Malaria in Nicaragua

A review of control status, trends, and needs

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PATH

This document is part of a larger case study on Nicaragua's health system and diagnostic needs. The health system case study employed two main methodological approaches. The first was a review of official Ministry of Health (MINSA) data and epidemiological reports, as well as publications in peer-reviewed journals. The second was a concurrent series of field visits in 2008 to provide firsthand evidence of diagnostic needs and difficulties. A more detailed account of these methodological approaches can be found in the methodology section of the health system case study.

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About PATH

PATH is an international nonprofit organization that creates sustainable, culturally relevant solutions, enabling communities worldwide to break longstanding cycles of poor health. By collaborating with diverse public- and private-sector partners, PATH helps provide appropriate health technologies and vital strategies that change the way people think and act. PATH's work improves global health and well-being.

Cover photo: PATH/Tala de los Santos

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Glossary

CNDR	Centro Nacional de Diagnóstico y Referencia (National Diagnostic and Reference Center)
Col-vol	Volunteer collaborators, local to municipalities, who diagnose and treat malaria cases and carry out vector eradication activities.
CTAM	Malaria Technical Advisory Committee
Global Fund	The Global Fund to Fight AIDS, Tuberculosis, and Malaria.
GMCS	Global Malaria Control Strategy
MINSA	Ministerio de Salud (Ministry of Health)
NGO	Nongovernmental organization
PAHO	Pan American Health Organization, a regional office of the World Health Organization
PATH	Program for Appropriate Technology in Heath
POCT	Point-of-care test
RBMI	The Roll Back Malaria Initiative
RDT	Rapid diagnostics test
RAAN	Región Autónoma del Atlántico Norte (North Atlantic Autonomous Region)
RAAS	Región Autónoma del Atlántico Sur (South Atlantic Autonomous Region)
SD	Standard diagnostics
SILAIS	Sistemas Locales de Atención Integral de Salud (Local Comprehensive Health Care Systems, which are the Nicaraguan health system's 17 administrative units corresponding to the country's departments and autonomous regions)
WHO	World Health Organization

Introduction

Malaria is endemic to Nicaragua and is tracked by MINSA's National Epidemiological Surveillance Program. MINSA defines suspected malaria as any case of acute fever accompanied by symptoms such as shivering, sweating, headache, muscle ache, or vomiting. To be counted as a confirmed case, the patient's blood sample must test positive for a malaria-causing pathogen (species of the genus Plasmodium).[1]

Nicaragua has made significant advances in the fight against malaria over the last 50 years. Increased government efforts in detection, treatment of suspected cases, and vector control has significantly reduced malaria's prevalence and incidence.[2,3] As a result, WHO considers Nicaragua one of five Latin American countries at the malaria pre-elimination stage.[a]

The Government of Nicaragua decentralized vector control efforts in the early 1990s, giving more responsibility to the Local Comprehensive Health Care Systems (SILAIS). Unfortunately, this coincided with significant reductions in the health ministry budget for tropical diseases.[4] At the same time, the government replaced its long-standing and ambitious concept of malaria eradication with a control program, matching the 1992 Global Malaria Control Strategy (GMCS) adopted internationally in Amsterdam.[5]

The tremendous devastation caused by Hurricane Mitch in 1998 was a turning point in the fight against malaria in Nicaragua. With funds from the international community flowing into Nicaragua, the government seized the opportunity to implement a comprehensive and systematic malaria control program alongside national reconstruction efforts. By 1999, Nicaragua was one of 21 countries in the Americas with active malaria transmission that had aligned its control programs with GMCS, which stressed case management rather than traditional vector control.[6] GMCS is based on four principles: 1) early diagnosis and prompt treatment; 2) implementation of protective and preventive measures, including vector control, for the individual, the family, and the community,; 3) development of the capacity to predict and promptly contain epidemics; and 4) strengthening local capacities in basic and applied research to permit and promote the regular assessment of a country's malaria situation.[2,7]

As part of the world struggle to overcome malaria, Nicaragua has committed to a series of national and international goals, including halving the malaria burden by 2010 and stopping local malaria transmission by 2015. In 2000, Nicaragua adopted the strategy of the Roll Back Malaria Initiative (RBMI), introduced by WHO in 1998 to complement GMCS's activities. It has six main components: 1) structured and integrated interventions at different levels (national/regional/local); 2) integration of resources, including the use of community health workers, to expand coverage of general health services; 3) assuring the availability and quality control of anti-malaria medications; 4) strengthening diagnostic and treatment capabilities; 5) creation of various "resource networks" to help implement malaria control policies; and, 6) intensifying vector control.[6,8]

Nicaragua is committed to achieving by 2015 the Millennium Development Goal of halting the local transmission of malaria.[9] With this goal, and with the parallel aims of tackling both HIV/AIDS and tuberculosis, Nicaragua successfully submitted a proposal to the Global Fund to Fight

a Pre-elimination and elimination of malaria: when the slide positivity rate of all febrile patients with suspected malaria is less than 5% or the incidence is less than 5 per 1,000 people at risk, the country, or district in some cases, could consider transitioning into "pre-elimination." When a country achieves an incidence rate of less than 1 per 1,000 people at risk it enters into the elimination stage. Elimination is officially defined as reducing to zero the incidence of locally acquired malaria infection in a specific geographic area through deliberate efforts (World Malaria Report, 2008).

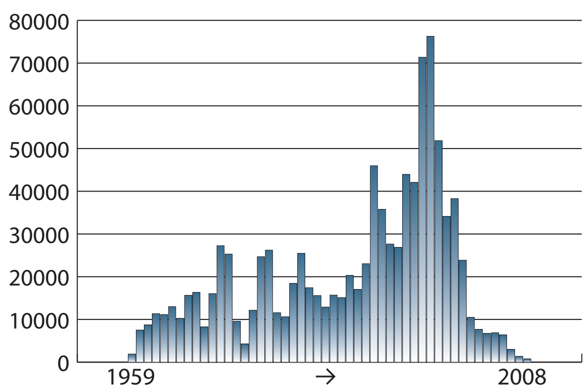
AIDS, Tuberculosis, and Malaria Global Fund under the Millennium Development Goal and RBMI umbrellas.[10] In response, the Global Fund granted Nicaragua US$5 million for malaria control efforts between 2004 and 2009. Together with technical support from the Pan American Health Organization (PAHO), this financial support was a critical factor in allowing the government to strengthen and sustain the momentum of malaria control efforts.

Disease trends, burden, and distribution

Recent trends

The strategies adopted by the Nicaraguan government have resulted in steady progress against malaria as measured by various indicators. The number of malaria cases has declined drastically in the last decade. From a high of over 70,000 in 1996, the number of confirmed cases dropped to 762 in 2008. That corresponds to an incidence rate of only 0.13 per 10,000 inhabitants (Figure 1),[11] a number just above one of the criteria required for designation as pre-elimination stage.

FIGURE 1: **Cases of malaria in Nicaragua, 1959–2008**



Source: Nicaragua Ministry of Health

Historically, the malaria peak season has coincided with the end of the rainy season. As the number of malaria cases nationwide has decreased, however, the seasonality of malaria cases has become less pronounced, especially in 2006 and 2007. This is particularly true in previously hard-hit areas like the North Atlantic Autonomous Region (RAAN) on Nicaragua's Caribbean coast.

The number of *Plasmodium falciparum* cases has also dropped dramatically, from a high of around 5,500 per year in 1979 to 106 in 2007 (Appendix, Figure 1).[4] In 2004, eight out of every ten cases of malaria were caused by *P. vivax*. By 2007, *P. vivax* was responsible for almost all cases (94.5%), with the rest attributed to *P. falciparum*. There were no reported cases of infection by *P. ovale* or *P. malariae*.

