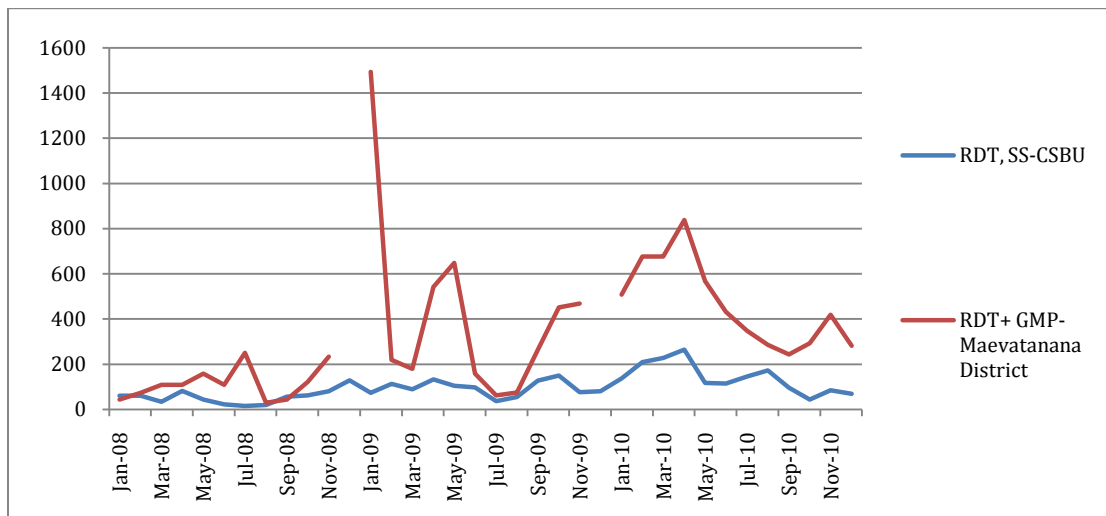
**Figure 14: Slide positivity rate for Maevatanana District collected by GMP (2008-10).**



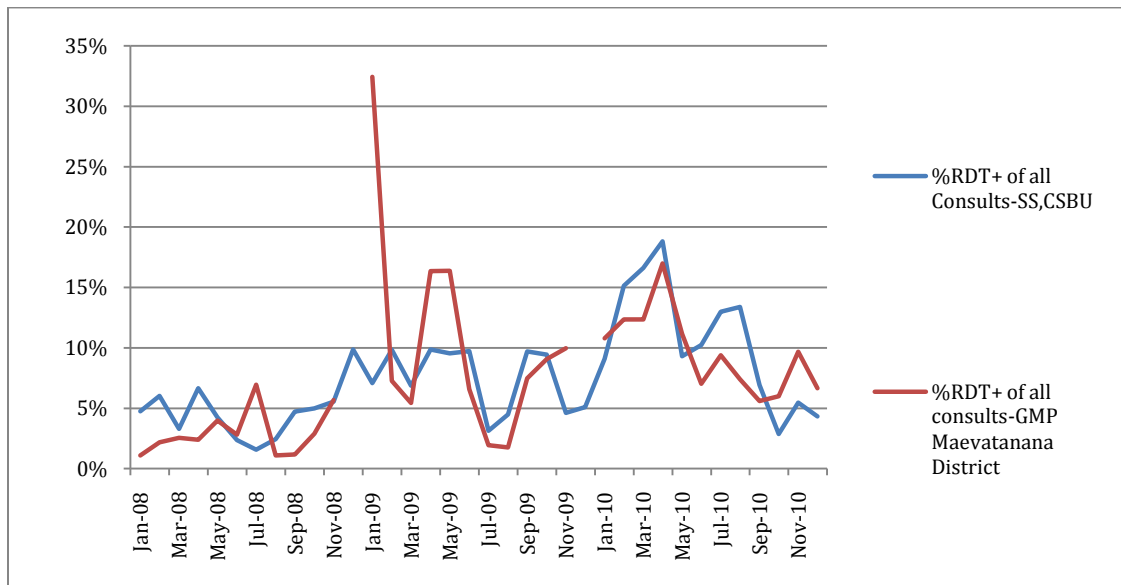
**Figure 15: Slide positivity rate for the Betsiboka region collected by GMP (2008-10).**

Moreover, other data sources corroborate the trend seen in the Sentinel Site data from the CSBU. As shown in Figure 6, the loess curves for both HMIS and Sentinel Site data sources demonstrate an increase in reported malaria cases between 2008 and early 2010, and then a decrease between mid-2010 to the end of 2010. Also, the GMP data source reporting RDT+

malaria cases by district show an increase in percent RDT+ malaria cases of all patient consults in Maevatanana district between 2008 and 2010 (Figures 16 and 17).



**Figure 16: Comparison of reported RDT+ malaria cases in GMP data for all CSBs in Maevatanana district and Sentinel Site data for the CSBU in Maevatanana (2008-10). The number of patient consults and RDT+ malaria cases in January 2009 are probably outliers or aggregated data from previous months that were not reported.**



**Figure 17: Comparison of the percent of reported RDT+ malaria cases of all patient consults from GMP data for Maevatanana district and Sentinel Site data for the CSBU in Maevatanana (2008-10).**

In terms of the impact of malaria control interventions on Maevatanana district, DHS and MIS surveys of LLIN ownership and utilization in the western region of Madagascar show increasing protection from malaria transmission between 2004 and 2011 (Table 2). The

proportion of reported ownership and usage of LLINs increased in each successive survey, which was expected to result in a decrease in the proportion of patient consults reportedly due to malaria. Furthermore, the percentage of children with reported fever that received anti-malarial treatment increased, which was also expected to result in a decrease in malaria transmission.

