# MALARIA LABORATORY DIAGNOSIS AND MONITORING PROJECT

Nine Years of Action for Improving Quality of Malaria Laboratory Diagnosis and Case Management Services in Ethiopia







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#### **FOREWORDS**

#### U.S. President's Malaria Initiative

Since 2005, Ethiopia has made significant steps to expand coverage of key malaria control and prevention interventions throughout the country. The United States Agency for International Development (USAID) in collaboration with the United States Centers for Disease Control (CDC), through the U.S. President's Malaria Initiative (PMI), has provided substantial support to the Ethiopian Ministry of Health to achieve its goals in combatting malaria

PMI's contributions, together with those of other partners, have led to dramatic improvements in the coverage of malaria control interventions in Ethiopia. Of the major areas that PMI supports, the Malaria Laboratory Diagnosis and Monitoring (MLDM) Activity was instrumental in improving the quality of malaria diagnosis and treatment in Ethiopia. As a result of PMI's support for diagnosis and treatment, a large proportion of at-risk populations, served by MLDM-supported facilities are benefiting from quality-assured malaria diagnosis. Nine years ago, when we started supporting diagnosis and treatment of malaria in Ethiopia, there were only a limited number of facilities in Oromia Region that were targeted for the support. PMI has expanded the initial support to all nine regions in Ethiopia and over 1,000 health facilities across the country with the core objective of reducing malaria mortality by 40% and morbidity by one-third from 2015 levels respectively.

This booklet was created to share information about PMI and MLDM achievements and lessons learned with all stakeholders. Collaborating together we can build upon current gains and further improve the quality of malaria diagnosis and treatment in Ethiopia.



#### **ICAP**

Ethiopia has achieved a major scale-up of anti-malaria interventions since 2005. Hundred percent access to effective and affordable malaria diagnosis and treatment is one of the strategies set by the Federal Ministry of Health (FMOH) to prevent, control and eliminate malaria in Ethiopia. This requires improving diagnosis of malaria cases using microscopy or multispecies rapid diagnostic tests (RDTs), and providing prompt and effective malaria case management at all health facilities in the country. Thus, malaria diagnosis and treatment are essential components of anti-malaria interventions in the country.

Funded by the President's Malaria Initiative (PMI) through USAID, ICAP at Columbia University implemented Malaria Diagnosis and Monitoring (MLDM) Project from 2009 to 2017 in Ethiopia supporting and strengthening the FMoH, EPHI, regional health bureaus, regional reference laboratories and facilities to achieve the national goal for malaria control. Over the period since 2009, ICAP has provided technical, strategic, and operational supports for the implementation and strengthening of malaria laboratory diagnosis and case management in 1,026 health facilities across the country. ICAP has been implementing the MLDM project primarily in the Oromia, Amahara, Tigray, Southern Nations, Nationalities and People's regions and Dire Dawa city administration. Other regions have also received support from the project.

This booklet summarizes some of the achievements gained so far through the MLDM project in improving the quality of malaria diagnosis and treatment in Ethiopia. The booklet is produced with the aim of sharing the success gained and lessons learned so that it can stimulate institutions and experts that have committed themselves to improve the quality of malaria diagnosis and treatment in Ethiopia and beyond. Stakeholders are encouraged to use this booklet to build on the gains and unite to keep the momentum towards ending malaria for good.

### MALARIA SITUATION IN ETHIOPIA

Malaria is a leading health problem in Ethiopia. Approximately 60% of the total population live in malaria-endemic areas in Ethiopia, chiefly at altitudes below 2,000 meters. Due to the unstable nature of malaria transmission, major malaria epidemics had been one of the serious public health emergencies in the country. Recently, however, because of scale-up and sustenance of key anti-malaria interventions throughout the endemic areas of the country, Ethiopia managed to record significant reduction in number of reported malaria cases and deaths. Moreover, there have not been any major malaria epidemics in the country for the last fourteen years.

