Malaria Elimination Task Force
Activity Report
May 2014-March 2018

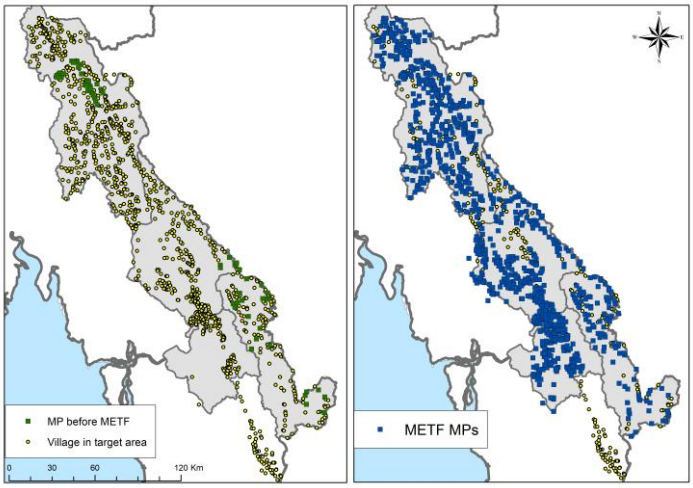
Content

The objective of the Malaria Elimination Task Force (METF) is to rapidly eliminate *Plasmodium falciparum* malaria in Eastern Karen/Kayin State, Myanmar. The specific target is the elimination of **artemisinin resistant** falciparum malaria. The METF started activities in May of 2014 in four townships of Karen/Kayin State. The task force is supported by the Global Fund Regional Artemisinin Initiative – Inter Country Component (GF-RAI-ICC) and the Bill & Melinda Gates Foundation (BMGF). The METF operates under the governance of an Executive Committee (EC) representing the major health-related organizations in the area.

This report in an update to the previous METF report which was ending in December 2016.

Summary of achievements: May 1st 2014- 30th March 2018

Mapping and geographic information system (page 20):
The Geographic Information System and subsequent maps contain data from over 1200 villages, spanning a geographic area of approximately 18000 km^2, divided into 3 areas (Area 1 = 6747 km^2; Area 2 = 6405 km^2; Area 3 = 4850 km^2) (FIG 1). The estimated population covered by MPs is 365303 (95% CI: 352381.4 – 378223.2). There are important differences between the areas in terms of population density, settlement patterns, transportation capabilities, communication infrastructure and access to electricity and water. The original geographic survey indicated that only 14% of villages in the project area had functioning MPs. This percentage has increased to >80 % of mapped villages (FIG 1). Geo-spatial analysis of the malaria surveys indicates that hotspot villages tend to occur in clusters, with nearby villages having similar malaria prevalence.



Community engagement (page 21):
The CE team has organized many meetings and workshops. Activities were concentrated particularly in the villages selected for the sub-microscopic prevalence surveys and in hotspots treated with MDA. The most important determinant of the effectiveness of MDA in the elimination effort is probably the level of participation in the MDA campaigns. Over 80% of village inhabitants received at least one round of MDA (i.e. one treatment course necessary for reservoir elimination). The proportion of participants who received the full 3 courses (needed for protection) was 62%. Overall the feedback from the population has been very positive.

Malaria posts (MP) (page 22):
As of March 2018, more than 80% villages of Hpapun, Myawaddy, Hlaingbwe and Kawkareik townships have a MP. The METF has trained 1648 MPWs, 133 MP supervisors, 47 Zone coordinators and opened 1226 MPs (FIG 1). A total of 341,808 fever cases were seen by the MPWs and 343,344 RDTs were used. Eight deaths related to malaria and 47 severe malaria cases were reported.

Real-time data collection and reporting (page 22):
Of the 1226 MPs, 866 (70%) presented no gap in their data reporting while 331 (29%) had one or several one-week gaps. Only 167 MPs (13%) had reporting gaps of more than one week. Many of these delays resulted from transmission or data entry errors that were subsequently resolved by checking the paper records. Across all available data the median (IQR) delay in data reporting is eight (three to10) days but there is variation by method (i.e. paper versus electronic). Gradual introduction of smartphones resulted in a rapid reduction in delays: data transmitted by SMS were available after a median of one day (IQR=0-2 days), while data relying on porters (Area 1) were available after a median of 8 days (IQR=8-9). All data generated by MPs are available on a secured portal that is accessible to all stakeholders: National Malaria Programme, METF partners and donors. Monthly reports are also generated and circulated among stakeholders.