Own an LLIN			Utilization of LLINs by children<5			The Percentage of children with a fever who received anti-malarial for a fever			The Percentage of children with a fever who received anti-malarial treatment within the first 24 hours		
DHS 2003-04	DHS 2008-09	MIS 2010-11	DHS 2003-04	DHS 2008-09	MIS 2010-11	DHS 2003-04	DHS 2008-09	MIS 2010-2011	DHS 2003-04	DHS 2008-09	MIS 2010-2011
57.6%*	76.1% <sup>y</sup>	95.4%	51.8%*	76.4% <sup>y</sup>	89.6%	N/A	13.7% <sup>y</sup>	19.1%	N/A	5.15% (Any anti-malarial); 0.4% (ACT) <sup>z</sup>	7.9% (Any anti-malarial); 0.4% (ACT)

\*The average of proportions from two western provinces that were surveyed in 2003-04 DHS (Toliara and Mahajanga) and comprise the western epidemiologic zone of malaria transmission in Madagascar.

<sup>y</sup>The average proportion for seven regions (Boeny, Sofia, Diana, Betsiboka, Menabe, Melaky, Atsimo Andrefanana) that comprise western epidemiologic zone of malaria transmission in Madagascar, surveyed in DHS 2008-09.

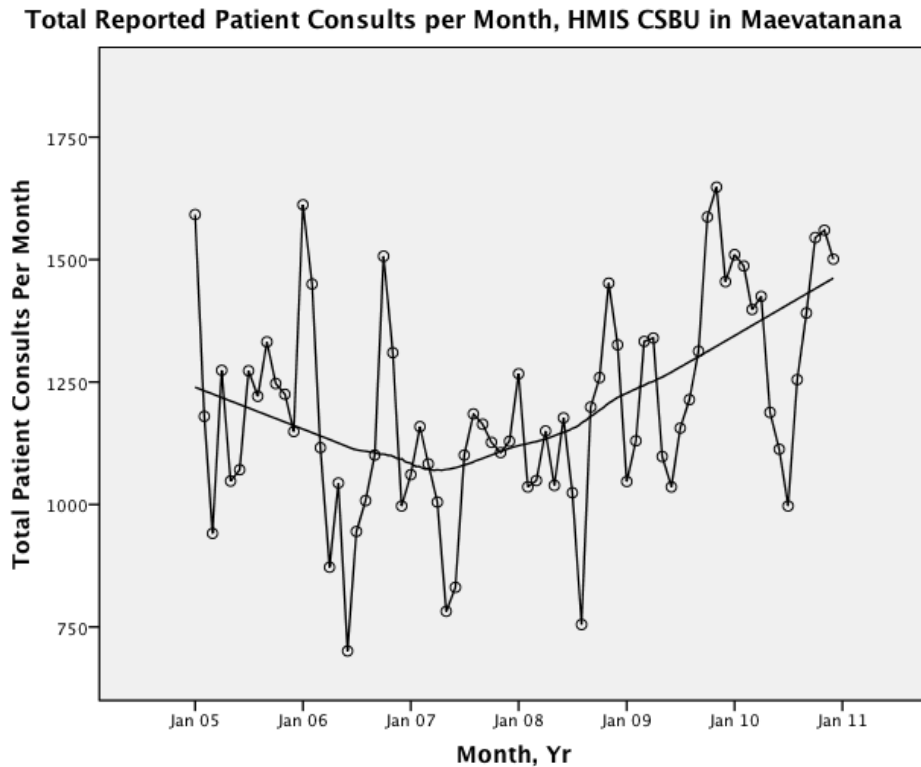
Table 2: Comparison of LLIN ownership, LLIN utilization by children <5 yrs, and treatment of fevers in children<5 yrs with anti-malarial treatment as reported in DHS and MIS demographic surveys for western Madagascar.

### **Explanation 1: Increase in reported RDT+ malaria cases in Sentinel Site may relate to changes in population behavior**

Reports from the Sentinel Site data from the CSBU show an increase in the number of RDTs used monthly, as well as the percentage of RDT+ cases of all RDTs used between 2008 and 2010, with higher monthly totals seen in the rainy season between November and March (Figure 8). This increase suggests a true increase in the number of patient consults with fevers and an increase in the proportion of RDT+ cases of those with fevers, or an increase in malaria capture ability by healthcare workers over time if health workers were not only testing symptomatic patients.

Furthermore, Figure 18 shows an increase in reported number of consults per month at the CSBU from HMIS data, especially from 2007 to 2010. Behavioral change communication is

included as a key component of malaria control interventions. It is possible that the number of people seeking care for fevers and subsequently being diagnosed with RDT-confirmed malaria increased between 2005 and 2010. Also, increases in patient consults could relate to the availability of free ACTs at the CSBU as a part of malaria control interventions.



**Figure 18: Number of reported patient consults from the HMIS data for the CSBU.**

While the number of patient consults also increases each year, the proportion of the additional patient consults that are RDT+ malaria cases is larger for each successive year, demonstrating that increases in patient consults have an increasing proportion of RDT+ malaria cases (Table 3). This trend could represent a true increase in malaria cases at the CSBU or could indicate better malaria case capturing as case management improves.