Since 2005, the Government of Ethiopia (GoE) has responded intensively to the health and socio-economic challenges posed by malaria through the support of development partners, primarily, the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM). The National Malaria Prevention and Control Strategic Plan, which is now revised for the period 2017-2020, direct the activities of the GoE. Major achievements to date include the distribution of over 90 million insecticide-treated bed nets (ITNs) and the introduction of rapid diagnostic tests (RDTs) as well as rollout of artemesinin-based combination therapy (ACT) to peripheral health facilities.

Although the Federal Ministry of Health (FMoH) has made tremendous progress, there are still critical gaps and challenges in malaria control, prevention and elimination efforts. Challenges include inadequate emphasis on malaria laboratory diagnostic services particularly in health center and hospital laboratories, limited implementation of quality assurance and control systems to monitor malaria laboratory diagnosis at the different levels, and the performance of rapid diagnostic tests (RDTs) under field conditions in Ethiopia. To address these gaps, the U.S. President's Malaria Initiative (PMI)/USAID Ethiopia is implementing the Malaria Laboratory Diagnosis and Monitoring (MLDM) project through ICAP at Columbia University in Ethiopia.

Approximately 60% of the total population of Ethiopia live in malaria-endemic areas



"I have benefitted much from the fever case management training. I have received very good updates on daily routine activities, especially on malaria cases."

Wondwosen Itefa, Health Officer, Jogir Health Center, Oromia, Ethiopia

### U.S. PRESIDENT'S MALARIA INITIATIVE (PMI) IN ETHIOPIA

Since 2008, Ethiopia has received support from PMI. This support, in combination with the five-year National Strategic Plan, aims to reduce malaria-related mortality by one-third from 2015 with proven malaria prevention and control interventions: ITNs, indoor residual spraying of households with insecticide (IRS), and improved use of diagnostics and case management. The PMI supported activities, which primarily targeted Oromia Regional State, the country's largest administrative regional state, which bears the brunt of the country's malaria burden, continued expansion of the activities to other regional states of the country in 2010/11, providing technical assistance to national structures, and offering technical and programmatic support and commodities to the Regional States.

Support activities continued to be focused on scaling up long lasting insecticide treated nets (LLINs), Indoor residual sprays (IRS), and improved diagnosis and case management, along with supportive activities such as SBCC, strengthening supply chain management and strategic information (e.g., surveillance, epidemic detection, and commodities micro-planning).

PMI's support to Ethiopia is in line with the GoE's HSTP (2015/16 - 2019/20) and national malaria strategic plan 2017–2020. Funding is targeted to fill gaps in activities that are not already supported by the FMoH, Global Fund, or other donors. PMI support also has been targeted to translating best practices to areas and activities currently supported by other funding agencies.

#### **ICAP OVERVIEW**

ICAP, based at Columbia University Mailman School of Public Health, is a global health leader that tackles the world's most pressing health threats and implements transformative. Since 2004, ICAP has been working with one central goal: to improve the health of families and communities.

ICAP is dedicated to delivering high-performing health system strengthening initiatives that improve access to quality and affordable health care. ICAP works hand-in-hand with partners at every level of the health system—from patients to health care providers to government officials. With its roots in comprehensive, family-focused HIV services, ICAP is known for capacity building and for innovative, effective, and ethical programs that are implemented in the most challenging resourcelimited settings. ICAP employs a collaborative and supportive approach to strengthening government health systems and local partners' capacity to deliver quality health services. To date, ICAP has worked to address major public health challenges and the needs of local health systems in more than 5,200 sites across 20 countries.

In Ethiopia, ICAP has been working with the FMoH and regional health bureaus (RHBs) and other partners since 2005 to scale up HIV prevention, care and treatment services and to strengthen the broader health system. ICAP supports HIV-related services in all 11 regions of Ethiopia and has supported over 700 health facilities, enabling them to enroll more than 465,500 patients in HIV care and to initiate more than 342,000 patients on HIV treatment. Today, ICAP's work addresses many major health threats, including tuberculosis, maternal and child health, malaria and non-communicable diseases. ICAP collaborates with local and national institutions in countries in sub-Saharan Africa and Central Asia, and in the U.S. to strengthen health systems and to implement innovative and sustainable health solutions.