Malaria mortality has been reduced to a minimum expression in half a century (Appendix, Figure 2). While more than 700 Nicaraguans died from malaria in 1961, no one has died from the disease since 2006. In addition, the reduction in deaths from malaria has been more noticeable in recent years, with eight deaths registered in 2002, seven in 2003, one in 2004, and six in 2005, for a mortality rate of 0.13 per 100,000 for the latter year.12 No malaria deaths were reported in 2007 and 2008.[4,11] With malaria indicators showing a steady downward trend over the last two decades, Nicaragua's commitment to eliminating local transmission of malaria by 2015 may be feasible, provided that adequate funding continues and the control strategies applied to date are consolidated.

Geographic distribution

The main vector for malaria transmission in Nicaragua is the Anopheles albimanus mosquito, which is widely distributed throughout the country, with the Anopheles pseudopunctipennis mosquito also responsible to a lesser degree.[4] The age group most affected by malaria is children between the ages of 5 and 14 years, followed by 15- to 40-year-olds. Slightly more cases are observed among males (55%) than females.[11]

Prior to the implementation of a national comprehensive control program in 1998, malaria was common in most parts of the country. In 1995, cases of malaria were reported in 13 of Nicaragua's 17 SILAIS. Ninety-five percent of cases were concentrated in 11 SILAIS: Chinandega, León, Managua, Granada, Nueva Segovia, Jinotega, Matagalpa, Chontales, Río San Juan, the RAAN, and the South Atlantic Autonomous Region (RAAS).[2]

According to MINSA, 36 high-risk municipalities represented 93% of the national malaria burden by 2004 and were considered to be strongholds of *P. falciparum*.[11] These municipalities are located primarily in Nicaragua's Caribbean coast region and the country's central region, in the RAAN and RAAS and in the departments of Matagalpa, Chontales, Jinotega, and Nueva Segovia. The higher malaria incidence in those geographical regions also reflects the disease's association with factors related to extreme poverty, low education levels, and social inequality. The populations in these areas are primarily indigenous and have greater difficulties accessing health care services.

By 2007, the only remaining malaria strongholds were in the RAAN, although cases have also been reported in Matagalpa, Chinandega, the RAAS, and Managua. Taken together, these areas account for 90% of all malaria cases (Appendix, Table 1).

Although the RAAN still has the largest number of malaria cases, there has been remarkable progress in disease control in the region. From 2006 to 2007, there was a 56% drop in the number of confirmed cases in this area (from 1,259 to 551), with a constant sample size. Most of the cases have been found in the RAAN municipalities of Siuna, Puerto Cabezas, and Waspam (Appendix, Table 2).

The RAAN has the additional distinction of having the most cases of falciparum malaria in the country, although the ratio of *P. vivax* to *P. falciparum* cases held constant in 2006 and 2007. In 2006, the majority of *falciparum* malaria cases were found in Siuna, Rosita, Puerto Cabezas, and Waspam. With the exception of Waspam, all of these municipalities reported a significant decrease in *falciparum* cases in 2007, especially Rosita, where cases dropped by 92%. Waspam, on the other hand, saw an increase of 45%.

According to the National Malaria Program Coordinator, Julio Rosales,[b] the persistence of malaria in these municipalities can be attributed to factors including:

- Environmental and geographical conditions that create many mosquito breeding sites (e.g., swamps).
- Cultural practices, such as reliance on traditional indigenous medicines, which can lead to delayed or incomplete treatment.
- High rates of illiteracy and poverty that lead to reduced awareness of the importance of treating malaria as well as reduced means for seeking care and following through with the prescribed course of treatment.
- The remoteness of the region and the lack of paved roads, making the area inaccessible and hindering visits from SILAIS health programs.
- Financial constraints, including a lack of human resources, which can result in insufficient vector control activities.

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[b] Personal communication with Julio Rosales, October 19, 2008.

National malaria control strategy

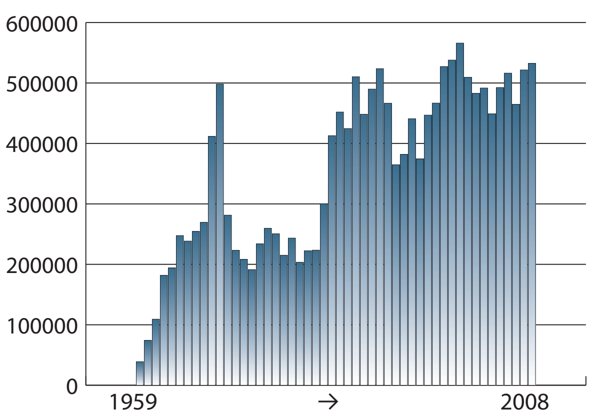
As its primary control strategy, the government relies on a network of health units (hospitals, health centers, and health posts) and a larger network of volunteer collaborators (known as "col-vols") to diagnose and treat malaria cases and carry out vector eradication activities in municipalities where positive malaria cases are found.[1]

Current diagnostic practices

Thick blood smear microscopy

Thick blood smear microscopy tests have been widely performed to monitor malaria transmission in the population, with about half a million blood samples tested annually since 1997 (Figure 2). In 2007, blood samples were collected from 521,464 people—about 9% of the Nicaraguan population. Of total samples, 0.26% tested positive, compared to 0.67% in 2006 and 1.2% in 2005.[11]

FIGURE 2: **Annual malaria testing with thick blood smear microscopy, Nicaragua, 1959–2008**[4]



Source: Nicaragua Ministry of Health

Blood samples are collected by about 7,100 community-based col-vols and by health workers from a network of around 1,200 health units. There is a nationwide network of 197 laboratories that prepares and sends sample slides to local laboratories capable of slide processing and analysis. Each SILAIS conducts quality control testing by sending 10% of negative and 100% of positive specimens to the National Diagnostic and Reference Center (CNDR).[1]

The entire process usually takes about two weeks to complete, although it can take twice as long—up to 30 days—in the country's most remote regions. According to Dr. Francisco Acevedo, Director of Applied Epidemiology at MINSA, the National Malaria Program has recently initiated microscopy technique training programs in more remote regions to improve the network's coverage and reduce delays in receiving diagnostic results. Pilot programs have been set up in the RAAN municipalities of Puerto Cabezas and Siuna, where auxiliary nurses have been trained in basic microscopy techniques. If these prove successful, the National Malaria Program aims to replicate the model in other SILAIS.[c]

The qualifications of microscopy technicians vary depending on whether they work for hospitals, health centers, or field-based programs. Hospital-based technicians usually have a five-year university degree or technical diploma and perform a wide range of diagnostic tests and procedures. Health center laboratory technicians usually have two to three years of laboratory training. Like their hospital counterparts, they also perform other basic laboratory tests in addition to thick smear microscopy. People working for the Malaria Control Program (usually six to eight per SILAIS) have the least training, usually two to three months, and are restricted to performing the thick smear microscopy test for malaria. Despite this, many are highly proficient, as they often have ten or more years of experience working in the same post and program.

[c] Personal communication with Dr. Francisco Acevedo, October 19, 2008.

Rapid diagnostic tests

With financial help from the Global Fund, the National Malaria Control Program began using rapid diagnostic tests (RDTs) in selected regions in 2005.[13,14] Unlike blood smear microscopy, RDTs allow col-vols in the field or in peripheral health posts to conduct diagnostic testing for malaria. This greatly reduces delays in receiving diagnostic results from the laboratory network.

The program started with the OptiMAL-IT® RDT, which differentiates infection with P. falciparum from other types of Plasmodium infection. The program initially purchased only 10,000 units for two reasons. First, budgetary limitations required a smaller purchase order. Second, this was the pilot case for using RDTs in the country, and MINSA felt it needed experience with RDTs before committing to larger volumes. The following year (2006), MINSA procured 15,000 RDTs.