Monitoring of MP(page 23):
Data was collected from 547 malaria posts visited since the beginning of the activity (August 2016). 74% of the surveyed MPs reported having never closed for more than 24 hours. At the time of survey, 44 (8%) of the MPs were out of stock of ACT or RDTs, indicating that 92% of the MPs are functional. 37 (7%) of the MPs declared that they suffered ACT or RDT stock-outs of more than two consecutive days in the previous month. 74% of MPs had received at least one visit from their supervisor over the previous two months.

Overall, 81% of consultations occurred between zero and 48h of fever onset, 13% of consultations occurred between two and three days and less than 6% after three days. These data suggest that most *P. falciparum* clinical cases were treated prior to the parasites becoming infectious (before the start of gametocyte production), and shows a strong mobilization of the community.

Surveys and mass drug administration (page 25):
272 prevalence surveys were completed. The prevalence of malaria was highly variable: ranging from 0% to 35% for *P. falciparum* and 0% to 64% for *P. vivax*. Out of these 272 surveys, 69 villages meeting hotspot criteria were identified. Most of these villages were located in Area 1. Sub-microscopic malaria hotspots tend to cluster spatially. Most malaria hotspot villages occur within five km of another high prevalence village and this pattern remains when examining at *P. falciparum* or *P. vivax* independently.

MDA was conducted in 61 communities. The proportion of villagers that received at least one round was high (median: 92%; IQR: 86-95). The median proportion of the population receiving the three rounds of MDA (complete coverage) was 64%

(IQR: 50-78). The difference between these proportions is explained in part by the population mobility which was lower in the communities of METF Area 1 than those from Areas 2 and 3. Furthermore, no severe adverse events were recorded following MDA. On average, 19% of individuals present in a village during a given month of intervention did not receive a curative course. These were grouped in three categories: 13% refusing, staying at home, or could not be reached; 4.5% not meeting inclusion criteria; and 1.3% who started the treatment but did not complete it.

Impact on malaria (page 27):

Impact of the MP network

Overall RDT-positivity for malaria was 12%, and 40,213 malaria cases were treated (14,001 *P. falciparum* and 26,212 *P. vivax*). Eight deaths related to malaria and 43 severe malaria cases were reported. This translates in a case-fatality rate of 0.6 deaths/1,000 *P. falciparum* cases, below what was measured in the area

before the METF project started (1.8/1000 cases). Results indicated that the incidence of *P. falciparum* started declining in the communities as soon as an MP was set up. The decrease in incidence was slower in the communities with the highest malaria burden, warranting specific intervention to speed up the elimination. Similar declines in cases were not seen for *P. vivax* and this resulted in significant changes in the Pf/Pv ratios that correlated with the duration of MP operating (FIG 2A and 2B).

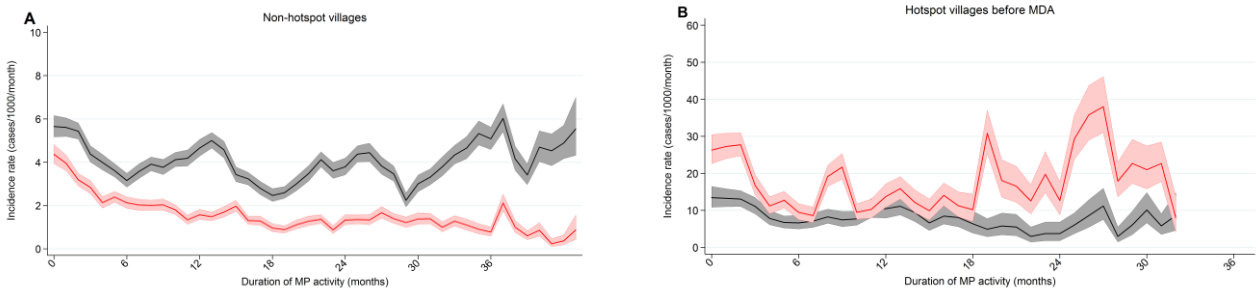


Figure 2 A and B Malaria incidence according to the age of the post and the hotspot status

