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Zambia Trip Report

Project DIAMETER (Diagnostics for Malaria Elimination Toward Eradication)

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Abbreviations

ACS	active case surveillance
ACT	artemisinin-based combination therapy
Active ID	active infection detection
AEIOU	Activity, Environment, Interaction, Object, and User
CHWs	community health workers
DBS	dried blood spot
DFID	Department for International Development
DHIS 2	district health information system 2
DIAMETER	Diagnostics for Malaria Elimination Toward Eradication
ELISA	enzyme-linked immunosorbent assay
GPS	global positioning system
HRP2	histidine rich protein-2
JOC	Jobs-Outcomes-Constraints
JSI	John Snow Incorporated
MACEPA	Malaria Control and Evaluation Partnership in Africa
MIS	Malaria Indicator Survey
MOH	Ministry of Health
MSAT	mass screen and treat
NMCC	National Malaria Control Center
NMCP	National Malaria Control Program
NMSP	National Malaria Strategic Plan
OPD	outpatient department
OTSS	outreach training and support supervision
PCD	passive case detection
PCR	polymerase chain reaction
PDA	personal digital assistant
PMI	President's Malaria Initiative
QA	quality assurance
RDT	rapid diagnostic test
Reactive ID	reactive infection detection
TB	tuberculosis
TPP	target product profile
USAID	United States Agency for International Development

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Introduction

Project DIAMETER

The goal of Project DIAMETER (Diagnostics for Malaria Elimination Toward Eradication) is to define the diagnostic needs unique to malaria elimination settings with sufficient clarity so that all stakeholders can act with confidence to develop, commercialize, and efficiently implement the most promising, cost-effective, and impactful technologies for malaria elimination.

Recent progress in malaria control has enabled countries to reduce malaria transmission rates. Existing diagnostic technologies—microscopy and rapid diagnostic tests (RDTs)—have played a critical role in this success by enabling many regions to achieve transmission rates near the threshold that defines the elimination phase. However, it is not clear whether these same tests are the most efficient and cost-effective tools to achieve accurate infection detection at low levels of parasitemia, which is critical to achieving elimination goals. Furthermore, there is a lack of clarity and agreement on the use scenarios, target product profiles (TPPs), standardized methods of assay validation, and market potential for the malaria diagnostic tools best suited for cost-effective detection in elimination settings. The resulting ambiguity hinders the development of new infection detection technologies as well as strategic application of existing and nearly ready tools.

PATH has developed a rigorous approach to identifying the most promising solutions to diagnostic challenges in low-resource settings. This involves aggregating and analyzing user needs, market needs, and technical requirements to generate the comprehensive evidence base necessary to inform product development, commercialization, and strategic program operations. Thus, through extensive field research and collaboration with malaria elimination experts, the DIAMETER team will evaluate and hone the use scenarios and TPPs for infection detection in elimination settings. To this end, stakeholder interviews will be conducted in a selection of countries in Asia, Africa, and South America that are nearing malaria elimination. Information gathered will be collated to inform product development of new diagnostics and areas where further research is required. This report presents findings from stakeholder interviews conducted in Zambia in August 2013.

Background on malaria in Zambia

Zambia is a land-locked country bordered by eight countries in southern Africa. It has a population of about 13.4 million, which is largely rural, with about 35% living in urban areas. Zambia is currently in the process of re-demarcating the boundaries of its districts and provinces; as of August 2013, there were 83 districts and 10 provinces.

Malaria transmission occurs throughout the year with a peak during the rainy season from November through April. The predominant parasite species is *Plasmodium (P.) falciparum* with *P. malariae* and *P. ovale* accounting for less than 5% of all infections. The 2010 Malaria Indicator Survey (MIS) recorded an overall prevalence of 16%, up from the prevalence of 10% obtained during the 2008 MIS**.** This upsurge

has been attributed to reduction and/or delays in funds that led to three provinces' inability to deliver malaria control interventions as planned.[1] The overall prevalence obtained during the 2012 MIS was 14.9%.[2] Almost two-thirds (64%) of households were reported to own insecticide-treated nets (ITNs) and 23% of households had been sprayed with indoor residual spraying (IRS) during the 2010 MIS. In recent years, evidence from routine health information, national surveys, and other focused studies has demonstrated a consistent decline in malaria prevalence. In order to better focus its control activities, the National Malaria Control Program (NMCP) characterized the country into three epidemiological zones.[3] This was based on the prevalence of malaria during the 2010 MIS and the level of malaria control in these areas. The categories of epidemiological zones are:

Category 1 - Areas where malaria control has markedly reduced transmission, and parasite prevalence in young children is less than 1%. This zone covers Lusaka city and its environs, where about 17% of the country's population live.

Category 2 - Areas where sustained malaria prevention and control has markedly reduced transmission, and parasite prevalence is between 1% and 14% in young children at the peak of transmission. This zone comprises the Central, Copperbelt, Northwestern, Southern, and Western provinces, with a population of about 6.4 million (49%).

Category 3 - Areas where progress in malaria control has been achieved but not sustained and lapses in prevention coverage have led to resurgence of infection and illness, and parasite prevalence in young children is ≥ 15% at the peak of the transmission season. This zone is made up of the Eastern, Luapula, Muchinga, and Northern provinces and is inhabited by 34% of the country's population.