Dr. Acevedo commented that at the beginning of the project top MINSA officials, himself included, were skeptical about col-vols using RDTs in the field. In the RAAN, for instance, health officials were particularly concerned about how well col-vols could perform the test, given their very limited levels of formal education. Some problems were indeed encountered in the early months, most of which were related to difficulties in interpreting test results. According to Dr. Acevedo, these problems were addressed through more training sessions and standardization of training methods. As the col-vols gained more experience using the tests, their performance improved. He added that all positive RDT results from col-vols and health units are reported to the SILAIS and to the MINSA central level (MINSA Central); however, quality control is not systematically conducted for RDTs. Furthermore, MINSA does not currently have a systematic way of tracking the number of tests performed in each region. Indeed, during the first months of their use, lack of coordination between MINSA Central and the local SILAIS resulted in an inconsistent supply of RDTs, and communities ran out of supplies.

During the introduction period, the RDTs were performed in conjunction with thick smear blood microscopy. In the first year of use, MINSA conducted a study comparing the OptiMAL-IT® and thick smear test results for 442 febrile patients in six SILAIS (Chontales, Jinotega, RAAN, RAAS, Matagalpa, and Nueva Segovia). The study revealed good concordance between the two tests for the detection of *P. falciparum*. The RDT detected 17 cases of malaria; blood smear microscopy detected 16 cases. One microscopy sample that corresponded to a positive RDT was discarded because of poor sample quality. These results dispelled many of MINSA's earlier concerns, and paved the way for increasing the number of RDTs used in the country.

In 2007, the National Malaria Program encountered difficulties in acquiring a reliable supply of the OptiMAL-IT® test. As an alternative, program leaders subsequently selected the Standard Diagnostics (SD) rapid immunochromatographic strip test (SD Malaria Ag point-of-care test). They continue to procure this type of RDT. The SD Malaria Ag has several advantages. It is easier and more convenient to procure. It costs less (US$1.90) and is both a P. falciparum and pan-malaria test.15 Because Nicaragua does not have P. ovale or P. malariae, the National Malaria Program assumes that a test result that is positive for pan-malaria and negative for P. falciparum is indicative of P. vivax infection.

Although more RDTs were procured in 2007, the 20,000 tests were equivalent to only 4% of the approximately 500,000 blood smear tests conducted annually. This is due to the national program's strategy, based on risk stratification, of making RDTs available only in select SILAIS with the highest incidence of malaria, namely the RAAN and RAAS, Matagalpa, Jinotega, and Nueva Segovia. Within these SILAIS, the use of RDTs is restricted to areas that are considered inaccessible and remote, with inadequate access to blood smear microscopy.

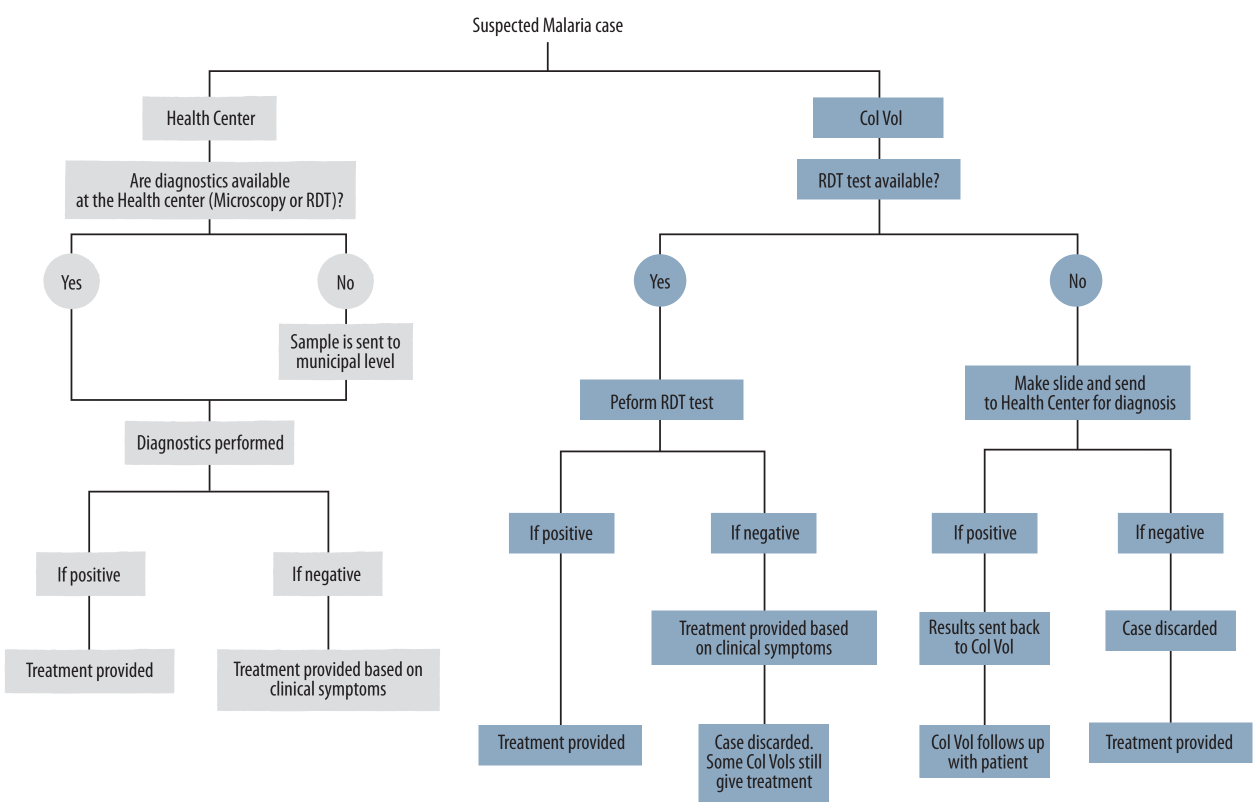
Overall, the National Malaria Program considers RDTs to be a very useful and important component of its malaria elimination strategy. The RDTs have good field performance and their use is well accepted in communities where they are employed (98% in studies conducted).15 Col-vols feel motivated and empowered through conducting the test. Patients are more likely to comply with treatment following positive results and non-treatment when results are negative. The National Malaria program considers RDTs very important in special field-based initiatives, such as medical missions to find cases of malaria, especially in isolated communities.13,14,15

Treatment

When febrile patients with suspected malaria turn up at a hospital or health center, treatment is supposed to be initiated only following a positive malaria diagnostic test result. This is usually the case in areas of low malaria prevalence, such as the Pacific coast. In higher prevalence areas, however, suspected cases are often treated with a short-course regimen, without waiting for a positive test result. This is particularly true in areas staffed by col-vols, not all of whom have access to RDTs. Patients who live in remote areas or who have limited access to health services often wait long periods before receiving microscopy results from the laboratory network. As a result, treatment is frequently initiated based on the clinical symptoms of malaria. Although the col-vol will still prepare the blood smear slide, this is done primarily for surveillance purposes. Should a positive result return weeks later, the col-vol provides the patient with the remaining medication to complete a 14-day treatment regimen. Figure 3 summarizes the interaction between a febrile patient and the health system for the diagnosis and treatment of suspected malaria.

In the absence of rapid tests—a common situation—col-vols give short-course malaria medication to all fever cases in their communities, as stipulated in the MINSA guidelines. In a context of pre-elimination, with the malaria incidence rate already near zero, a large number of people may be unnecessarily receiving treatment. Furthermore, in some high prevalence regions treatment is sometimes initiated even when the diagnostic test is negative for malaria. Although

FIGURE 3: **Flow chart of the treatment of febrile patients in the Nicaraguan health system**



no chloroquine-resistant strains of P. falciparum have been found in Nicaragua, the pervasiveness of presumptive malaria treatment presents a risk of their emergence.