Impact of MDA on hotspots

The prevalence of *P. falciparum* infection was estimated 12 months after MDA in 46 hotspot villages. All villages showed a sustained reduction of prevalence compared to baseline, *P. falciparum* infection prevalence decreased by 92% in median (IQR=81;100, n=46). The decrease in *P. vivax* prevalence only decreased by 19% (IQR=47% lower; 8% higher). The total number of clinical *P. falciparum* episodes originating from hotspots was reduced 5 folds after MDA and no rebound has been observed. MDA, in combination with MPs, had a rapid and sustained impact on the reservoir of *P. falciparum* and on the incidence of clinical cases in hotspot villages.

Approximately 72% of the villages in METF target region are under or have reached the WHO threshold of elimination of < 1 case/1000 person/year.

No increase in resistance

No increasing proportion of artemisinin resistance mutant (Kelch13) is observed in METF implementing 4 townships with accelerated malaria elimination interventions, average K13 mutants distribution around 40% from 2014-2017. There is no evidence for emergence of piperaquine resistance (plasmepsin2). However, we detect parasites with an amplified Pfmdr1 gene in the north that could indicate emergence of resistance to lumefantrine.

Entomology results

Seventy entomological surveys were conducted in 43 villages. A total of 116,353 *Anopheles* mosquitoes were collected and morphologically identified. Moreover, 9,536 specimens were analysed by allele specific multiplex PCR (AS-PCR) in order to discriminate between sibling species of malaria vectors and 15,441 specimens were analysed by quantitative real-time PCR *Plasmodium* in order to assess infection rates in the area. The abundance and species distribution was highly variable in time and space, suggesting high heterogeneity in malaria exposure across Kayin State. Malaria vectors in the region have a strong tendency to feed early and outdoors therefore the transmission that is not prevented by insecticide impregnated bed nets ("residual" malaria transmission) probably accounts for most of the transmission. Our results also confirm the low infection and high biting rates of malaria vectors in the area.

Conclusion

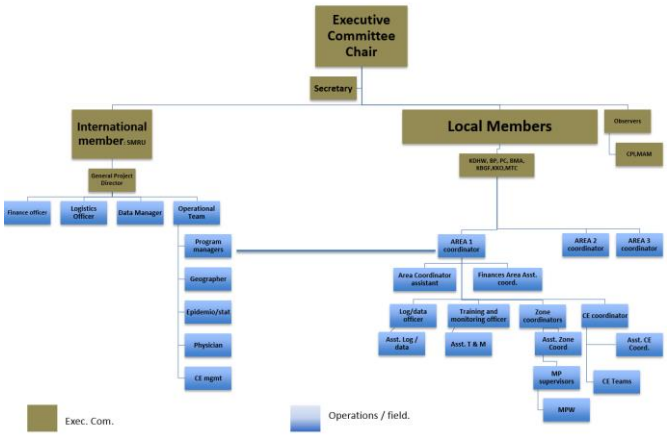
The METF programme provides a comprehensive and effective approach to malaria elimination and is the largest implemented so far in the Greater Mekong Region [27]. The METF is embedded in the community. It is evidence-based, reactive, adaptable and responsive. After 47 months of operation it now covers over 1220 villages, many in hard-to-reach areas of the eastern Karen/Kayin State. The success of the programme derives from a deep knowledge of the population and robust evidence gathered from over 30 years of malaria research in the area. The impact on *P. falciparum* has been spectacular, with a sharp reduction in the number of new clinical cases and entomo indices. The majority of the villages are now below the elimination threshold. This is attributed to the deployment and continued support of effective MPs and the rapid elimination of sub-microscopic infections by MDA. Continued success will depend on coverage of all villages in the area, effective MPs and the sustained efficacy of the drugs used. The objective for 2018-2020 is to maintain a tight early detection and treatment system to prevent re-introduction. Later, elimination of *P. vivax* malaria will provide substantial additional health benefits and critically will sustain the surveillance necessary to maintain elimination of *P. falciparum.* These results should encourage similar programs to be deployed elsewhere in Myanmar and across the Greater Mekong Subregion. As resistance to artemisinin and combination therapies is quickly spreading, we are clearly racing against time. The results of the METF project provide clear evidence that the rapid reduction and elimination of *P.falciparum* is feasible.