In 2004, Zambia began to progressively introduce artemisinin-based combination therapy (ACT), with full national scale reached by 2005. It is estimated that only 13% of all malaria cases are confirmed. The NMCP aims by 2015 to have all patients with suspected malaria undergo parasitological testing via microscopy or an RDT, and all confirmed cases to receive early, effective treatment.[3] Some of the main strategies to be used include:

- Strictly enforce malaria diagnosis and treatment policies in both the public and private sectors.
- Provide malaria diagnosis and treatment guidelines to health facilities at all levels in the public and private sectors.
- Strengthen quality control/assurance capacity in malaria diagnosis and case management in the public and private sectors.
- Strengthen supervision at all levels.
- Establish a malaria reference center for quality control, training, and research.
- Ensure timely availability of adequate diagnosis/case management commodities.
- Explore emerging technologies in malaria diagnosis and treatment.

Malaria control is considered a national priority and the NMCP has strategically been placed within the Directorate of Public Health and Research at the Ministry of Health (MOH). It has a well-established national coordinating body, the National Malaria Control Center (NMCC). The Zambian NMCP recently finalized a new National Malaria Strategic Plan (NMSP) for 2011–2015. The vision of this NMSP is to achieve progress toward a "malaria-free Zambia by 2030" through equity of access to quality-assured, cost-effective malaria prevention and control interventions close to the household. The NMSP aims to achieve the following three goals by 2015: 1) reduce malaria incidence by 75% of the 2010 baseline; 2) reduce malaria deaths to near zero and reduce all-cause child mortality by 20%; and 3) establish and maintain five "malaria-free zones" in Zambia.[3] The NMCP is funded by the Government of Zambia, the Global Fund, Department for International Development (DFID), President's Malaria Initiative (PMI), Bill & Melinda Gates Foundation through the Malaria Control and Evaluation Partnership in Africa (MACEPA), World Bank, and United States Agency for International Development (USAID).

Role of MACEPA

MACEPA supports the Zambian government to plan and implement malaria control interventions. MACEPA has categorized its interventions into three steps, and it engages the services of Akros Research to implement some of its activities. To ensure that good quality data are obtained at the district and sub-district levels and made available in a timely manner for planning purposes, MACEPA has supported the MOH to design and introduce a rapid reporting system—the district health information system 2 (DHIS 2). In this reporting system, health workers send specific malaria data to a central server each week via mobile phones. This information is immediately available to program managers at district, provincial, and national levels, allowing them to focus interventions on specific needs. This is referred to as Step 1 of MACEPA's interventions. It was first piloted in 25 districts and is being scaled up. Step 2 is the Test and Treat campaign, in which entire communities are proactively tested and treated for malaria during specific periods of the year. This was initially piloted from December 2011 through January 2012 in 10 health facility catchment areas where malaria prevalence was low. It was subsequently expanded to 21 health facilities in 4 districts in 2012, and more health facilities have been added in 2013. Step 3 involves reactive infection detection (ID), and is carried out in areas where malaria prevalence is less than 5%.

Purpose of the report

1. To consolidate and document country-specific information derived from stakeholder interviews.
2. To disseminate summarized information to key informants who participated in the data collection process, to PATH staff in-country, and to other stakeholders.

Methods

In order to capture a complete picture of the current state of malaria elimination in each country, Project DIAMETER combines thorough desk research on malaria control and elimination efforts with theory-driven qualitative research targeting the opinions and actions of key players within the country's malaria program.

Desk research

Prior to initiating the qualitative research component, a literature review of relevant documents was undertaken. This desk research helped the team to position Zambia along the spectrum from control to elimination, clearly understand the strategies and priorities of the NMCP, and gain perspective on previously completed and ongoing research in the country. Based on this desk research, qualitative data collection tools were developed and key informants were identified.

Qualitative research with key informants

Sixteen key informant interviews and two focus group discussions were conducted along with visits to four health facilities and the NMCC lab. A list of stakeholders is provided in Appendix A. Interview guides and observation checklists were developed in advance to encourage systematic and uniform data collection techniques within the tenets of Contextual Inquiry methodology and using a hybrid of two frameworks—Jobs-Outcomes-Constraints (JOC) and Activity, Environment, Interaction, Object, and User (AEIOU)—to organize concepts. Contextual Inquiry approaches qualitative data collection with the objective of describing how actors, objects, and rules influence and are influenced by the larger system in which they exist. This method exposes tacit knowledge that informants may not be aware of and encourages the informant (rather than the reviewer) to prioritize concepts.

Interview guides and observational checklists were used for each category of key informant: program manager, thought leader, laboratory personnel, clinician, and community health worker. The data collection tools were developed using a hybrid JOC-AEIOU framework, which prompted the interviewees to describe the main elements of the system (AEIOU) and then define the barriers to successfully achieving the intended objectives (JOC).

Following data collection, key concepts from each interview were summarized by the research team, mapped to the corresponding use scenarios and settings, and aggregated across twelve data sets (five observational visits and seven interviews). A spreadsheet mapping key concepts to use scenarios and settings is included as Appendix B.

Malaria diagnostic tests used in Zambia

In 2008, the Zambia MOH adopted a policy of universal laboratory diagnosis of malaria using microscopy or RDT (where microscopy is not available) prior to treatment. Microscopy was to be used where the equipment and trained staff were already present; otherwise RDTs were used.[3] According to information from PMI (2013), 417 health facilities in Zambia have laboratories with microscopy. The national guidelines stipulate that microscopists should not read more than 40 blood slides per day (personal communication, NMCC chief parasitologist). Therefore, microscopists switch over to RDTs once they have read 40 slides. This is to reduce the likelihood of errors in reading slides as a result of fatigue. Thus, all health facilities with capacity for microscopy also use RDTs. A major constraint with the use of microscopy is human resources.