The different treatment regimens in Nicaragua have included (Figure 4):

- Radical treatment for 14 days, which is the PAHO treatment protocol.16
- Radical treatment for a shortened course of 7 days (this has been the preferred approach, using the same total amount of medication as the 14-day protocol).
- Short-course treatment for 3 or 5 days (total dose also reduced).
- 3-day multiple-dose treatment, known locally as "single dose" (total dose also reduced).

The 14-day radical malaria treatment (chloroquine 25 mg/kg/day x 3 days and primaquine 0.25 mg/kg/day x 14 days) has been recommended by the World Health Organization (WHO) as a standard treatment that guarantees the elimination of the parasites (hypnozoites) that establish themselves in the liver and cause relapses. While this treatment is effective, it is also very difficult to supervise. Furthermore, its long duration, side effects, and the perception of being cured when the fever disappears during the first days of treatment significantly influence the patient's decision to abandon the treatment early. This makes ensuring the patient's compliance a real challenge.

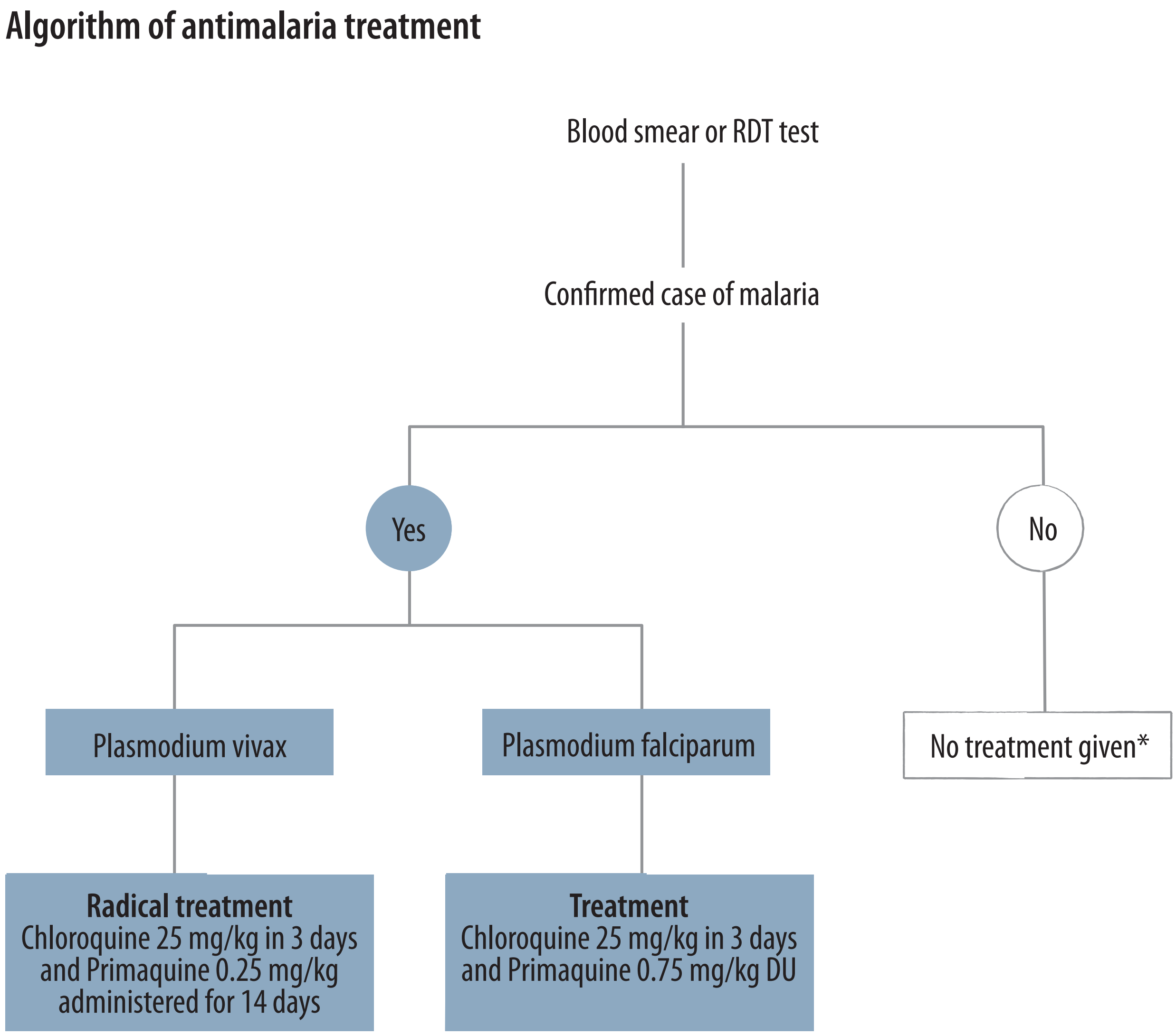
The negative aspects of the 14-day radical treatment triggered research to establish a more pragmatic but equally efficacious protocol, particularly in South America. In several published studies, researchers have investigated the issue of establishing efficacy for a shorter treatment course for malaria patients. Several medication courses have been tested, including 5-day and 7-day treatments. Unfortunately, most of these studies have had weak methodologies, and there is a need to further evaluate efficacy and adherence, as well as to rule out the potential for parasite resistance.

In Nicaragua, the 7-day radical treatment was adopted and widely implemented by MINSA, particularly to respond to the challenge created by remote and inaccessible populations where it is very difficult to administer and supervise a treatment protocol that lasts for 14 consecutive days. This shortened malaria treatment maintains the same total medication as the standard 14-day protocol. Chloroquine is given for the same 3 days as the WHO 14-day radical treatment, but the daily dose of primaquine is doubled and applied for just one week, thus administering the same total amount in half the time (chloroquine 25 mg/kg/day x 3 days and primaquine 0.5 mg/kg/day x 7 days) (Table 1). A local MINSA study conducted in Chinandega revealed 0% therapeutic failure with this variation, which has the advantage of reducing the supervision of treatment to just one week. In 2002, another MINSA study, this time in Rosita, found the negativization of microscopy

TABLE 1. **The 7-day radical malaria treatment**

Age group	Day and dosage		
	Day 1 Chloroquine, 250 mg tablet	Days 2 and 3 Chloroquine, 250 mg tablet	Days 1 to 7 Primaquine, tablet dose as indicated
< 6 months	¼	¼	
7–11 months	½	½	1 (5 mg)
1–2 years	1	½	2 (5 mg)
3–6 years	1	1	3 (5 mg)
7–11 years	2	1½	4 (5 mg)
12–14 years	3	2	2 (15 mg)
15–59 years	4	3	2 (15 mg)
> 60 years	3	2	2 (15 mg)

Figure 4: **Summary of the treatment algorithm for *P. vivax* and *P. falciparum* cases in Nicaragua**



test results to be 78% after 3 days of treatment and 100% after 6 days. Symptoms went into remission in 100% of cases after 3 days of treatment, without any relapses during 28 days of monitoring.

Communities selected by the National Malaria Program recently adopted the "single dose" 3-day multiple-dose treatment (chloroquine and primaquine). The treatment regimen is based on the concept that, in malaria-affected communities, certain people living in certain houses with particular characteristics repeat and maintain malaria transmission. Year after year, these people are the main source of malaria in the community. This modality, therefore, prioritizes surveillance of the treatment, epidemiological surveillance, and periodic visits. It also ensures 3-day treatment administered every 3 months and for 6 treatment cycles; i.e., for 18 months of follow-up. This treatment regimen has proved useful in both Nicaragua and Mexico and was adopted to contribute to the rapid elimination of malaria in communities of Chinandega and Nueva Segovia where malaria transmission persisted.