Year	Consults	RDT+	Proportion RDT+ of all Consults	Change in number of yearly consults	Change in RDT+ malaria cases per year	Ratio of change in RDT+ malaria cases of change in consults
2008	13532	666	0.049			
2009	15464	1136	0.073	1932	470	0.243
2010	16496	1681	0.102	1032	545	0.528

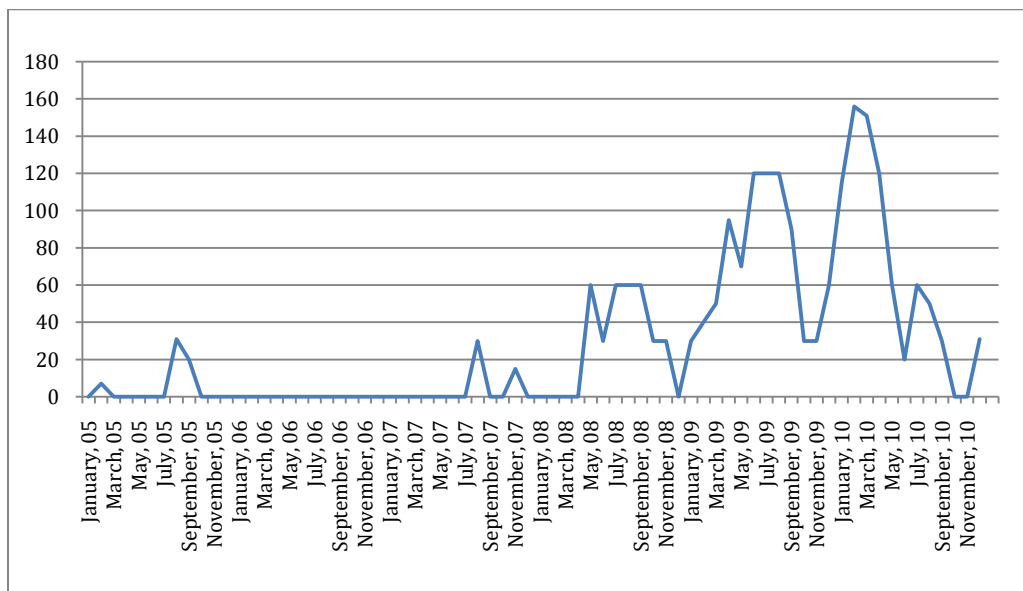
Table 3: Analysis of increases in RDT+ malaria cases of all patient consults as reported in the Sentinel Site data for the CSBU (2008-10).

Further investigation is needed to understand health-seeking behavior in this area. First of all, each of the intervention districts had Community-based Integrated Management of Childhood Illness (c-IMC) programs established, and therefore population health behaviors across districts should be relatively similar (PMI-Madagascar, 2011). Secondly, it is assumed that the populations in each intervention district have familiarity with malaria symptoms and are likely to seek treatment at a public health facility, private facility, or pharmacy when sick, and that trends in behavior would be similar across sites. It is therefore of interest to investigate changing patterns in healthcare-seeking behavior in relation to malaria incidence to see if there are specific differences between Maevatanana and the rest of Madagascar.

**Explanation 2: Increases in reported RDT+ malaria cases correlates with increases in stock-outs of ACT**

In terms of programmatic gaps, HMIS reports limited information about ACT stock-outs at CSBs, and show an increase in the number of days of ACT stock-out at all CSBs in Maevatanana district between 2005 and 2010, which corresponds to higher reported malaria (Figure 19). This trend suggests that malaria incidence has increased and has possibly caused ACT stock-outs, that the stock-outs have resulted in increases in malaria

incidence as less protection against transmission is available, or that patients are returning to the clinic for treatment and being re-recorded as a malaria case when there are stock-outs. However, data about stock-outs are consistently incomplete in monthly reports collected by HMIS and the reasons for stock-outs are not reported. It would be of interest to investigate why stock-outs are occurring and what impact they have on health-seeking behavior as well as health workers' treatment of malaria cases (i.e. with other lesser-quality drugs) at the CSBU and in other intervention districts in order to identify potential problems such as re-infection in the population and potential resistance to malaria treatment.



**Figure 19: Aggregated monthly number of days of ACT stock-out at all CSBs in Maevatanana district from HMIS data (2005-10).**

**Explanation 3: Increases in reported RDT+ malaria cases are contradictory to expectations when the entomological inoculation rate (EIR) is low**

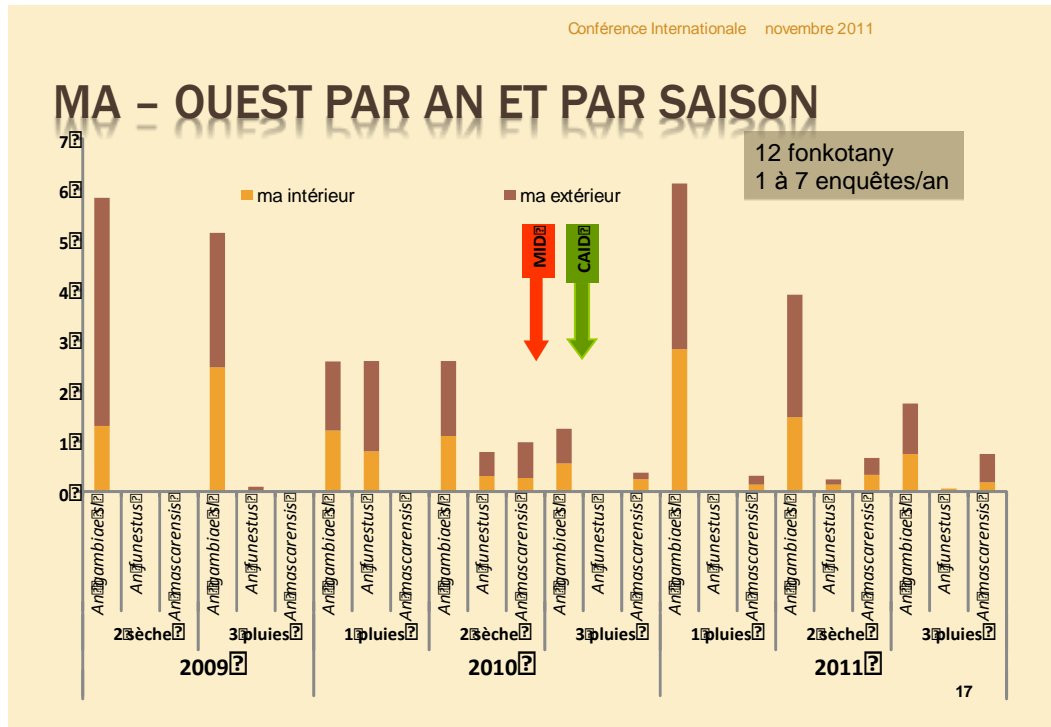


Figure 20: Presentation slide depicting EIRs in the western region of Madagascar from 2009 to 2011 (Rakotoson, 2011).