RDTs are available in all public health facilities and these facilities are responsible for supplying community health workers (CHWs) in their catchment areas with RDTs. The NMCC has a committee that

quantifies RDT needs based on previous consumption and also reviews product specifications based on feedback from end users. This information is shared with various partners such as PMI, DFID, MACEPA, John Snow Incorporated (JSI), and Global Fund. Each partner then takes up the responsibility of procuring a proportion of the projected RDT needs using its own institutional procurement procedures, although all deliveries are made to the central medical stores. Delivery of RDTs is not coordinated and may therefore occur at different times, thus having a negative impact on the supply chain system. The procurement cycle from the tender process through delivery of RDTs can take as long as a year. Local distributors often have an edge over international ones in the bidding process, as taxes on any profits they make go back to the Government of Zambia. Because of this, their quote per unit test is adjusted to a lower rate than bids obtained directly from the manufacturer (thus making them competitive in the tender process). SD BIOLINE (*P. falciparum*) is the RDT brand currently being used, but First Response Malaria Ag HRP2[i] and ICT Malaria *P. falciparum* have also been used in the past.

Some of the technical specifications that the MOH has recently used in procurement include:

- Product should be among the first 10 on the malaria RDT performance results of the World Health Organization (WHO)/Foundation for Innovative New Diagnostics (FIND) product testing of RDTs.
- Must be a *P. falciparum* cassette.
- The sampling device should be an inverted cup as this makes the test more accurate and is user friendly at lower levels, especially among CHWs.
- Sensitivity at low parasite densities (200 parasites/µl) should be between 95% and 100%.

The key constraint to RDT use among all users interviewed was the recurring stockouts of test kits. Also, the frequent changes in brands of RDT led to errors in the use of the buffer solutions among users, even among trained laboratory technicians. This occasionally led to wastage of tests when buffer solutions run out. While laboratory technicians were satisfied with the pipette as a transfer device, CHWs preferred the inverted cup because of its ease of use. It has also been observed that patients who have been on treatment still test positive with RDTs.

Quality assurance

Three years ago, Zambia initiated a quality assurance (QA) system: outreach training and support supervision (OTSS) for malaria diagnostics. In this program, supervisors use standardized checklists to observe use of RDTs and microscopy, recheck select malaria smears, and also collect information on provider adherence to laboratory results and stockouts. These supervisors also provide onsite training and corrective action as needed. All of the health facilities with labs that we visited reported that OTSS was taking place regularly. Supervisory activities were carried out on a quarterly basis in the first year and biannually thereafter. A comparison of some indicators in the first and fourth visits showed some improvements: the average percentage of microscopy tasks performed correctly increased from 66% to 80%, average percentage of RDT tasks performed correctly increased from 78% to 86%, and the

[i] Histidine rich protein-2

proportion of health facilities that achieved a concordance greater than 85% with supervisor slide readings increased from 74% to 85% (PMI, 2013).

Malaria diagnostic scenarios in Zambia

The districts we visited in Zambia were all within the MACEPA intervention areas, and the malaria diagnostic use scenarios included passive case detection, reactive ID, mass screen and treat (MSAT), and malaria indicator surveys (MIS). Passive case detection and MIS are possibly the main use scenarios in non-MACEPA intervention areas, which constitute a greater part of the country.

Passive case detection

Passive case detection (PCD) occurs in public and private health facilities as well as at the community level. There is limited information available from the private sector.

A. Health facility level

As per the national guidelines, public health facilities may use either RDTs alone or a combination of RDTs and microscopy depending on the availability of a laboratory with a microscope and a laboratory technician. The implementation of these guidelines, however, varied in all three health facilities we visited that used both microscopy and RDTs. At one health facility (a district hospital), RDTs were used to test all febrile patients, and those who tested positive were treated. Microscopy was mainly used for inpatients and for patients for whom a clinician had specifically requested microscopy. This strategy markedly reduced pressure on the only available microscope and allowed the microscopists to spend more time on other non-malaria related evaluations. In another facility (a mission hospital), RDTs were used to screen all febrile patients at the outpatient department (OPD) and those who tested positive were sent to the lab for another blood sample to be taken for microscopy. Occasionally, when the OPD nurses are overwhelmed, all febrile patients are sent to the lab for RDT screening and subsequent microscopy when necessary. In the third health facility (a large health center in an urban setting), microscopy was performed for all patients until the microscopist had read 40 slides. Thereafter, RDTs were used. In this same facility, RDTs were also used for patients who are too sick to walk to the lab during regular working hours and after the lab had closed at 4:00 pm except in situations of RDT stockouts, whereby patients are referred to other health facilities. Because all the health facilities we visited were located within the MACEPA intervention areas, they were all involved in the rapid reporting system and therefore reported the following information weekly via cell phone: total number of OPD patients, total number tested by RDT, total number testing positive by RDT, total number tested by microscopy, total number testing positive by microscopy, all positives younger than 5 years old, all positives older than 5 years old, artemether-lumefantrine (Coartem) dispensed and stock remaining, and RDT stock remaining.

Constraints: The most frequent constraint associated with RDTs was stockouts. This led to patients being treated presumptively or delays in patient care because they had to be referred to other health facilities. Also, the frequent switching of RDT kit vendors led to difficulties in adherence to the kit protocol as test kits often differed with respect to volume of buffer used, time to results, or blood transfer devices. Finger pricks are painful and this led to difficulties in drawing blood, especially in children. Constraints

pertaining to microscopy were power outages (infrequent), power fluctuations, lack of back-up generators, and challenges with obtaining fuel for generators. Laboratory technicians were also concerned about the poor quality of blood slides prepared for inpatients by nurses. Although not a common occurrence, the use of expired reagents was an issue of concern. There were also challenges with human resource as there were not enough trained staff conducting quality microscopy.