WHO considers Nicaragua's malaria control program well established.[3] There is extensive community volunteer involvement, which helps increase both vector control activities and the population coverage of malaria detection and treatment. In 2007, MINSA identified 521,464 suspected cases of malaria. Of these, about 93% (483,363) are considered "passive discoveries" in which the patient sought treatment for fever at a health unit (326,123) or from a community health volunteer (157,240). The remaining 7% (38,101) of the cases were identified through active searches in which health workers visited a community to check for febrile illnesses, mainly for epidemiological research or control.[11]

Although the ratio of suspected cases identified through the health units to those identified through col-vols is almost 2:1 (326,123 to 157,240), proportionately more confirmed cases come from the col-vols. About 0.24% of patients seeking care from health units were confirmed positive, compared to 0.34% of those seeking care from col-vols. Overall 1,356 confirmed cases of malaria were recorded nationwide for 2007, representing 0.26% of all suspected cases. Passive discovery accounted for most of the positive cases (97%), with 781 detected by health units and 530 by col-vols, while 45 cases were identified through active searches.[11]

Vector control activities

The National Malaria Control Program promotes comprehensive vector control activities, stressing risk stratification and community education and participation. When a confirmed positive malaria case is identified, the following steps are taken:1

- The patient, other members of the household, and relatives in the community are given the 7-day course of anti-malaria medication (the radical treatment).
- A search for other febrile cases in the immediate vicinity is conducted, along with RDTs, if available. If the results are positive, treatment is provided accordingly.
- The patient's house and nearby houses are sprayed with insecticide.
- The community participates in searching for Anopheles mosquito breeding sites, which are destroyed using larvicides.
- Family members and the community receive updated information on how to maintain an environment that reduces the risk of re-infestation of Anopheles mosquitoes.
- Demographic data and the results of the malaria tests (for *P. falciparum* or *P. vivax)* are collected for entry into the national tracking system.
- The geographic coordinates are collected for all positive cases and breeding sites using geographic positioning systems, when available.
- If not already present in the community, the col-vol network is reactivated or installed.

Recent activities

Several reports highlight a number of vector control actions in recent years, including treatment of mosquito breeding sites, house fumigation, and distribution of permetrin-treated mosquito nets.[2,11,13,14] Breeding sites are typically treated with the larvicides Bacillus sphaericus or Bacillus thuringiensis israelensis. In 2007, 10,573 breeding sites were treated in the country, covering a surface area of 2,808,777 square meters. Backpack spray dispensers are most commonly used for small breeding sites, while a helicopter is sometimes employed for spraying the coast of Lake Managua.

For indoor spraying, etofenprox is typically used with an application schedule of every six months. In 2007, 166 communities rated as high risk for malaria were treated with etofenprox, which is equivalent to 98% coverage of priority areas. Of the almost 13,000 houses sprayed, 48% were in the RAAN, 16% in the RAAS, 16% in Chinandega, 8% in Jinotega, 8% in Nueva Segovia, 2% in Estelí, and 2% in Río San Juan.

Mosquito nets pretreated with permetrin have been distributed in 525 communities over the past two years, including communities in Jinotega, Matagalpa, the RAAN, the RAAS, Nueva Segovia, Chinandega, and Chontales.

Education and social participation

The network of col-vols has played a critical role in educating and preparing the population for malaria control over the years. These volunteers distribute educational materials, such as posters and brochures, and lead meetings during which people discuss the importance of getting tested for malaria, complying with the full course of treatment, and practicing prevention methods. MINSA also organizes annual "anti-epidemic days" to highlight these efforts and to support the col-vols in their house-to-house visits.

A 2007 study of col-vols by MINSA found that they often had extensive experience with this volunteer work (an average of 10 years). They also had a low level of formal education (65% had only primary education) and tended to be middle-aged (average age of 40 years). In addition, 41% were housewives and another 41% were farmers. The study also documented a high degree of organization and active participation in community health activities, such as actions aimed at eliminating mosquito breeding grounds.

MINSA has formed health commissions in 22 high-priority municipalities to coordinate an integrated and comprehensive approach to local health problems. Commission members include representatives from health authorities, nongovernmental organizations (NGOs), and local small private businesses, as well as educators and col-vols. All commission members commit themselves to promoting community participation in addressing health concerns through planning and implementing vector control actions. Both col-vols and commission members are unpaid. MINSA also has created a national-level Malaria Technical Advisory Committee (CTAM) for the Malaria Control Program. MINSA permanently presides over CTAM, which includes representatives from government and NGOs.

Examples of regional control strategies

According to Dr. Juan José Amador, former MINSA director of epidemiology, Chinandega, Nueva Segovia, and the RAAN are good examples of Nicaragua's malaria control strategy in small communities. The field researchers for this study found that the strategy has been employed in SILAIS with high incidences of malaria and has the following features:

- The first step is to identify areas that are high risk for malaria transmission. A high-risk area is defined as a community with a confirmed positive case of malaria. RDTs are available for use in Chinandega to help with malaria diagnosis.
- Epidemiological surveillance is then carried out every 3 months for the following 18-month period through local health posts and col-vols.
- All other inhabitants are given either the 3-day treatment every 3 months within the same 18-month time frame or the 7-day radical treatment.
- All communities are geo-referenced to monitor sites of known Anopheles mosquito reproduction, and to compare the monitored sites with sites where malaria transmission has been previously found.
- Mosquito nets treated with 1% permetrin are distributed in the identified high-risk areas. Vector control activities such as indoor spraying and the application of larvicide to potential mosquito breeding sites are also initiated.

Chinandega

Chinandega is a flood-prone area with a historically high incidence of malaria. As a result of these multifaceted approaches, the number of malaria cases in Chinandega continues to drop. In 2006, 0.46% of samples tested were confirmed as positive (300 out of 65,118). By 2007, this figure had dropped by more than half, to 0.21% (175 confirmed positive out of 83,473) (Appendix, Table 3). We were unable to determine the number of RDTs used in this region, however, or the number of RDTs with positive results.

In Chinandega, people working on large sugar plantations, such as San Antonio and Monte Rosa, are monitored closely for malaria. These plantations historically have had high incidences of malaria due to the internal movement of migrant workers from other regions of Nicaragua and the environmental conditions in the plantations. The latter include artificial lakes and cramped living quarters for the thousands of workers, both of which favor mosquito infestation and increase the risk of malaria transmission.

Community education and participation is a key feature of the malaria control program in Chinandega. This involves school workshops and environmental sanitation campaigns, as well as competitions for the cleanest houses and yards in an effort to reduce potential breeding areas for the Anopheles vector.

Nueva Segovia

During the 1980s, Nueva Segovia was a war zone in which the Contras operated, and malaria was out of control. But the malaria situation there has improved dramatically, with only two cases confirmed in 2007. In the first half of 2008, there was only one confirmed case out of almost 11,000 samples.[2]

Nueva Segovia has a strong col-vol network, which forms the basis for surveillance, detection, and treatment in the area. Col-vols perform follow-up work and notify the community health posts. SILAIS health personnel facilitate coordination between the network of col-vols and MINSA vector technicians regarding spraying houses and communities, availability of medication, and reporting surveillance and education activities.

As in the rest of the country, malaria diagnosis in Nueva Segovia is still mainly based on microscopy, although limited amounts of RDTs are also available. From January to July 2008, only 250 RDTs were made available in the region. Most (70%) were sent to health posts and the rest to col-vols. In field visits to the communities of Teotecacinte, Chusli, Tauquil, El Corozo, and Namasli, we confirmed that col-vols were using RDTs. The SD Malaria Ag POCT is currently in use, but the lots they had access to had an expiration date of May 2007.

In discussions with col-vols, we found that RDTs have a high level of acceptability. Col vols were particularly happy with the SD Malaria Ag POCT, as it is easier to use than the OptiMAL-IT® test they had used the previous year. Unfortunately, RDT distribution has been irregular and the col-vols said they were unsure whether they would continue to have access to the tests.