EIR or the number of bites per person by infected anopheles estimated by a proxy baseline study in Maevatanana was found to be 9 (bites/person) in 2007 (Rzakandrainibe, 2009). Figure 20 shows the most recent estimates of EIR in the western region of Madagascar (including Maevatanana district and Betsiboka region), demonstrating that these rates decreased to 6 in 2009, then to 1-3 in 2010, with most of the decrease in EIR being in bites occurring outdoors. Increases in RDT+ malaria cases seen in the Sentinel Site data are contradictory to what would be expected with lower EIR measurements identified between 2007 and 2010. On the other hand, prior studies in other locations in Madagascar have shown that even with low EIRs, such as 2.49 in the central area of Madagascar, malaria prevalence remains high at 10.7-51% per month (Robert, 2006). Lower EIRs therefore should be further examined in their relation to continual high malaria prevalence reported in the Sentinel Site data from the CSBU.

**Explanation 4: Increases in reported RDT+ malaria cases may be due to resistance to insecticides and malaria treatment**

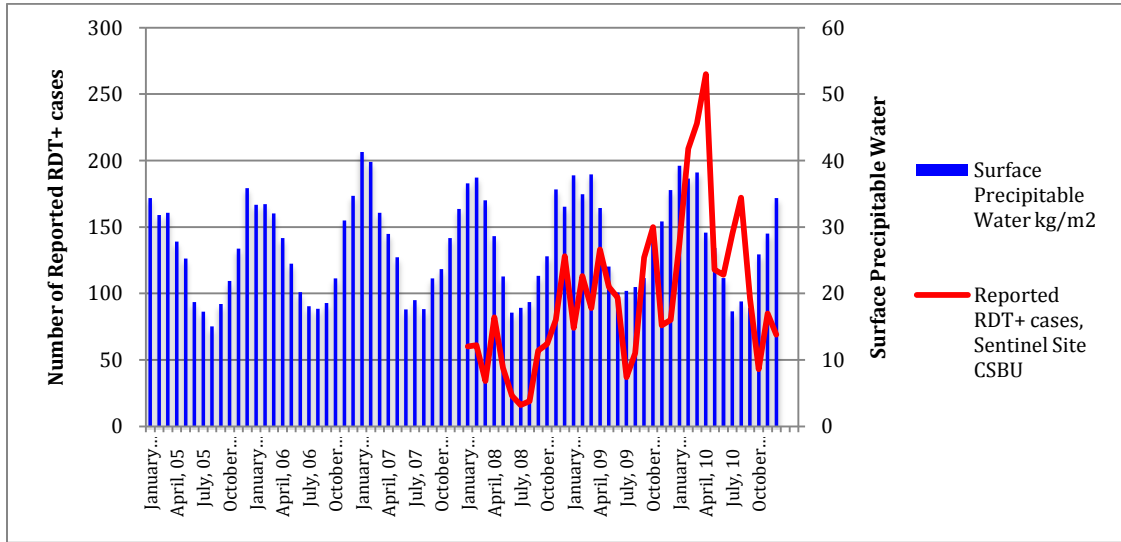
East	Central Highlands	Fringe Sites	South	West
<i>An. gambiae sl</i> Résistance au DDT, Pyréthrinoides et Bendiocarb	<i>An. gambiae sl</i> Résistance au DDT, Pyréthrinoides et Bendiocarb	<i>An. gambiae sl</i> Résistance au DDT, Pyréthrinoides et Bendiocarb	<i>An. gambiae sl</i> Résistance au DDT, Pyréthrinoides et Bendiocarb	<i>An. gambiae sl</i> Résistance au DDT, et Bendiocarb Résistance confirmée aux Pyréthrinoides
<i>An. funestus</i> Pas de données	<i>An. funestus</i> Pas de données	<i>An. funestus</i> Tolérance au DDT et Pyréthrinoides		<i>An. funestus</i> Pas de données
<i>An. mascarensis</i> Pas de données				

**Figure 21: Presentation slide of findings in insecticide resistance in 2010 from IPM and PMI/CDC investigations (Rakotoson, 2011).**