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# MALARIA LABORATORY DIAGNOSIS AND MONITORING (MLDM) PROJECT IN ETHIOPIA

#### **Project objectives**

Through the MLDM project funded by PMI/USAID, ICAP aimed to strengthen the laboratory malaria diagnostic capacity and case management in Ethiopia by addressing critical gaps in malaria laboratory diagnosis, supporting best practices in clinical management of acute illness with fever, promoting appropriate treatment for malaria illness and conducting operational research for the control and prevention programs. The major objectives of the MLDM project are summarized in Figure 1.



MLDM Project

#### Specific objectives of the MLDM project:

- (i) Strengthen the partnerships and coordination of the national malaria laboratory diagnosis and monitoring activities involving all important malaria stakeholders in Ethiopia.
- (ii) Scale up and strengthen the quality assurance (QA) activities and laboratory systems related to malaria laboratory diagnosis in collaboration with Regional Reference Laboratories and what is now Ethiopian Public Health Institute (EPHI) (previously EHNRI).
- (iii) Train selected malaria program, clinical, and laboratory health professionals in malaria laboratory diagnosis and laboratory quality assurance and quality control (QA/QC) systems.

- (iv) Conduct operation research projects as directed by PMI.
- (v) Improve fever/malaria case management at PMI project sites and in Ethiopia.
- (vi) Strengthen the linkages between malaria, HIV, and TB diagnostic and treatment services at health centers and hospitals in Ethiopia.



MLDM micro-planning workshop, December 03-04, 2008

# Establishment of malaria laboratory diagnosis and monitoring project activities

ICAP Ethiopia started the implementation of malaria laboratory diagnosis improvement activities by conducting micro-planning workshop at the beginning of the project. The aim of the workshop was to review the existing major gaps and obstacles in standardizing malaria laboratory diagnosis and case management at national level. ICAP facilitated the participation of the National Malaria Control Program (NMCP), EPHI, the Oromia Regional Health Bureau (ORHB), and other key partners and stakeholders in malaria prevention and control in the workshop. Consequently, key intervention areas in terms of strengthening the malaria laboratory diagnosis and case management were identified.

The gaps illustrated in the diagram to the right were identified in the micro-planning workshop to be addressed during subsequent years of the MLDM project.

> Gaps identified in the micro-planning review workshop

# Table 1: Number of health facilities with baseline assessment conducted on malaria laboratory diagnosis (n=180)

Major gaps identified in health facilities	Number of facilities (Number, proportion)
Without functional microscope	42 (23%)
Without Giemsa stain supply	84 (47%)
Without supply of lancets	53 (29%)
Nithout supply of microscope slides	57 (32%)
Without microscope slide storage box	88 (49%)
Without slide staining troughs	136 (76%)
Without timers	54 (30%)
Without immersion oil	64 (36%)
With no electricity supply	33 (18%)
With frequent electric interruptions	111 (62%)
No in-service training on malaria microscopy	169 (94%)
No quality assurance/quality control protocols	167 (93%)
No regular regional external quality assessment (EQA) scheme	180 (100%)

No national diagnostic guidelines

No national malaria EQA guidelines

**No** training materials (diagnosis & case management)

**No** in-service training programs (diagnosis & case management)

**No** EQA program across the tier laboratory system

**No** standard & regular supervision & Mentoring

**Most lacked** functional microscope and HCT centrifuge

**Most lacked** quality reagents and other supplies for malaria laboratory diagnosis

Most lacked electrical power or had frequently interrupting electrical power

# Identifying gaps critical for malaria laboratory diagnosis through baseline assessment

Before starting MLDM project activity implementation, baseline assessment of the laboratory diagnostic capacity of health facilities is first assessed in order to identify the existing major gaps.