B. Community level

At the community level, passive case detection is carried out by volunteer CHWs; their information feeds into Step 3 of the MACEPA interventions, active ID. About 3 to 16 CHWs are attached to a health facility. They obtain their supplies of RDT and Coartem from these facilities. After undergoing training for 4 days, these CHWs are attached to the health facility for 2 weeks, where their activities are directly supervised. Thereafter, the CHWs carry out their activities within the community. Each CHW decides on the days and times that he/she will see sick people at a designated site, which could be in their home, under a tree, in a makeshift structure, etc. The information recorded for each patient is name, age, sex, address, complaint, any travel history, test result, and treatment given. CHWs are only allowed to treat people with Coartem when they test positive with an RDT; sick people who test negative are referred to the health facility for further investigation. One CHW is selected as a reporter and he/she collates information from the other CHWs every month for submission via cell phone, usually by Day 10 of the following month. Akros staffs usually follow up when submission of information is delayed as it could mean the phone has been lost. Akros also conducts regular supervisory activities and collects the hard copy registers from the CHWs once a year to enter all the data into a computerized system. Data entered is compared to the monthly reports submitted by the CHWs. The information submitted for each CHW is the number of people seen, number testing positive, number that had travelled, and number treated.

Constraints: Frequent stockouts of RDTs and vendor switching with resultant errors in buffer volume, read times, and blood transfer were major issues. Some CHWs feared pushing the lancet into the finger pad firmly. Although CHWs have been provided with containers for waste, these were only disposed of at the health facilities occasionally and storage of hazardous waste at the CHWs' homes was a problem, especially when there were children around. CHWs' homes or stations where they see patients do not have reliable sources of electricity or water. There were challenges with using cell phones for data entry and transmission. Sometimes the CHWs inserted their personal SIM cards for use with the phone and this affects the built-in software for data entry.

Reactive infection detection

Reactive ID constitutes Step 3 of the MACEPA interventions and is carried out in rural and urban settings. This activity is termed active case surveillance (ACS) in rural settings and reactive ID in urban settings.

A. Active case surveillance

Active case surveillance is conducted by CHWs. These are the same CHWs who conduct the passive case detection within the communities. ACS is initiated when a case is identified during passive case detection. The CHWs follow up within a week to the index household and neighboring households within a 140-

meter radius, where they test everyone. People who test positive are treated. The CHWs move in a clockwise direction and aim to cover an area equivalent to one and a half times a football field. The CHWs record all data in a register. Every month they provide a summary of the data recorded to the CHW reporter for submission via mobile phone. The information includes the number of households visited, number of persons who have travelled outside the district, total number tested, number that tested positive, number treated, and number not treated.

Constraints: In addition to the constraints already outlined for passive case detection by CHWs, there were additional constraints unique to reactive ID. Because of the frequent RDT stockouts, CHWs tend to reserve their supply of RDTs to use for PCD when people are actually symptomatic. There were also reports of community mistrust of the purpose of the test as there was the perception that blood was being collected for rituals or for HIV testing. However, it was noted that RDT kits with an image of a mosquito on the box alleviated those concerns.

B. Active infection detection

Cases are passively identified at the health facilities. If it is determined that these index cases have not had malaria in the past month, have not traveled in the past month, and live within the catchment area, a follow-up visit is made to their household and nine neighboring households. A team made up of a CHW, environmental health technician, nurse, and sometimes a laboratory technician carry out the active ID activity. The nurse usually supervises the CHW to perform the RDTs and also administers treatment. The environmental health technician takes global positioning system (GPS) coordinates of the household and educates people on vector control activities. The team carries out the active ID activities on weekends when they are likely to find people in such urban settings at home. On occasions when only one or two patients are identified in a week at the health facility, the active ID is deferred to the following week to allow them get an appreciable number of households for follow-up. This is mainly due to problems with logistics. Follow-up visits are not deferred for more than three weeks, however. Once follow-up activities are scheduled, a request is made to the district for a vehicle.

Constraints: The team has limited access to transportation for active ID. Therefore, they are often unable to conduct revisits to households where people were missed during their initial follow-up. Sometimes RDT results are read earlier than prescribed because they are hard-pressed for time. Teams also noted that there was inadequate space on the cassette to write patient information.

Mass screen and treat

This is Step 2 of MACEPA activities, and is referred to as Test and Treat. It is carried out by teams of CHWs and enumerators who are attached to health facilities. The CHWs' role is to perform the test and treat while the enumerators enter all the data into a personal digital assistant (PDA). They obtain their supplies from the health facilities daily, and work within the catchment areas of the health facilities. The Test and Treat campaigns are carried out three times a year from May through October. Each round lasts a month, and there is a month's break between rounds. Each pair (CHW and enumerator) works from 6 am to 2 pm each day and visits 9 to 14 households per day depending on the household size and the distance between households, because they walk within the community. Household size varies from about 9 to 18 and they spend an average of 30 minutes per household. The CHW tests and treats family

members as appropriate after informed consent has been obtained. Generally, informed consent is obtained from all household members during the Test and Treat campaigns. They label the test cassettes for all household members and arrange them in the same order as the names of the household members appear in the PDA. The tests are run concurrently and mobile phones are used to time the tests. The enumerator completes a short questionnaire on a PDA, records the test results, and takes GPS coordinates of the households. If some household members are missed, revisits are made to households toward the end of each Test and Treat round.

Constraints: School children are often missed when Test and Treat activities are carried out when school is in session. There are also occasional refusals from members of a particular religious group. Sometimes, there are shortages of gloves but the team improvises by using plastic bags. Occasionally, the PDA devices turn off during data entry, which requires the enumerator to restart the device and the data entry process, thus prolonging the time spent in one household. They do not have access to mains electricity or water.