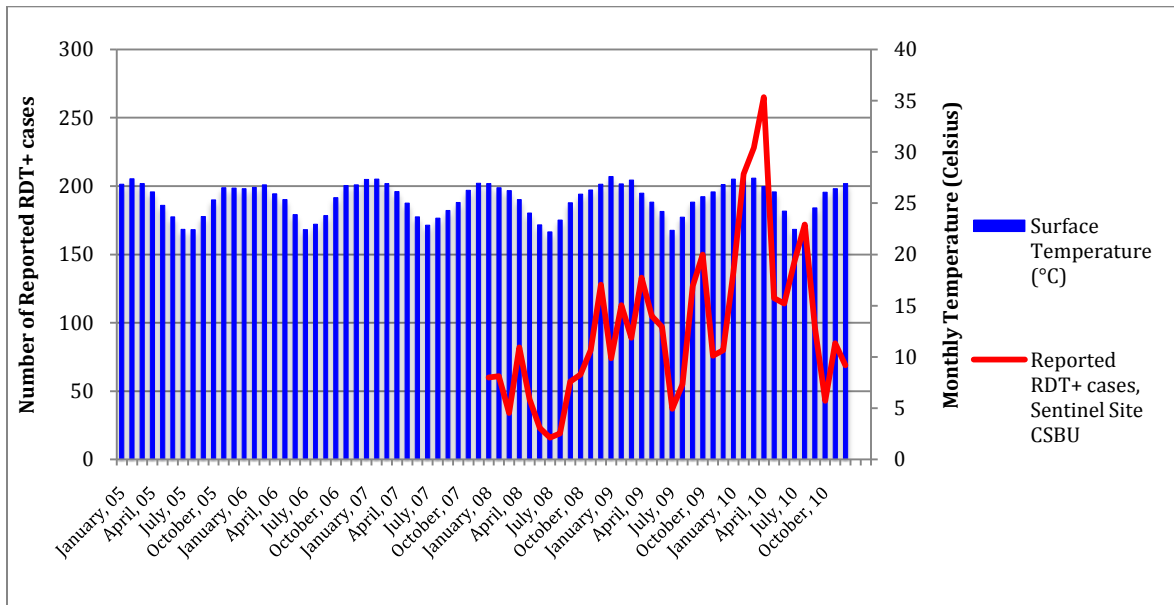
Resistance to pyrethroids, the insecticides used in LLINs and IRS in Madagascar, has been confirmed throughout Madagascar, including in western regions during PMI/NMCP sampling surveys in 2010 (Figure 21) (WHO, 2012). This could cause increased or unabated malaria incidence in Maevatanana district and the rest of Western Madagascar. On the other hand, Sentinel Site data in the other regions where resistance has been discovered have not reported increases in malaria incidence after the 2007 interventions. This suggests that resistance to pyrethroids may not be the major determinant of malaria trends seen in the Sentinel Site data from the CSBU. Alternatively, this could be the first evidence of an increase in incidence associated with resistance, which other studies in Africa have shown to counteract malaria control efforts if widespread (Ranson, 2011). Furthermore, another study of resistance to quinolines in *P. falciparum* shows different distributions of mutated genes throughout Madagascar, which may account for differing malaria trends seen at the CSBU (Andriantsoanirina, 2009) (see Appendix II). It would be of interest to examine the nature of and

possible differences in vector susceptibility to insecticides and malaria treatments periodically in Maevatanana and other districts with Sentinel Sites in order to further investigate the impact of resistance on trends in reported RDT+ malaria cases.

**Explanation 5: Recent increases in reported RDT+ malaria cases at the CSBU may be associated with changes in climatic cycles in Maevatanana district**



**Figure 22: Reported RDT+ cases per month from the Sentinel Site data for CSBU compared to surface precipitable water in Maevatanana district (2005-10).**



**Figure 23: Reported RDT+ malaria cases from Sentinel Site data from CSBU compared to average monthly temperature (°C) for Maevatanana District (2005-10).**

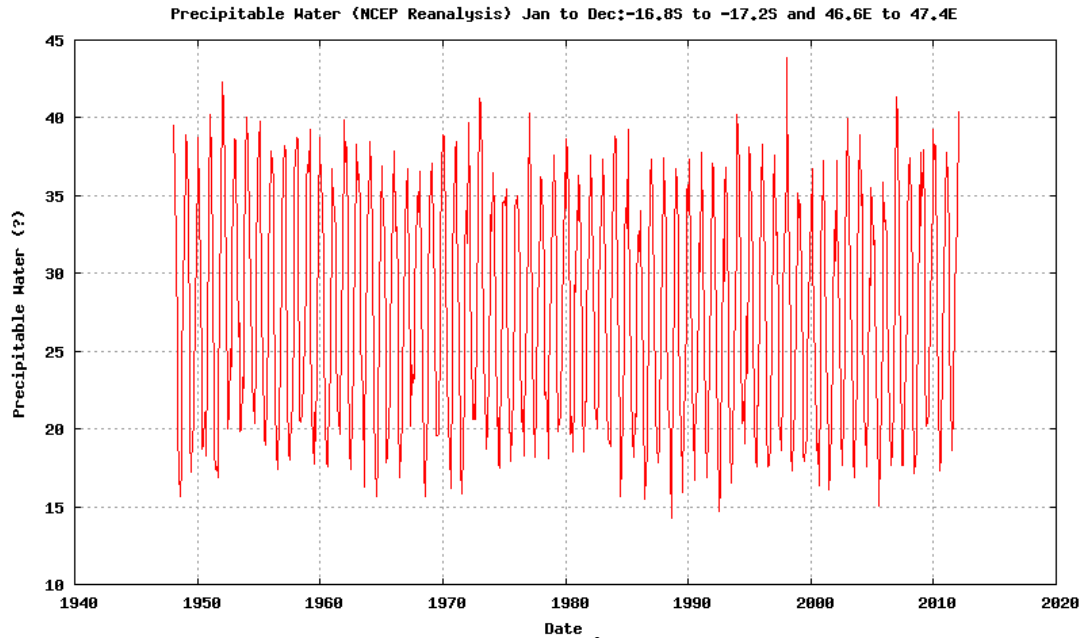


Figure 24: Monthly total surface precipitable water ( $\text{kg/m}^2$ ) in Maevatanana district, 1950-2011 (Earth Science Research Division, 2012)