The identified gaps to the left significantly affect the quality and accessibility of malaria diagnosis. The results of the assessment were critical for developing and distributing the necessary guidelines, manuals, SOPs, formats and log sheets; for purchasing microscopes, supplies and consumables; for supporting regional health bureaus to undertake trainings of the health professionals in malaria laboratory diagnosis and case management; and, for conducting regular supportive supervisory and mentoring visits and external quality assessment in the facilities supported by the project.

# GEOGRPHIC COVERAGE OF ICAP'S PMI MLDM PROJECT SUPPORT

The project, which started its activity in 70 health facilities in five zones of Oromia region, has expanded its operation in the last nine years to 1,026 health facilities with the highest coverage in Oromia (705), followed by Amhara (162), SNNPR (94), Tigray (41) regions, and with complete coverage in Dire Dawa (17), the national malaria reference laboratory and 13 regional and sub-regional reference laboratories across the country.





# Total number of health facilities by region

Total number of health facilities by type



Among the 1,026 health facilities supported by the project, 947 (92%) of them are health centers and the remaining are health posts, hospitals, malaria control centers, national and regional reference laboratories.

# STANDARDIZING NATIONAL MALARIA DIAGNOSIS AND CASE MANAGEMENT

# Developing and updating policy guidelines and technical documents

Subsequent to the major gaps identified in the micro-planning workshop, ICAP facilitated and technically supported the development of the following policy guidelines, manuals, standard operating procedures, standardized laboratory registers, and job & bench aides displayed below.





Today all these materials are used by the national program and are distributed to the regional health bureaus and all stakeholders in malaria control and prevention



# National review workshop on malaria laboratory diagnosis

After two years of project implementation in 59 health facilities in five zones of Oromia, ICAP facilitated a national annual review meeting to expand the best experiences to health facilities in all zones of Oromia. The national review meeting included 69 experts. Among them were the malaria program managers from all zones of Oromia, malaria program officers from regional health bureaus, and laboratory heads of regional laboratories across the country and other partners. The gaps were identified and the strengths of project implementation were clearly outlined. Major recommendations were made to scaling up of project support to as many health facilities as possible. A proceeding of the annual review meeting was produced and distributed to all stakeholders.



National review workshop on malaria laboratory diagnosis and quality assurance programs

# Establishment of national slide bank of malaria microscopy slides

For introducing an internationally standardized training within a country and to strengthen the National EQA scheme through use of Proficiency testing (PT), the MLDM project has collaborated with EPHI to establish the nation's first malaria slide bank. ICAP supported the establishment of national malaria slide bank at EPHI by supporting the mass production, validation (by WHO) and storage of 10,742 standardized slides comprising P. falciparum, P. vivax and malaria negative slides and properly

furnished the bank. This slide bank is a key source for malaria laboratory EQA program through proficiency testing, national and international trainings and competency assessments. Facilitated the development of a memorandum of understanding (MOU) for malaria blood film slide exchange between countries in Africa so that the malaria slide banks in the countries will have all species of malaria parasites.



Standardized slides produced for the National Archive of Malaria slides, March 27, 2012, Adama

Preparing slides for staining with Giemsa, March 27, 2013, Adama.

Quality checks for selecting out slides with defects, March 30, 2012, Adama



### Other key national accomplishments

#### Through its PMI-funded MLDM project, ICAP in Ethiopia:

Supported the development and revision of national malaria guidelines, national malaria strategic plans, malaria elimination related guidelines and manuals and related documents;

Became an active member of the National Technical Advisory Committee (TAC), hosted by the FMOH, and the National Laboratory Technical Working Group (NLTWG), hosted by EPHI, to advocate and provide technical assistance on malaria laboratory diagnosis and case management.

Provided technical support in the development and revision of the national malaria guidelines (2012, 2017) and to the FMOH's launched dissemination workshop on the new malaria guidelines. ICAP prepared and presented the case management part of the guidelines to participants during the dissemination workshop.

Provided technical support to the development and revision of the national malaria strategic plans (2011-2015, 2014-2020 and 2017-2020)

Provided technical support to the development of the National Malaria Case Management training manual that is being used as a national document to train clinicians at hospitals and health centers across the country.