The RAAN

The RAAN has historically had a high incidence of malaria, although incidence has been dropping in recent years. In 2007, the RAAN col-vol network reported 36,615 suspected cases and 551 confirmed cases, which is down from the 1,259 positive cases in 2006. Nonetheless, certain factors make malaria control in the RAAN more challenging than in other SILAIS.

The RAAN's geography and economy favor malaria. Almost the entire region is in a state of extreme poverty, while the limited number of roads makes certain communities very isolated. There is inadequate housing, and local conditions create a favorable environment for mosquito breeding sites. In addition, reliance on indigenous practices means that some patients may not seek malaria tests and treatment in a timely manner. The region's health budget does not cover local needs, which translates into a lack of human resources and a weakened local health infrastructure, including a laboratory network with a limited capacity for blood smear microscopy. Finally, the region's remoteness and inaccessibility make it difficult and expensive to carry out malaria control activities.

Financing and partnerships

The sustainability of malaria control in Nicaragua depends heavily on financial capacity and the transfer of financial resources from the central level to the SILAIS level. MINSA assigns funds for anti-malarial control activities, providing resources for each SILAIS and salaries for about 1,000 field workers across the country. In addition, $750,000 is allocated each year for purchasing insecticides. Another $2 million are available for control of transmissible diseases, of which approximately 30% are allocated to fight malaria.

Two international agencies—PAHO and the Global Fund—have also made big contributions to Nicaragua's Malaria Control Program. PAHO has provided both technical and financial support, with financial support currently amounting to about $100,000 per year. The Global Fund has played an especially important role and has provided extensive financial support, amounting to $1 million or more annually. RDTs obtained through the Global Fund are used mainly in communities with the greatest incidence of malaria.

The first and second phases of the Global Fund project in Nicaragua were executed between 2004 and 2009. A new project that will run through 2012 will provide funds and implement activities for vector and parasite control. This includes indoor residual spraying, ultra-low volume fumigation for outbreak controls, anti-larval measures, selective medications, general medication, and col-vol network activities. The Global Fund also finances clinical and administrative supplies, entomological materials, insecticides and larvicides, microscopes for blood smear tests, and RDTs. Dr. Josefina Bonilla, director of the NicaSalud Network that administrates Global Fund financing, stated that while the next phase will continue to focus on diagnosis through blood smear microscopy, the Global Fund malaria control project also will provide access to RDTs in remote locations.

Unmet clinical needs

The following information comes mainly from individual interviews and group discussions described in the methodology section. It is limited to discussions applicable to malaria and is presented by health care level.

Primary health care level

Rapid tests

With Nicaragua in the malaria pre-elimination stage, the identification of new cases is of paramount importance. But despite the existence of an extensive network of volunteers and health personnel reporting all suspected cases of malaria, confirmatory laboratory results can take days or weeks to be returned to patients. People living in remote villages have to wait for up to a month to receive their thick blood smear results. To compensate for this long wait, treatment is given for all fever cases. This increases costs, may cause unnecessary side effects, and could even generate drug resistance.

Distributing rapid tests for malaria would provide doctors and nurses in health posts and community volunteers with diagnostic tools, enabling them to prescribe appropriate treatment based on quicker results. Rapid tests will strengthen field work, responsiveness, follow-up, and treatment.

"This health center receives RDTs for the col-vols, but the malaria program coordinator holds some back for when there is a shortage of lab staff. Sometimes the doctor will request an RDT at the hospital if he/she wants a quick result. This means the lab staff have to go look for the malaria coordinator and request an RDT from him. The lab staff prefer to do blood smears rather than RDTs because they can do multiple tests at the same time and can do other things while they prepare the slides." Malaria program technician, Kukra Hill Health Center.

Multiple diagnoses (multiplex) and the elimination of malaria

Recently, Nicaragua has seen a change in the epidemiological pattern. Malaria has been significantly reduced as one of the main causes of fever . At the same time, no cause has been identified for about half a million febrile cases every year. WHO has warned of the need to pay attention to both neglected diseases and to the presence of new pathogens that have not been properly investigated and could emerge as global diseases.

Nurses and doctors based in the country's health posts and health centers have expressed an urgent need for RDTs to identify the pathogens responsible for diseases among both children and adults. Health care personnel are particularly overwhelmed by fever cases during the Nicaraguan rainy season (May through November), which is usually accompanied by an increase in the number of infectious diseases, including dengue, leptospirosis, and respiratory infections. Under these circumstances, a multiplex rapid test would drastically improve epidemiological surveillance and help increase the quality of care.

"Around 10 patients with febrile symptoms are seen every day. During the rainy season this can increase to 40-50 cases, and we confirm the cause in 50% of them (acute respiratory infection, malaria, dengue, leptospirosis or urinary infection) but not in the other 50%." Female nurse, Kukra Hill Health Center.

"Last month, they had 22 cases of fever. Four were suspected dengue cases, but none tested positive. Ten to twelve were suspected malaria cases, but none tested positive." Female doctor, Pearl Lagoon Health Center.

Central administrative level and the CNDR

Improving epidemiological surveillance

Program directors and technical staff at the central administrative level agree on the need to study cases involving fever in order to identify pathogens that generate high morbidity and significantly contribute to infant and overall mortality. There is also an ongoing need to monitor emerging pathogens of epidemiological importance.

"We should increase the differential diagnosis of febrile diseases, such as western encephalitis virus, influenza, infectious mononucleosis, parvovirus B19, hantavirus, West Nile virus, leptospirosis, Chagas disease, brucellosis, and respiratory infections." CNDR Virology Department, MINSA Central, Managua.

User requirements

Sensitivity and specificity

A multiplex test should have high sensitivity and specificity for several diseases at a time. A new test would require review of protocols, algorithms, and quality control. It should also be accompanied by other interventions, such as providing staff with appropriate training, adjusting and implementing central-level quality control, strengthening the information system, and guaranteeing treatment for the diseases to be tested.

Affordability and Sustainability

Because Nicaragua's economy is dependent on international aid, sustainability is always an important concern. Cost is a very significant feature when developing a new test. Patient time, efforts, and costs could all be reduced through a new multiplex test. Such a test might make possible diagnoses of diseases caused by different pathogens, thus avoiding the need for separate test cycles and results. A thorough cost analysis could support this hypothesis.

Strengthening the health information system

If a rapid test and multiplex test were routinely available, doctors and nurses could quickly diagnose and distinguish among a variety of diseases. MINSA maintains at least three different information systems that are independent of each other, making it difficult to track cases. Program directors and technical staff agree on the need to strengthen the health information system, which would help make the pre-elimination and elimination of malaria increasingly feasible.

Barriers and facilitating factors for new diagnostic tests

Barriers

Information system

Information flow is slow when conducting quality control tests and returning results. In addition to the lack of infrastructure, many processes are unnecessarily long. The information system is also "fragmented" in the laboratory area, with weak monitoring and supervision, and there is no flow of information to the laboratories from the thousands of col-vols in the community-based health network.

Irregular medical supplies

Stock-outs are very common at health facilities. The constant lack of reagents is a problem for health centers with laboratories and represents an important barrier to point-of-care tests. Reagents and supplies can be requested monthly, but several months can go by without a response.

Budget

Nicaragua is the second poorest country in Latin America and the Caribbean, with the lowest per capita health investment. Public investment in health is very low, and the demand for health care is growing. Sustainability is of paramount importance for any initiative aiming to create new diagnostic tools. Given that donations have been decreasing, MINSA has been reducing the budget for purchasing medical supplies, and much of the laboratory funding comes through specific Health Ministry programs.

Facilitating factors

The network of community health volunteers

At the primary health care level, the experience of community health volunteers and col-vols conducting rapid tests represents a major advantage in the new phase of malaria control. New rapid test and multiplex strategies should therefore seek to build on this initial experience.