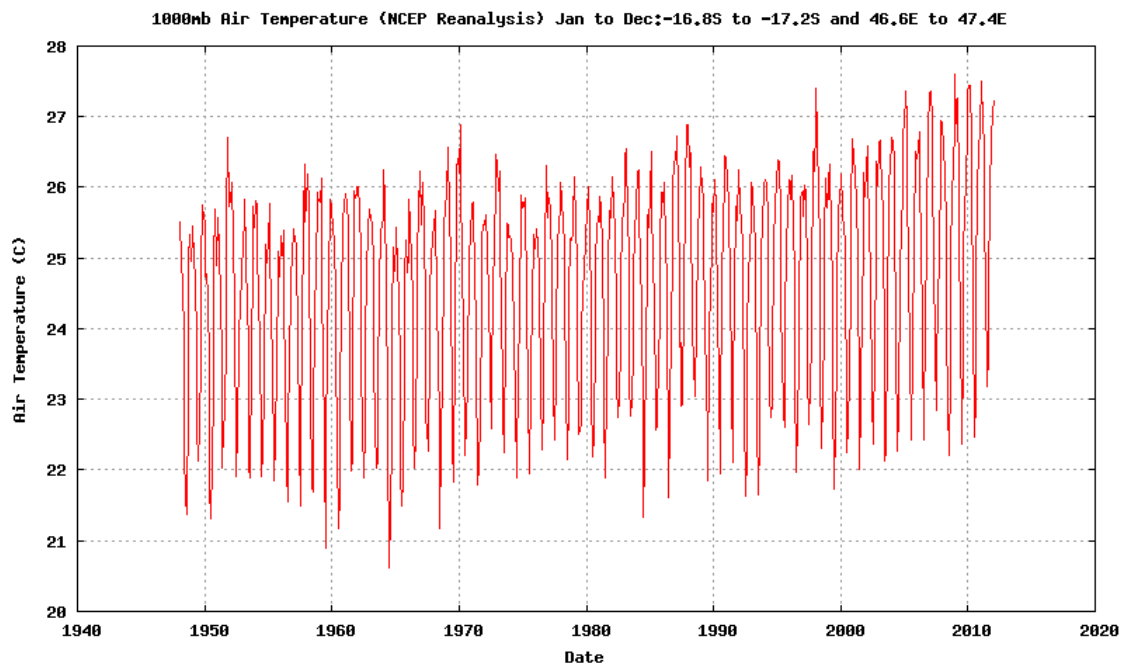


Figure 25: Average monthly temperature ( $^{\circ}\text{C}$ ) in Maevatanana District between 1940 and 2011 (Earth Science Research Division, 2012).

Climate is linked to parasite development, with higher temperatures, higher relative humidity, and higher precipitation levels associated with faster anopheles development and parasitic

extrinsic cycles (Krefis, 2011; Ye, 2007). In Figures 22 and 23, the number of reported RDT+ cases of all consults from the Sentinel Site data for the CSBU is compared with monthly surface precipitation levels and temperatures (°C) for Maevatanana district. Higher numbers of reported RDT+ cases correspond to periods of higher monthly precipitation and temperatures. The Sentinel Site data show an increase in the number of RDT+ cases with each successive rainy season and hot season from 2008 to 2010; however the amount of precipitation as well as relative humidity (not pictured) have remained the same during the study period (2005-10) and since 1950 (Figure 22) (Earth Science Research Division, 2012). On the other hand, average temperature during the study period and between 1950 and 2010 have increased, which may correspond to increases in malaria cases, though there are few studies that model a direct relationship between changes in temperature and malaria incidence for a clinic or community (Figure 23).

## **Discussion**

The triangulation methodology was helpful in cataloging different data and surveillance sources regarding malaria incidence at the CSBU and evaluating different reported trends; however, its inability to prove causality characterizes this methodology as mainly a hypothesis-generating activity. The methodology was helpful in determining the main causes of the decreasing trend in reported malaria cases in the HMIS data. When attempting to compare HMIS and Sentinel Site data from the CSBU, two different case definitions of malaria were used between 2005 and 2010. This led to contrasting trends in malaria incidence as health care management of fever cases changed with the introduction of RDTs. The decreasing trend seen in the HMIS data likely corresponds to an increase in RDT utilization by health workers and subsequently, the elimination suspect malaria cases from the HMIS data.

On the other hand, the triangulation methodology was not conclusive in regards to increases in reported RDT+ cases demonstrated in the Sentinel Site data for the CSBU; therefore, the methodology was used for hypothesis generating. The increase in RDT+ cases in the Sentinel Site data from the CSBU is troubling because it contradicts what was expected after control interventions were implemented in Maevatanana district, and the trend is different from Sentinel Site data from other districts. This trend raised the question of whether the 2007 malaria control interventions were inadequate in Maevatanana district, or if variations in population health behaviors, climate, or parasitemia distribution and resistance impacted malaria incidence.

The DHS and MIS survey data show that reported LLIN ownership and utilization, as well as reported treatment of malaria with anti-malarial treatment increased during the investigation period, though these are self-reported results and are subject to reporting bias. Moreover, EIRs dropped in Western Madagascar, demonstrating little evidence of programmatic gaps or an increase in bites. Furthermore, changes in precipitation and humidity did not occur between 2005 and 2010, though increases in temperature may play a role in increasing malaria incidence, and requires further investigation. On the other hand, increases in patient consults as well as the increase in the number of RDTs used (or suspect cases presenting) at the CSBU between 2008 and 2010 could indicate a true increase in malaria cases or an increase in the number of cases reported, though whether or not the increase is a departure from prior malaria incidence cannot be ascertained without accurate baseline data. In this sense, the effect of control interventions may have been masked by increases in patient consults and the introduction of RDTs, but the fact that the increasing number of patient consults were also RDT+ malaria cases suggests that a true increase was occurring. Findings such as increases in stock-outs of ACT between 2005 and 2010 in Maevatanana district, as well as the confirmation of resistance to

pyrethroids and quinolines in the western region of Madagascar, could correspond to an increase in malaria incidence at the CSBU and warrant further investigation. Unfortunately, the Sentinel Site data are limited because they cannot be compared to data from before the control interventions were implemented in 2007. Also, more than two years of data after malaria interventions will be needed to assess the impact of control interventions in Maevatanana district. It would also be useful to investigate whether trends in ACT stock-outs, climate, health-seeking behavior, resistance, and EIRs are similar in other intervention districts.