Provided technical and logistic support to both 2011 and 2016 FMOH's malaria program review by participating in desk review and field validation activities.

Provided technical support to the development of the nation's first malaria elimination strategy and the Malaria Laboratory Diagnosis and Quality Assurance Manual for Malaria Elimination in Ethiopia.

Provided logistical and technical support to the planning and implementation of the Malaria Indicator Survey 2011(MIS2011 & MIS2015).

Developed an algorithm for acute fever in adults and provided technical support in the revision of fever section of the IMNCI algorithm.

Provided technical support to the FMOH's grant proposals submitted to the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM).

Supported the development, printing and distribution of malaria laboratory diagnosis external quality assessment (EQA) scheme guidelines, manual for laboratory diagnosis of malaria, malaria microscopy job aides, standard operating procedures, comprehensive laboratory register, bench aids, and different formats.

Provided 12 standard microscopes to strengthen the National Malaria Laboratory at EPHI and facilitate the examination of slides collected in the MIS 2011 and MIS 2015.

Supported the printing of IEC/BCC materials for the celebration of the World Malaria Day starting from 2010.

Led the diagnosis and case management thematic area for the FMOH and the WHO-led national Malaria Program Review (MPR) and technically assisted in reviewing the National Malaria Diagnosis and Treatment Guidelines.

Produced and handed over 3,241 malaria and Borellia species positive slides to be used by Universities, health science colleges, national and regional reference laboratories across the country to help standardize malaria microscopy pre-service and in-service trainings across the country.

Participated in a series of and provided technical inputs to USAID's Country Development Cooperation Strategy (CDCS) Trends Analysis and consultative meeting on creating a new CDCS for Ethiopia

### REGIONAL AND HEALTH FACILITY LEVEL CAPACITY BUILDING

#### Provision of malaria laboratory commodities

ased on the results of baseline assessment, malaria laboratory diagnosis equipment, reagents and consumables were purchased and provided to MLDM project supported health facilities. Microscopes, mirrors and spare bulbs, led lights; hematocrit centrifuge, microscopic slides, Giemsa stock solutions, methanol, pH buffer tablets, staining jars, drying racks, lancets, gloves, etc. are among the laboratory commodities provided to the facilities to strengthen the quality of malaria microscopy. Multithreaded teaching type microscopes were also provided to Adama and Nekemte regional laboratories.



Donation of malaria laboratory commodities to a health facility



Teaching-type microscope donated to Adama and Nekemte regional laboratories

#### EQA and ssupportive supervision and mentoring



ICAP provided the health facilities under the MLDM project support with the EQA guidelines and other necessary documents, as well as SOPs and malaria laboratory commodities. ICAP trained their laboratory professionals and then continuously engaged in external quality assessment through on-site evaluation and blind rechecking. The respective regional laboratories continued to assess the health facilities under the MLDM project by rechecking the slides archived from the routine patient management. Feedbacks were prepared joint regional laboratories' and ICAP malaria laboratory advisors provided mentoring and supportive supervision. A significant improvement was observed in the EQA performance of facilities.

A stakeholders (EPHI, ORHB and USAID/PMI) review meeting on the lessons learned produced key recommendations on new approaches for strengthening and scaling up the malaria EQA scheme. This included certifying facilities to graduate from the blind rechecking scheme if the annual average performance is over 85% on the slide reading agreement after three consecutive rounds of EQA. In every four months, the graduated facilities are to be followed by on-site evaluation, supportive supervision and mentoring to subsequently address for any identified gaps to ensure that standards are maintained.