Surveys

Malaria indicator surveys are conducted on nationally representative samples. The MIS has been conducted biennially since the first survey in 2006. Blood samples are obtained from children under six years for RDTs, preparation of thick and thin smears for microscopy, and dried blood spots (DBS). Results from the RDTs are used to guide treatment of children with parasitemia during the survey. The ICT Malaria *P. falciparum* RDT was used during the 2010 MIS. All stained blood slides were independently read by two microscopists and discrepancies were reanalyzed by a third reader. The DBS have been stored in a freezer at the NMCC and are yet to be analyzed. The used RDTs have also been stored in a freezer at the NMCC for possible future DNA extraction.

Apart from the national MIS, small-scale surveys referred to as “mini MIS” or “follow-up MIS” are conducted between MIS survey years in the MACEPA intervention areas to assess the impact of malaria control activities. Blood samples are collected for RDT, blood smears, and DBS. The DBS from these mini surveys are yet to be analyzed.

Constraints: The NMCC lab is not fully set up with equipment, reagents, and human resource to analyze the DBS samples. No interviews of MIS survey staff were conducted to identify constraints during sample collection.

Malaria diagnostic settings in Zambia

Of the 1,882 health facilities in Zambia, 79% are government-run, 14% are in the private sector, and 7% are affiliated with religious organizations. The three levels of public health facilities are hospitals, health centers, and health posts; the hospitals are further divided into primary (district), secondary (provincial), and tertiary (central) facilities (Table 1). Geographic access to health facilities varies greatly between urban and rural areas: 99% of urban households reside within five kilometers of a health facility, compared to 50% of rural households.

Table 1. Distribution of health facilities in Zambia.[4,5]

Facility type	Number	Population covered per facility	Diagnostic tests likely in use
Health post	275	3,500 in rural areas and 7,000 in urban areas	Rapid diagnostic test (RDT)
Rural health center	1,060	10,000 or a catchment area of 29 km radius	RDT only or RDT and microscopy
Urban health center	436	30,000 to 50,000	RDT only or RDT and microscopy
Primary hospital (district)	84	80,000 to 200,000	RDT and microscopy
Secondary hospital (provincial)	21	200,000 to 800,000	RDT and microscopy
Tertiary hospital (national)	6	≥800,000	RDT and microscopy
Total	**1,882**		

Our team visited four health facilities and the NMCC lab. The health facilities were the Siavonga district hospital; the Mtendere mission hospital, which serves as the district hospital in the Chirundu district; and the Chainda and Chelstone health centers in Lusaka.

District hospital

The Siavonga district hospital lab is equipped with one microscope, a blood chemistry analyzer, and a CD4 machine (which was broken down during our visit). There is no back-up generator, but power cuts are infrequent as there is a hydroelectricity plant located in the district. Patients with fever are tested with RDTs at the outpatient department, and this significantly reduces the pressure on the only microscope, which is also used for tuberculosis (TB) diagnosis and other diagnostic tests. The OPD has a dedicated screening room where RDTs are performed.

Constraints: The constraints to RDT use are stockouts. Patients who have been in treatment still test positive with RDTs; the laboratory technician has therefore advised clinicians that such patients be referred to the lab for microscopy. Constraints identified with microscopy were the occasional power cuts and human resource issues; also, there was a need for more qualified microscopists.

Mission hospital

The Mtendere mission hospital receives support from Italian missions; however, it is now functioning as the district hospital of the newly created Chirundu district. There are four laboratory technicians, three of whom perform malaria microscopy. They alternate roles in preparing, staining, and reading the blood slides. Febrile patients are screened with RDTs in the OPD, and those testing positive are referred to the

lab for microscopy. They process about 20 slides daily including those of inpatients. Previously, they could process about 40 slides daily; they attribute this decline in number of slides to the Test and Treat activities. The lab has two functioning microscopes and a spare one. There is a back-up generator that switches on automatically within 30 seconds of a power cut; power cuts are not too common, however. There is an in-house equipment maintenance system in place. Other tests performed are TB microscopy, urine and stool examination, blood chemistry, and histopathology. The lab is open for eight hours daily and there is always a laboratory technician on call for emergencies.

Constraints: The constraint associated with microscopy was the occasional poor quality of smears prepared by nurses for inpatients. For RDTs, the constraints were a lack of a quality control (QC) system, patients testing positive even after treatment, and challenges with adherence to instructions on the number of drops of buffer due to the frequent changes in RDT brands.

Health centers

The Chainda health center is located in peri-urban Lusaka. It does not have a lab and uses only RDTs for malaria diagnosis. A simple set-up in a corner of the OPD serves as the area for rapid diagnostic testing, and all febrile patients are referred for testing here. Patients requiring further lab evaluation are referred to the much larger Chelstone health center.

The Chelstone health center has a lab managed by three laboratory technicians. The lab has two functioning microscopes, and the tests performed include malaria microscopy, urine microscopy and chemistry, stool microscopy, sputum microscopy for TB, hematology. The lab offers blood transfusion services as well. There are no problems with electricity. There were problems with replacement microscope bulbs in the past, but they now use newer microscopes and do not have such problems. There are technicians who come in to fix broken equipment on the same day they are called. Blood smears are air-dried but an electric heater is used for drying stained slides. RDTs are mainly used by nurses at the OPD and by laboratory technicians when they have read a maximum of 40 slides in a day.

Constraints: The nurses and laboratory technicians spend a lot of time on malaria smears compared to other tests, and blood smears take a longer time to air-dry during the winter months. Generally, there were no constraints with the use of RDTs except for the frequent stockouts.