Typically, regional NMCP program managers in Madagascar use HMIS data and do not routinely compare this data with other sources. The additional step of triangulating malaria trends from different data sources can be useful when contrasting trends are seen in different data sources for specific locations. However, triangulation methodology was unable to conclusively identify reasons for the trends seen in the Sentinel Site data from the CSBU when specifically focusing on the Betsiboka region, and further research using data sources from other districts in comparative manner may be able to further address this research aim (HIV Triangulation Resource Guide, 2009). In general, triangulation methodologies can be helpful for NCMP program managers when analyzing malaria trends to resolve inconsistencies in the data and generate hypotheses for further investigation as malaria control efforts continue.

## **Recommendations**

Based on the findings in this triangulation study, the following recommendations are proposed for continued research and monitoring of malaria trends at the CSBU in Maevatanana and elsewhere in Madagascar:

- Regional malaria programmers should have access to Sentinel Site data, GMP data, as well as DHS and MIS data, and they should be encouraged to compare and track trends in malaria incidence in these different sources through the development of annual reports.
- Teams of regional, district, and CSB malaria program managers should have regular meetings to discuss trends in malaria incidence and programmatic impact, and they should investigate data reported in data sources that report in their area.
- The NMCP of Madagascar should attempt to standardize monthly reports based on a collaborative determination of case definitions of malaria.
- Regional and central malaria program managers should work together to develop and refine malaria indicators to monitor programmatic impact. Suggested measurements and information for routinely monitoring and evaluating malaria control programs should include the following:
  1. Definition of “malaria case” across data sources, as well as the numerator and denominator
  2. Number of RDT+ cases by age group (<5, 5-15, >15) and by sex
  3. Number of recurrent cases per month (people who present with malaria more than once in one month)
  4. Number of days of RDT and ACT stock-outs
  5. Proportion of children<5 and persons>5 who use LLINs (assessed through yearly surveys)
  6. Seasonal EIRs in high-transmission areas in regions with Sentinel Sites

7. Seasonal measurements of pyrethroid and quinoline resistance in regions with Sentinel Sites
8. The number of patients tested with RDTs and treated with ACTs or other drugs at pharmacies and by community health workers

## Appendix I: Data source matrix for CSBU, Maevatanana Triangulation study

Data Source	Data Collection	Measures of Interest	Malaria Case Definition	Denominator	Years	Population
Sentinel Site, CSBU Maevatanana (and 13 other sites for comparison)	Data sent daily to central level by SMS technology. Reports are received daily >95% of the time, and only 5% require correcting. Weekly feedback is available in IPM newsletter summarizing trends in all Sentinel Sites.	Total outpatient visits, total number of fever cases, number of fever cases tested with RDT, number of RDT+ malaria cases.	RDT+	CSBU patient visits per month	Jan 2008-Dec 2010	Patient population attending the CSBU, Maevatanana (and 13 sites)
DHS Reports (2003-04, 2008-09)		Demographic data, behavioral, prevention and treatment data (possession and use of LLINs and treatment of fevers in children<5)	None	Survey sample of the general population in Western Madagascar	2003-04, 2008-09	General population of Western Madagascar and other regions for comparison
MIS Report (2010-11)		Demographic data, behavioral, prevention and treatment data (possession and use of LLINs and treatment of fevers in children<5)	None	Survey sample from regions in Western Madagascar	2010-11	General population in Madagascar
HMIS CSBU, Maevatanana RMA	Collected monthly by the SSD 2005-10; 100% completion	Number of outpatient visits by age, malaria cases by age	RDT+ and suspect	Patient visitors at 22 CSBs per month	2005-2010	Patient Population CSBs Maevatanana, Betsiboka
HMIS Maevatanana District, RMA	Collected monthly by the SSD 2005-10; 90% completion	Number of days of ACT stock-out	None	22 CSBs per month	2005-2010	22 CSBs in Maevatanana district, Betsiboka
Global Malaria Programme, WHO (GMP) Aggregated data from all districts	Centrally collected by NMCP; >95% complete	Number of outpatient visits, number of RDTs used, and number of RDT+ malaria cases per month	RDT+	Patient population of CSBs in all districts	2008-2010	Patient Population from CSBs in all districts
Annuaire des Statistiques de Secteur Santé de Madagascar (SSS)	Collected yearly, HMIS system; Average of <80% completion rate	Number of outpatient and inpatient visits by age, number of malaria cases by age, number of malaria mortalities by age	RDT+ and suspect cases	Patient population of CSBs and CHDs/CHRRs in all regions	2005-2010	Patient Population of CSBs and CHDs in all regions

**Appendix II: Distribution of *Plasmodia* carrying mutations that correspond to resistance to quinolines (Andriantsoanirina, 2009).**