Funding opportunities

Another facilitating element has been the technical and financial support received for several years from cooperation agencies such as PAHO and the Global Fund. Global Fund support will continue for the next six years under the Axis of Prevention and Control of Malaria in Mesoamerica project.

Monitoring by the CNDR

The CNDR has over 20 years of experience in supporting and supervising the country's laboratory network. It also supports day-to-day epidemiological surveillance and rapid responses to outbreaks. It has over 100 differentiated diagnostics.

Conclusions and recommendations

In September 2000, Nicaragua took on the Millennium Development Goal of reducing the incidence of malaria by 2015. During the last decade, national epidemiological surveillance has revealed a continuous reduction in the indicators related to illness and death from malaria, to such a degree that the country is moving toward possible elimination of local transmission of malaria. In this new epidemiological context, it is important to strengthen case detection capabilities and treatment in remote communities, where health personnel are scarce and col-vols are closely involved in malaria treatment and follow-up.

One of the lessons learned in Nicaragua is that long-term impact can be achieved only when a strategy ensures the participation of community organizations and multiple institutions. It must also combine actions related to health care, prevention, education, and the improvement of environmental health and living conditions. Adequate financing is essential to ensure that activities continue to be intensively conducted at the community level and sustained over the coming years. Such activities include keeping people informed about and involved in the identification of malaria cases, distributing treated mosquito nets and spraying houses, and planning and conducting other vector control activities. Ensuring the success of a strategy to eliminate malaria, therefore, requires participation from institutions outside the health sector.

In the last decade incidences of malaria have been dramatically reduced in Nicaragua, but malaria remains a problem in specific, remote zones. Favorable malaria indicators over the past year suggest that to sustain the downward trend in malaria-related morbidity and mortality, timely diagnosis and treatment must be ensured even in these remote places. Persistent cases of suspected malaria with no diagnostic confirmation will require further investigation, potentially including the use of improved methods to quickly determine the cause of febrile illness in a country with a shifting epidemiological profile. Sufficient funding is needed to effectively implement RDT and multiplex testing throughout the country so that local transmission can finally be ended.

Investment in strengthening epidemiological surveillance by means of rapid testing is important to control malaria and reduce chances of a reversal in the current malaria trend. Given the sustained reduction in malaria cases, decision-makers could mistakenly shift attention and funding from this disease. Malaria, however, could potentially return with parasite resistance, generating a greater number of lethal cases. Several other threats also persist. Extensive internal and external migration could make it hard to control disease transmission. Natural disasters and emergencies might create environmental conditions that favor continued malaria transmission. Easy access to anti-malaria medication can also lead to incomplete and inappropriate treatment, as well as parasite resistance. Further success will require additional work to strengthen the diagnostic network. RDTs, including multiplex tests, will play an important role in areas with no access to the microscopy network. This network provides an important opportunity to implement immediate control measures, such as epidemic focus controls and active searches for malaria cases.

Nicaragua's advantages and opportunities in the area of malaria control include high levels of community participation through the network of col-vols, technical and financial assistance from PAHO and the Global Fund, and strategic alliances formed both nationally and internationally. Meanwhile, collaboration by NGOs, such as PATH, can provide much-needed support for efforts to eliminate malaria from the country. a review of the treatment algorithm to prevent subsequent drug resistance could also influence future success, and lead to appropriate treatment for the vast majority of suspected malaria cases in a country where the incidence has dropped so significantly.

Recommendations for the Malaria Control Program in Nicaragua

The results of this case study were presented during a meeting of experts held in December 2008. MINSA Malaria Program officials, other national malaria experts, and the local PATH research team participated (Appendix, Table 4). These recommendations could greatly contribute to fundraising efforts if presented as part of a country proposal linked to the elimination of malaria.

1. Increase research into febrile disease cases when the diagnostic test is negative for malaria. Only one in every 500 febrile cases in which malaria is suspected is actually confirmed, so the etiology of most remains undetermined. Experts agreed on the need to establish differential diagnostics for febrile patients and that there are still enormous diagnostic gaps.

2. In relation to the national malaria guidelines:

   2.1) Review the operational definition of malaria cases to strengthen clinical practice and epidemiological surveillance within the pre-elimination stage. The determination of malaria cases and the adaptation of the diagnostic algorithm and treatment could provide the basis for a proposed extension of the current project or a new proposal for the Global Fund. This redefinition of malaria cases would involve a number of changes to the organization of services, which would necessarily imply added costs.

   2.2) Establish precise guidelines on whether to medicate febrile patients who have negative microscopy results, considering the kind of test used, confidence in its quality, and the fact that Nicaragua is in a pre-eradication stage. No such guidelines currently exist.

   2.3) Differentiate the treatment guidelines for suspected cases in areas with different levels of endemicity. In 2008, MINSA control measure eliminated malaria cases from the country's Pacific zone and drastically reduced those in most communities of central Nicaragua; however, transmission of malaria persists in the Caribbean coast region.

   2.4) Define guidelines (protocols) for implementing RDTs and microscopy and strengthening record keeping and treatment. Positive results from microscopic diagnosis are now less frequent than in previous years. In 2008, fewer than 1,000 cases were recorded. Fewer positive results reduces the practical experience and diagnostic ability of the new human resources using thick blood smear, which could affect sensitivity and specificity and increase the number of false positive cases. Rapid tests offer an increasingly advantageous alternative to microscopy, due in part to the ease with which they can be taken to at-risk communities that have not had access to laboratory services. The CTAM should review these new situations.