National Malaria Control Center lab

The NMCC lab is situated in Lusaka near the main teaching hospital. There is an insectary used for rearing relevant vector colonies. There is also a microscopy lab that is used for reading MIS slides and occasionally for diagnosing patients referred from the nearby hospital. In a separate stand-alone building, there is a laboratory dedicated for molecular work. It is equipped with a conventional polymerase chain reaction (PCR) system that has been used for parasite DNA work as well as vector genetics. The NMCC has recently acquired a container biosafety level 2 lab from South Africa. This new lab is being set up to run quantitative PCR on existing MIS DBS samples currently stored in the freezer. These two labs have the infrastructure and equipment that is standard to any lab running molecular assays: freezers, refrigerators, enzyme linked immunosorbent assay (ELISA) readers, gel boxes, thermocyclers, water still,

reagent storage, etc. A backup generator is available for power outages. Reagents and other consumables are generally acquired from abroad.

Constraints: A major constraint identified was lack of staff training and retention to perform molecular work. The two current laboratory technicians are on attachment as interns from university and could leave the NMCC once they get a more permanent employment opportunity. There is no specific budget line for full-time molecular biologists within the MOH/NMCC. There is, therefore, a high staff turn-over rate and retraining is rather burdensome.

Equipment breakdown is another constraint; the water distillation machine, for instance, has not been functioning for more than a year and they have had to purchase double-distilled water from a local vendor. The DNA extraction step is tedious and labor intensive, as is loading the sample into the master mix because they use a single pipette. There are also problems with supply stockouts; at the time of our visit they had run out of eppendorf tubes and had substituted used cryovials for extraction instead. Also, they are unable to run gels when they run out of DNA ladder. Under such circumstances, they store the plates in a refrigerator until they receive a new supply of ladder. However, this does not happen too often.

At the moment, the new container lab is not fully operational to analyze the MIS samples. A significant amount of optimization of assay protocols will be required before high throughput testing of MIS samples can begin.

Challenges

The following were identified as potential challenges to Zambia's elimination efforts:

RDT supply chain system

The most frequent problem encountered was RDT stockouts. The tender process appears to be cumbersome, taking almost a year from time of tender to delivery. Multiple donor agencies fund the purchase of RDTs, and each agency has its own procurement process and delivery schedule. This may contribute to the frequent stockouts and changes in test kits; the rampant changes in test kits adversely affect adherence to test protocols. There were reports of utilization of health services located in the border regions by citizens from neighboring countries, but the extent to which this impact stocks of RDTs is not known. However, projected needs are based on previous consumption, to which some upward adjustments are made. The factors contributing to the erratic supply of RDTs appear to be complex, and accurately ascertaining them is beyond the scope of this exercise.

Sustainability

Although the NMCC is encouraging district ownership of strategies directed toward malaria elimination, elimination efforts are currently being driven and supported by MACEPA. About 83% of Zambia's population still lives in relatively high transmission areas, and achieving a malaria-free Zambia by 2030 may be difficult without continued donor support.

High importation risk of malaria

Because Zambia is land-locked, there is a substantial amount of trade in goods and services, resulting in the net movement of people across borders. Zambia is much more advanced in its malaria control efforts than its neighboring countries, making it vulnerable to importation risk. Furthermore, Zambia has large areas with high malaria transmission in-country. Although there have been discussions on regional initiatives to coordinate malaria control activities, this has not reached an advanced stage.

Human resource needs

Limited human resources is one of the challenges the NMCC faces as it builds up its lab's capacity to carry out real time PCR assays. The lab currently relies on interns and the turn-over rate is high. A lot of time and effort is therefore spent on training new interns. This is burdensome and has the potential for disrupting work and errors.

There aren't enough trained microscopists and the few available are often overburdened with malaria microscopy as well as microscopy for other infections such as TB. Microscopy centers also face the challenge of maintaining the competency of staff as malaria transmission drops.

Impact of HRP2 deletions on RDTs in use

One potential challenge currently being investigated is the possibility of genetic mutations in circulating parasite strains that would preclude them from detection using current RDTs that detect HRP2 proteins. This follows observations made in Peru.[6] The NMCP, however, has plans to start surveillance for these strains.

Summary

Zambia aims to eliminate malaria in five areas by 2015 and is being supported by MACEPA to achieve this goal. In addition to the routine passive case detection and MIS, new strategies such as mass screen and treat and reactive ID have been introduced in selected districts in the southern part of the country. There is a huge reliance on community health workers to carry out these strategies. The primary means of diagnosing malaria are microscopy and RDT. The use of molecular methods, such as conventional PCR and ELISAs, are in place and the NMCC is adding capacity for real time PCR for the analysis of MIS samples and other genomic work. The main constraints identified by microscopists were time spent preparing and reading smears compared to their other duties, maintaining skills in a time of low transmission, and the need for more qualified microscopists. Major constraints associated with RDTs are the stockouts and vendor switching, which results in procedural errors.

References

[1] Ministry of Health (MOH). *Zambia National Malaria Indicator Survey 2010.* Zambia: MOH; 2010.

[2] Miller JM, Hamainza B, Silumbe K, et al. National malaria indicator survey 2012 demonstrates continued success in malaria control progress with key interventions. An abstract submitted to the Zambia National Health Research Conference 2013. Lusaka; October 2013.

[3] Ministry of Health (MOH)/National Malaria Control Program (NMCP). *National Malaria Control Program Strategic Plan for FY 2011–2015.* Zambia: MOH/NMCP; 2011.