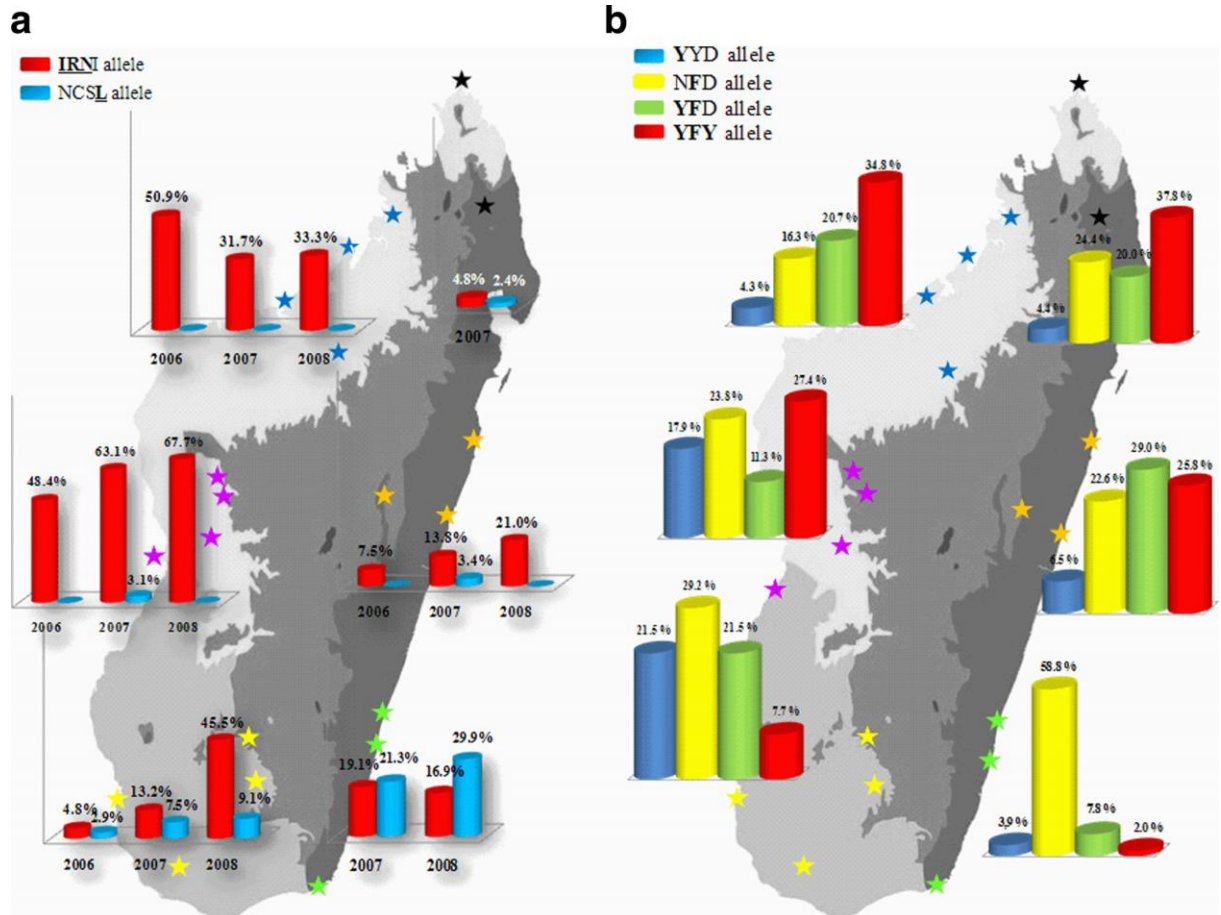


FIG. 2. Spatial-temporal distribution of the most prevalent *P. falciparum* dihydrofolate reductase and multidrug resistance gene 1 haplotypes at the sites involved in the antimalarial drug resistance surveillance network in Madagascar, 2006 to 2008. The 20 sites in six areas are presented as colored stars: black for the northeast (Antsiranana, Andapa), blue for the northwest (Antsohihy, Analalava, Mahajunga, Maevatanana), orange for the central east (Toamasina, Moramanga, Betsizaraina), purple for the central west (Tsiroanomandidy, Ampasimpotsy, Miandrivazo, Morondava), green for the southeast (Tolanaro, Farafangana, Manakara), and yellow for the southwest (Ihosa, Iakora, Toliara, Ejeda). (a) The total numbers of isolates analyzed in 2006, 2007, and 2008 were as follows: 0, 42, and 0, respectively, in the northeast; 53, 60, and 42, respectively, in the northwest; 40, 29, and 81, respectively, in the central east; 95, 130, and 62, respectively, in the central west; 0, 47, and 77, respectively, in the southeast; and 104, 53, and 11, respectively, in the southwest. The **IRNI** allele with triple mutations was particularly frequent in the northwest and the central west of Madagascar, displaying the same prevalence found in the Comoros Islands. Between 2006 and 2007, its prevalence significantly increased in the central west ( $P = 0.04$ ), and between 2007 and 2008 its prevalence significantly increased in the southwest ( $P = 0.03$ ), supporting its spread in the western part of Madagascar. However, the allele with the single 164L mutation was essentially observed in the south of Madagascar: it was first detected in 2006 in the southwest and increased in prevalence between 2007 and 2008 ( $P = 0.04$ ); this allele remains the most frequently observed allele in the southeast and represented approximately one-third of the alleles in 2008. (b) The total numbers of isolates analyzed in 2006 and 2007 were 45 in the northeast, 92 in the northwest, 31 in the central east, 168 in the central west, 51 in the southeast, and 130 in the southwest. No significant differences in the proportions of alleles were found between 2006 and 2007; but the distribution of the three most frequent alleles was heterogeneous: the **NFD** allele was significantly more frequent in the southeast than in the other areas ( $P < 0.05$ ); the **YFY** allele was significantly more frequent in the north ( $>30\%$ ), intermediate in frequency in the central west/east ( $>20\%$ ), and low in frequency in the south ( $<10\%$ ); and the **YYD** allele was the most prevalent in the central or southwest ( $>15\%$ ) compared to its prevalence in the other parts of the country ( $<7\%$ ).

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