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Appendix

Figure A-1: ***P. falciparum* cases, Nicaragua, 1956–2008.**

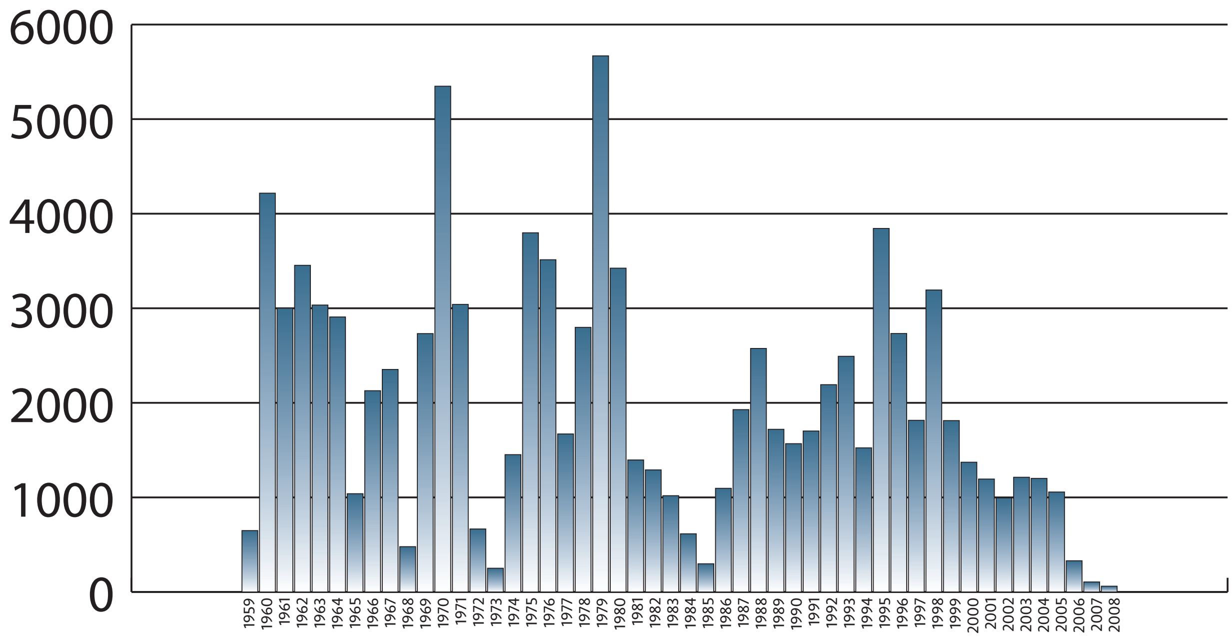

Figure A-2: **Deaths attributable to malaria, Nicaragua,1961–2008**

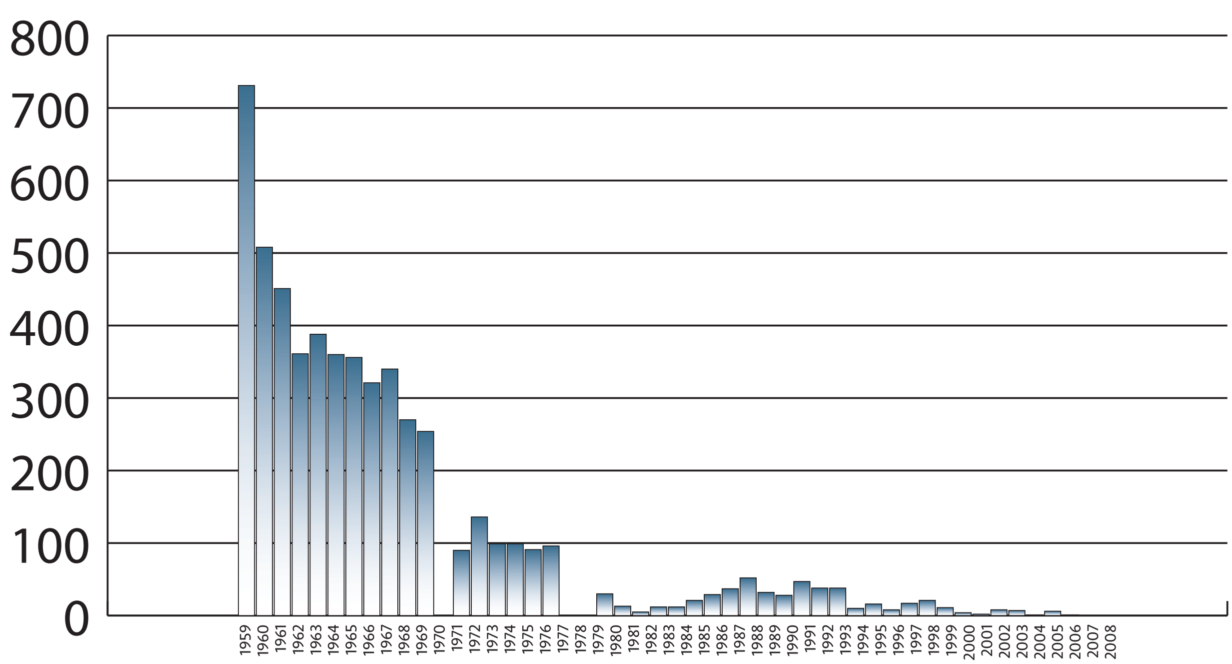

TABLE A-1: Cases of malaria in Nicaragua by SILAIS. Comparison, 2007 to 2008

SILAIS	All malaria						Falciparum only						
	Cases per year			Percentage of all malaria cases			Cases per year			Percentage of all malaria cases			
	2006	2007	2008	2006	2007	2008	2006	2007	2008	2006	2007	2008	2008 incidence rate
Boaco	44	13	4	1.41	0.96	M	8	1	1	2.42	0.94	1.63934	0.02
Carazo	0	1	2	0	0.07	M	0	0	0	0	0	0	0.01
Chinandega	300	175	160	9.63	12.91	21.1	1	0	0	0	0	0	0.39
Chontales	58	12	6	1.86	0.88	0.45	1	0	1	0.30	0	1.63934	0.02
Esteli	11	3	2	0.35	0.22	M	0	0	1	0	0	1.63934	0.01
Granada	0	0	3	0	0	0.45	0	0	0	0	0	0	0.02
Jinotega	129	23	3	4.14	1.70	1.83	1	0	0	0	0	0	0.01
León	44	75	35	1.41	5.53	5.04	0	0	0	0	0	0	0.09
Madriz	0	0	0	0	0	M	0	0	0	0	0	0	0
Managua	119	142	116	3.82	10.47	20.1	5	3	2	1.52	3	3.27869	0.08
Masaya	0	2	3	0	0	M	0	0	0	0	0	0	0.02
Matagalpa	481	187	105	15.45	13.79	18.3	15	6	2	4.55	5.66	3.27869	0.16
Nova Segovia	16	2	3	0.51	0	0.45	1	0	0	0	0	0	0.01
RAAN	1259	551	283	40.43	40.63	24.7	245	89	52	74.24	83.96	85.2459	0.98
RAAS	621	161	31	19.94	11.87	6.8	53	7	2	16.06	6.60	3.27869	0.22
Rio San Juan	16	8	3	0.51	0.59	M	0	0	0	0	0	0	0.03
Rivas	16	1	3	0.51	0	0.45	0		0	0	0	0	0.02
Total	3114	1356	762	100	100	100	330		61	100	100	100	0.13

*IPA: Incidencia Parasitaria Anual (Annual Incidence Rate x 1000)

TABLE A-2: Number of malaria tests and positive results for six RAAN municipalities, 2006 and 2007

	Malaria tests		Positive results		P. vivax		P. falciparum	
	2006	2007	2006	2007	2006	2007	2006	2007
Puerto Cabezas	7,492	7,236	256	127	215	110	41	17
Waspan	4,027	3,303	266	139	233	91	33	48
Rosita	6,146	5,740	238	68	190	64	48	4
Siuna	12,697	14,163	350	169	248	152	102	17
Bonanza	5,432	5,347	101	37	89	34	12	3
Prinzapolka	1,005	826	48	11	39	11	9	0
Total	36,799	36,615	1,259	551	1,014	462	245	89

TABLE A-3: **Number of malaria tests and positive results for 14 Chinandega municipalities, 2006 and 2007**

	Malaria tests		Positive results		*P. vivax*		*P. falciparum*	
	2006	2007	2006	2007	2006	2007	2006	2007
Chichigalpa	9,619	10,859	61	35	61	35	0	0
Chinandega	18,226	28,661	47	28	46	28	1	0
Cinco Pinos	1,292	1,351	1	0	1	0	0	0
Corinto	1,932	2,539	4	4	4	4	0	0
El Realejo	2,119	2,031	34	8	34	8	0	0
Viejo Norte	6,119	6,755	41	18	41	18	0	0
Viejo Sur	8,120	10,104	94	69	94	69	0	0
Posoltega	2,096	3,089	10	6	10	6	0	0
Puerto Morazan	2,716	2,901	5	1	5	1	0	0
San Francisco del Norte	1,090	1,274	0	0	0	0	0	0
San Pedro del Norte	934	779	0	1	0	1	0	0
Santo Thomas del Norte	793	1,329	0	0	0	0	0	0
Somotillo	4,383	6,205	0	4	0	4	0	0
Villa Nueva	5,679	5,596	3	1	3	1	0	0
Total	65,118	83,473	300	175	299	175	1	0

TABLE A-4: **Participants at the validation session for recommendations from the Malaria Case Study, December 18, 2008**

Dr. Francisco Acevedo	Director Applied Epidemiology	Ministry of Health (MINSA)
Betsabé Rodríguez	in charge of malaria, Department of Parasitology	MINSA
Dr. Aida Soto	Malaria Consultant	Pan American Health Organization (PAHO)
Dr. Jesús Maria Martínez	Transmittable Diseases Consultant	PAHO
Dr. Naxalia Zamora	Malaria Specialist for the Global Fund Project	NicaSalud
Dr. Juan José Amador	Director of Technology and Health Systems	PATH
Dr. Magda Sequeira	Global Health Diagnostic Consultant	PATH
Dr. Henry Espinoza	Consultant, Meeting Secretary	PATH

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