EQA participation showing progressive improvements of performance over time



Recognizing and certifying of facilities performing >85% slide agreement on regional EQA scheme

### HUMAN RESOURCE CAPACITY BUILDING

#### Summary of training on different thematic areas

In the first five years, ICAP's MLDM project provided trainings to about 1891 health care workers in different thematic areas as summarized in the table below:

# Number of trained health workers (October 2008 - November 2017)

#### Thematic area Total trained

ToT on malaria microscopy	352
Basic malaria/HIV laboratory diagnosis and quality assessment	3,762
External Competency Assessment of Malaria Microscopists (ECAMM)	37
Fever case management and malaria/HIV lab dx to clinicians	2,068
ientation on national malaria guidelines and fever case management	1,788
ever case management and malaria/HIV lab dx to program managers	337
Approaches to fever case management and malaria RDT diagnosis to HEWs	38

Total 8,382

"It is after that training that we are doing all that we are doing now. The training enabled us to differentiate all the malaria parasites including the stages. We never knew anything about EQA activities before we got the training. It would be helpful if we could also get refresher training"

> Gemechis Mesfin, Laboratory Head, Nedjo Hospital, Oromia, Ethiopia

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# Practical demonstration of malaria parasite detection and species identification

All laboratory staff in the supported health facilities received basic microscopic training, which included the transmission of theoretical knowledge and practical skills on parasite detection and species identification. Each trainee received a hands-on practical demonstration on every slide of P. falciparum, P. vivax, Borriella species and artefacts so that they can differentiate the parasite species and stage as well as quantify parasitemia per the standard. During the basic trainings in malaria microscopy, participants were subjected to a practical pre- and post-tests assessments on their skills and knowledge of parasite detection, species identification and parasite load.

Trainees' skill is evaluated before and after training using a standardized training evaluation database developed for this purpose and the result is compared as shown in the figure below.



# Improving malaria microscopy to international standards

ICAP in collaboration with other PMI partners implemented the WHO standardized External Competency Assessment of Malaria Microscopists (ECAMM) for national and regional reference laboratory malaria microscopists in Ethiopia. The course is designed to assess the competency of the professionals according to an international standard. In late 2016, as a preparation for this competency assessment, ICAP arranged for slides comprising of all human malaria parasites from the Research Institute of Tropical Medicine (RITM) in the Philippines to be provided for two rounds of intensive malaria microscopy refresher trainings for laboratorians of the national and regional reference laboratories. At the conclusion of the assessment, eight of the microscopists were recognized by WHO as level one expert readers and five as level two experts. This has increased the number of WHO certified level one expert microscopists in country by eight fold.

#### Training of trainers (ToT) on malaria microscopy

In order to expand the project support to as many health facilities in Ethiopia as possible, ICAP, in collaboration with EPHI, conducted a series of ToTs on malaria microscopy using the standard training modules and EQA guidelines. The ToT participants were selected from the national reference laboratory at EPHI, from regional reference laboratories, federal hospitals, hospitals of the uniformed forces, and other partners. Until today, about 190 laboratory professionals participated in ToT sessions. Further, ToT was provided to 162 instructors from colleges and universities in Ethiopia that train students in medical laboratory technology. The purpose of this training was to create awareness and to strengthen the pre-service training of students.



TOT on malaria laboratory diagnosis and quality assessment, August 07, 2011, Adama.

### Training on fever case management

With the intent to improve fever and malaria case management at the supported health centers and hospitals, ICAP developed an algorithm on managing adult patients with fever and has promoted the use of the IMNCI algorithm in children. In collaboration with regional health bureaus, ICAP has conducted trainings on approaches to fever/malaria management, and mentoring of health workers from the health facilities supported by the MLDM project. In such trainings, clinicians are taught and advised not to treat patients clinically without laboratory confirmation, nor to treat patients with negative blood film results (malaria negative) with antibiotics, but to assess thoroughly for other causes of acute

> Training on approaches to fever case management, March 03, 2010, Adama

febrile illnesses. So far, 2,405 clinicians and program managers, as well as 38 health extension workers and supervisors from 10 health posts participated in the fever case management training.



#### PERATIONAL STUDIES AND MAJOR FINDINGS

ICAP, in collaboration with FMOH, EPHI and the Regional Health Bureaus, has conducted operational studies in selected areas to inform policy decisions in malaria control and prevention activities. Part of the operational research on antimalarial drug efficacy (chloroquine and arthemeter-lumefantrine), antimalarial drug adherence, and burden of malaria/HIV co-infections has been completed and most findings have already been published.