[4] Ministry of Health (MOH). *Zambia National Health Strategic Plan 2006–2010.* Zambia: MOH; 2010

[5] President's Malaria Initiative (PMI). *President's Malaria Initiative Zambia Malaria Operational Plan FY 2013.* Zambia: PMI; 2013.

[6] Gamboa D, Ho M-F, Bendezu J, et al. A large proportion of *P. falciparum* isolates in the Amazon Region of Peru lack pfhrp2 and *pf*hrp3: implications for malaria rapid diagnostic tests. *PLoS ONE.* 2010;5(1).

Appendix A: List of stakeholders

Name	Position
Dr. Mulakwa Kamuliwo	Deputy director, National Malaria Control Center (NMCC)
John Miller	Technical officer, Malaria Control and Evaluation Partnership in Africa (MACEPA)
Kafula Silumbe	Monitoring and evaluation specialist, MACEPA
Thokozile Ngwneyna and Zunda	Surveillance specialists, Akros
Mwila Chipofya	Environmental health technician, Chainda Health Center
Collins Mulenga	Lab technician, Siavonga District Hospital
Ezelina Chalwe	Nurse, Siavonga Hospital Affiliated Health Center
Sister Lisa	Clinician, Mtendere Mission Hospital
Given Hampungani	Lab technician, Mtendere Mission Hospital
Gabriel Chipili	Lab technician, Mtendere Mission Hospital
Community health workers (CHWs) and enumerators	Attached to Mtendere Mission Hospital
Martha Mulenga	NMCC logistics officer
Rabecca Ngwira	Intern, NMCC lab
Nasilele Situmbeko	Intern, NMCC lab
Emmanuel Mukupa	Lab technician, Chelstone Health Center
Active infection detection team (nurse, environmental health technician, and CHW)	Chelstone Health Center
Sadik Seedak	Local rapid diagnostic test distributor
Moonga Hawela	Chief parasitologist, NMCC
Busiku Hamainza	Principal operations research officer, NMCC

Appendix B: Use scenarios for malaria diagnostic tests in Zambia

Use Scenario	Setting	Inputs				Outcomes	Constraints
		Diagnostics	Process	Human Resources	Infrastructure/Supplies		
Passive Case Detection (PCD)	Rural Community	Rapid diagnostic test (RDT) (SD Bioline Pf currently; different brands in the past)	• Sick people present to community health worker (CHW) • CHW tests by RDT	• CHW who has received training for four days and attachment to a health facility for two weeks	• RDT • Supply of coartem, sharps, and waste disposal • Notebook for record keeping • Cell phone to CHW who is responsible for data collation and submission	• Treat people who test positive • Obtain travel history • Record information in register • Generate list of household (HH) to follow up on for active infection detection (AID) • Refer sick people that test negative to health facility (HF) • Monthly collation of information from CHWs in a HF catchment area and submission via cell phone by one CHW • Periodic disposal of waste at HF	• Frequent RDT stockouts • Errors in quantity of buffer used due to frequent changes in RDT brands • Difficulty in using pipette • Results often read earlier than recommended time • Danger of storing hazardous waste at home • Challenges with using mobile phone for data transmission • No electricity and water
	Health Center (mid-level infrastructure with no lab in an area where there is AID - Step 3)	RDT (SD Bioline Pf currently; different brands in the past)	• Patients presenting with fever referred to a corner at outpatient department (OPD) for testing	• Nurses with three years training • Environmental health technician (EHT) with four years training • Volunteer CHW	• RDT • Register for record keeping • Cell phone for data submission • Electricity and water, but no lab • Table and bench	• Patients treated appropriately • Patient data entered in a register • Contact details obtained for those who test positive, have no travel history, live in HF catchment area and give consent for follow-up to HH • Weekly submission of data via cell phone	• Frequent RDT stockouts • Errors in quantity of buffer used due to frequent changes in RDT brands • Difficulty in using pipette • Patients sometimes treated presumptively during RDT stockout
	Health Center (mid-level infrastructure with access to lab in an area with mass screen and treat (MSAT) but no AID - Step 2)	RDT (SD Bioline Pf currently; different brands in the past) • Microscopy	• Patients present with fever • RDT tests performed and results sent to clinician • Clinician may request microscopy for some out- and inpatients	• Nurses with three years training • Laboratory technician with three years training	• Electricity • Water • RDT • Register for record keeping • Microscope • Reagents and consumables	• Patients treated appropriately • Patient data entered in a register • Weekly submission of summary data via cell phone • Slides subject to quality assurance (QA) system	• RDT stockouts • Fingersticks using lancets are painful, especially for children • Power cuts, though these are infrequent • No backup generator • Sometimes reagents expire • Poor quality of slides prepared for inpatients by nurses
	Health Center (high-level infrastructure - Step 3)	RDT (SD Bioline Pf currently; different brands in the past)	• Febrile patients sent to lab for microscopy • RDTs used at lab after microscopists have read more than 40 slides • Nurses test febrile patients with RDT when lab is closed	• Nurses with three years training • Volunteer CHW (assists nurse) • EHT with four years training • Laboratory technician with three years training	• Electricity • Backup generator • Water • Register for record keeping • Microscope • Reagents and consumables • Electric heater for drying slides after staining	• Diagnostic test results sent to clinician for patient management • Patient data entered into register • List generated for AID • EHT submits data via cell phone weekly	• Frequent RDT stockouts • Frequent changes in RDT brands lead to errors in use of buffer • Often run out of buffer as a result of errors in use of buffer • Difficulty in using pipettes (by nurses) • Patient referral to other HF with 24-hour lab service when lab is closed and during RDT stockout • Poor quality of slides taken by nurses for inpatients • Slides take a longer time to dry during winter months • Human resource issues - switch to RDT after microscopist has read 40 slides
	Mission Hospital (high-level infrastructure - Step 2)	RDT (SD Bioline Pf currently; different brands in the past) and microscopy	• Patients present with fever • Nurses screen with RDT and refer those who test positive to the lab for microscopy • Sometimes all febrile patients are referred to the lab for RDT screening and microscopy • Slides taken by ward nurses for inpatients	• Nurses with three years training • Laboratory technician with three years training	• Electricity • Back up generator • Water • RDT • Microscope • Reagents and consumables • Computer in lab for documentation • Register for record keeping • Cell phone for weekly reporting	• Results sent to clinician for patient management	• Frequent RDT stockouts • RDT stockouts lead to increased workload for microscopists • RDT stockouts sometimes lead to presumptive treatment of patients (may lead to overestimation of statistics) • Frequent changes in RDT brands lead to errors in quantity of buffer used • Patients may still test positive if they have been on treatment • No QC system for RDT • Human resource - need more qualified laboratory technicians
Reactive Case Detection (RACD)	Household in Rural Setting	RDT (SD Bioline Pf currently; different brands in the past)	• List of HH with index cases obtained from passive case detection (PCD) register • Test all index HH members and neighboring HH within a defined radius	• CHW who has received training for four days and attachment to a health facility for two weeks	• RDT • Supply of coartem, sharps, and waste disposal • Notebook for record keeping • Cell phone to CHW who is responsible for data collation and submission	• Persons testing positive are treated • Symptomatic people testing negative are referred • Information entered into register • Monthly collation of data by one CHW for submission via mobile phone • Periodic disposal of waste at HF	• Frequent RDT stockouts • Tendency for CHW to reserve RDT for PCD as a result of frequent stockouts • Frequent changes in RDT brands lead to errors in quantity of buffer used • Results often read earlier than recommended time as CHW gain more confidence in use of RDT • Difficulty in using pipette • Community mistrust of purpose of test • CHWs' fear of pushing lancet into the fingerpad • Challenges with use of mobile phone to transmit data • Danger of storing hazardous waste at home prior to disposal at HF
	Household in Urban Setting	RDT (SD Bioline Pf currently; different brands in the past)	• List of HH with index cases obtained from PCD register • Test all index HH members and nine surrounding houses	• Nurses with three years training • EHT with four years training • Volunteer CHW • Team receives one week training • Driver	• RDT • Supply of coartem, sharps, and waste container • Notebook for record keeping • GPS equipment • Vehicle • Mobile phone	• Persons testing positive are treated • Travel history obtained from persons tested • GPS coordinates of HH are obtained • Health education is provided by EHT • All field data entered in a register • Data is submitted monthly via mobile phone • Physical collection of paper registers by Akros bi-monthly	• Limited access to transportation to facilitate revisits • Difficulty with blood transfer from finger to device using pipette • Results are often read earlier when there is time pressure • Inadequate space on RDT cassette to write patient details
Mass Screening and Treatment (MSAT)	Household	RDT (SD Bioline Pf currently; different brands in the past)	• Carried out three times a year • Each round of activities takes 30 days • Pairs of CHW and enumerator cover 9-14 HH daily • Informed consent is obtained from HH members prior to testing • Revisits carried out toward end of round • Personal digital assistants (PDA) are charged daily at supervisor's home	• CHWs and enumerators trained for one week • Supervisor	• RDT • Supply of coartem, sharps, and waste container • Consent forms • PDA with GPS capability • Backpacks • Mobile phone	• Persons testing positive are treated • GPS coordinates of HH obtained • All data entered into PDAs • Summary data submitted on paper to supervisor daily • Mobile phone submission of data by supervisor • Information on PDA downloaded periodically by supervisors	• Miss out on children when school is in session • Some refusals, especially from certain religious groups • Occasional shortage of gloves (improvise with plastic bags) • PDAs sometimes shut down in the middle of data entry and a restart is needed • No electricity and water

Use Scenario	Setting	Inputs				Outcomes	Constraints
		Diagnostics	Process	Human Resources	Infrastructure/Supplies		
Surveys	National level - representative sample of households	RDT, microscopy, and dried blood spot (DBS)	• Survey of representative sample of HH • Blood samples obtained • Questionnaire administered	• Trained survey personnel	• RDT • Blood slides and other consumables for microscopy • Filter paper • Coartem	• Persons testing positive by RDT are treated • Prevalence determined from microscopic examination of blood slides • DBS and used RDTs stored for future DNA extraction and analysis	• DBS not yet analyzed due to lack of technical support and reagents, and incomplete lab set-up
	Selected districts	RDT, microscopy, and DBS	• Survey of representative sample of HH • Blood samples obtained • Questionnaire administered	• Trained survey personnel	• RDT • Blood slides and other consumables for microscopy • Filter paper • Coartem	• Persons testing positive by RDT are treated • Prevalence determined from microscopic examination of blood slides • DBS and used RDTs stored for future DNA extraction and analysis	• DBS not yet analyzed due to lack of technical support and reagents, and incomplete lab set-up
Determine Origin of Infection	Health Facility, Household	RDT	• Ask patients presenting at HF or to a CHW about travel history • Ask HH members during active infection detection activities about travel history	• Nurses with three years training • Volunteer CHW (assists nurse) • EHT with four years training • Laboratory technician with three years training	• Electricity • Back up generator • Water • RDT • Microscope • Reagents and consumables • Computer in lab for documentation • Register for record keeping • Cell phone for weekly reporting	• Travel history obtained and infection classified as local or imported	• This determination is not conclusive