Antimalarial drug efficacy study team

### EFFICACY OF ARTEMETHER-LUMEFANTRINE (AL) AND CHLOROQUINE (CQ) AGAINST PLASMODIUM VIVAX

Study was conducted between October and November 2009 in Bishoftu malaria control center and Bulbula health center.

Study was conducted according to the WHO standardized protocol and measured recurrent parasitemia, drug level and genotyping using microsatellite markers.

Using survival analysis, uncorrected patient cure rates at day 28 were 75.7% (95% confidence interval ((CI)) 66.8–82.5) for AL and 90.8% (95% CI 83.6–94.9) for CQ.

During the 42 days of follow-up, 41.6% (47/113) of patients in the AL arm and 31.8% (34/107) in the CQ arm presented with recurrent P. vivax infection.

Using microsatellite markers to reclassify recurrent parasitemias with a different genotype as non-treatment failures, day 28 cure rates were genotype adjusted to 91.1% (95% CI 84.1–95.1) for AL and to 97.2% (91.6–99.1) for CQ.

In the short term, both AL and CQ were effective and welltolerated for P. vivax malaria, but high rates of recurrent parasitemia were noted with both drugs.

CQ provided longer post-treatment prophylaxis than AL, resulting in delayed recurrence of parasitemia.

The co-administration of primaquine for treatment of P. vivax malaria needs to be urgently considered to prevent relapse infections.

For detailed information, see PLOS ONE May 2013 /volume 8/issue 5 e63433



Antimalarial drug efficacy study team enrolling a patient to a study, November 2012

### ADHERENCE TO ARTEMETHER-LUMEFANTRINE IN THE TREATMENT OF UNCOMPLICATED MALARIA IN ETHIOPIA

Study was conducted in 2010 in Asendabo health center and the nearby health posts of Merewa and Tikur Balto.

A total of 241 patients were assessed; 240 were enrolled for the day 3 follow-up visit. Only one patient was lost to follow-up and two were not included due to missing data.

In total, 237 persons were included in this analysis.

The total number of participants that were adherent based on the definition provided was 131 or 55% (i.e. 45% of the participants were classified as non-adherent).

Of the 106 participants who did not adhere to their treatment

- 50% took an incorrect number of doses
- 58% took an incorrect number of tablets per dose
- 6% reported sharing the pills with others
- 42% still had pills remaining at the time of the interview by report or pill count.

Adherence was lower for age groups 0-4 and 5-17 years when compared with participants older than or equal to 18 years.

Health facility type was not significant at the 0.05 level but did show a trend toward better adherence at health posts compared with health centers.

Higher adherence was observed in those who reported receiving three-part instructions.

### COMPARISON OF ARTEMETHER-LUMEFANTRINE AND CHLOROQUINE WITH AND WITHOUT PRIMAQUINE FOR THE TREATMENT OF PLASMODIUM VIVAX INFECTION IN ETHIOPIA

A one-year follow up study was conducted on 398 patients where the patients were randomized to four treatment arms. One group received CQ only (the current recommended treatment for P. vivax malaria in Ethiopia); the second group received CQ plus PQ; the third group received artemether-lumefantrine (AL) alone; and the fourth group received AL plus PQ. All patients were followed up for a year and were treated with the same treatment for every P. vivax malaria episode.

The risk of P. vivax infections at day 28 after treatment and also over 12 months was quantified. The risk of recurrence by day 28 and 42 was greater following AL than CQ. The addition of PQ to either CQ or AL reduced the risk of recurrence three-fold by day 42, and two- to three-fold over one year.

Patients treated with PQ had on average only 0.5 P. vivax malaria episodes per year, whereas patients not treated with PQ had on average two episodes per year. The efficacy of PQ treatment for recurrences, which was unsupervised, was three- to four-fold lower than that of the initial treatment, which was semi-supervised.

In Ethiopia there is evidence of CQ resistance; nevertheless, in this study CQ monotherapy had greater efficacy than AL therapy at day 42. The addition of PQ radical cure to either CQ or AL provided major benefits in reducing subsequent recurrent infection

For more details, see Abreha et al. PLoS Med 14(5): e1002299. https://doi.org/10.1371/journal.pmed.1002299

# BURDEN OF MALARIA AMONG ADULT PATIENTS ATTENDING GENERAL MEDICAL OUTPATIENT DEPARTMENT AND HIV CARE AND TREATMENT CLINICS IN OROMIA, ETHIOPIA

A comparative cross-sectional study among HIV-positive patients having routine follow-up visits at HIV care and treatment clinics and HIV-seronegative patients attending the general medical outpatient departments in 12 health facilities during the peak malaria transmission season was conducted from September to November, 2011. A total of 3,638 patients (1,819 from each group) were enrolled in the study. Provider initiated testing and counseling of HIV was performed for 1,831 medical outpatients out of whom 1,819 were negative and enrolled into the study. Malaria blood microscopy and hemoglobin testing were performed for all 3,638 patients. Data was analyzed using descriptive statistics, Chi square test and multivariate logistic regression.

Of the 3,638 patients enrolled in the study, malaria parasitaemia was detected in 156 (4.3 %); malaria parasitaemia prevalence was 0.7% (13/1819) among HIV-seropositive patients and 7.9% (143/1819) among HIV-seronegative patients. Among HIVseropositive individuals 65.4% slept under a mosquito bed net the night before data collection, compared to 59.4% of HIVseronegative individuals. A significantly higher proportion of HIV-seropositive malaria-negative patients were on cotrimoxazole (CTX) prophylaxis as compared to HIV-malaria co-infected patients: 82% (1,481/1,806) versus 46% (6/13) (P = 0.001). HIV and malaria co-infected patients were less likely to have the classical symptoms of malaria (fever, chills and headache) compared to the HIV-seronegative and malaria positive counterparts. Multivariate logistic regression showed that HIVseropositive patients who came for routine follow up were less likely to be infected by malaria (OR = 0.23, 95% CI = 0.09–0.74).

The study documented lower malaria prevalence among the HIV-seropositive attendants who come for routine follow up. Clinical symptoms of malaria were more pronounced among HIV-seronegative than HIV-seropositive patients. This study also reaffirmed the importance of co-trimoxazole in preventing malaria symptoms and parasitaemia among HIV- positive patients.

# THERAPEUTIC EFFICACY STUDY OF ARTEMETHER-LUMEFANTRINE OR DIHYDROARTEMISININ-PIPERAQUINE FOR THE TREATMENT OF UNCOMPLICATED PLASMODIUM FALCIPARUM AND DIHYDROARTEMISININ-PIPERAQUINE OR CHLOROQUINE FOR UNCOMPLICATED PLASMODIUM VIVAX INFECTION.

#### Objectives

To assess the therapeutic efficacy of AL or DP for uncomplicated Pf and DP or CQ for uncomplicated Pv infections based on parasitological, clinical, and hematological parameters.

#### **Specific Objectives**

1. To measure the clinical and parasitological efficacy of AL in patients aged more than six months with uncomplicated Pf malaria.

2. To measure the clinical and parasitological efficacy of DP in patients aged more than six months with uncomplicated Pf malaria

3. To measure the clinical and parasitological efficacy of CQ in uncomplicated Pv malaria patients

4. To measure the clinical and parasitological efficacy of DP in uncomplicated Pv malaria patients,

5. To differentiate recrudescence from new infection by molecular methods

6. To evaluate the incidence of adverse events

#### **Secondary Objectives**

1. To determine the polymorphism for known molecular markers of resistance

2. To determine the blood concentration of CQ

3. To determine parasite clearance rate, fever clearance rate, and gametocyte carriage rate

4. To assess hematological response

This research activity was completed and analysis is underway.



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