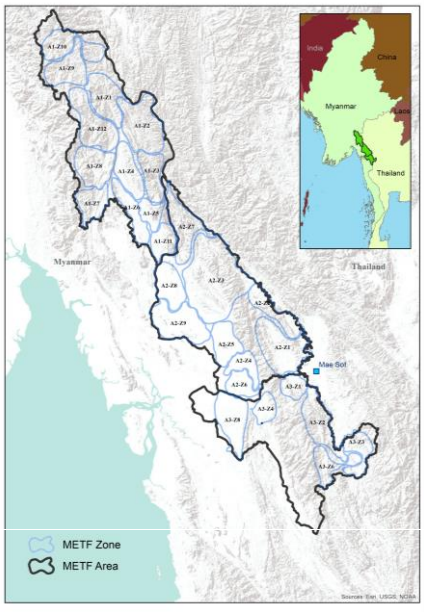
INTRODUCTION

The Malaria Elimination Task Force (METF) was set up in 2014 to conduct a large-scale project for *P. falciparum* elimination in 4 townships (Kawkareik, Myawaddy, Hlaingbwe, and Hpapun) of Eastern Myanmar (Karen/Kayin state). It is composed of one representative of local NGOs/CBOs (KDHW, MTC, BPHWT, BMA, KBGF, KPC, KKO, SMRU) [1]. Other organisations also involved in malaria elimination in Myanmar (MAM, CPI)[2] are invited as observers to the Executive Committee (EC).

A structure has been developed by the EC to facilitate communications, logistics, reporting, supervision and management (FIG 4).

- The project region is large and is divided into three 'Areas' under the responsibility of an area programme manager and a coordinator seconded by a technical team for CE, training/monitoring, data collection and administration (FIG 4).
- Each area is divided into zones, covering a stretch of land where health services are administered by one of the local NGOs/CBOs. (Fig 3)
- Each zone has a number of MPs (depending on the landscape and demographic concentration). An MP supervisor is responsible for 10 to 15 MPs.
- The central coordination team is composed of the area programme managers/coordinators, one epidemiologist/biostatistician, one geographer/spatial epidemiologist and a medical referent.
- This central coordination team is headed by a programme director and is based at SMRU in Mae Sot. SMRU provides support logistics, data management, grant management and laboratory support.





[1] KDHW: Karen Department of Health and Welfare; MTC: Mae Tao Clinic; BPHWT: Back Pack Health Workers Team; BMA: Burma Medical Association; KBGF: Karen Border Guard Force; KPC: Karen Peace Council; KKO: Klohtoobaw Karen Organization; SMRU: Shoklo Malaria Research Unit.

[2] MAM; Medical Action Myanmar; CPI: Community Partners International

The METF is supported by the Global Fund Regional Artemisinin Initiative – Inter Country Component (GF-RAI-ICC), the Bill & Melinda Gates Foundation (BMGF) and SMRU is supported by The Wellcome Trust of Great Britain. The aim of this project was to assess the feasibility of eliminating *P. falciparum* rapidly in the context of increasing artemisinin resistance. As such it can be considered as a study or pilot project aimed at answering operational or translational research questions and is endorsed by the Ministry of Health of Myanmar and the Karen Department of Health and Welfare (KDHW). It is approved by the Ethics Committee of the Myanmar Department of Medical Research. This report presents in detail the components of the elimination strategy and the results after 47 months of operation.

I. BACKGROUND

Malaria is endemic in Myanmar and a major cause of mortality and morbidity. The main plasmodial species involved are *P. falciparum* and *P.vivax*. Transmission is low and seasonal and caused by multiple anopheles vectors [4–6]. Along the border with Thailand, *P. falciparum* has become resistant to almost all available antimalarials including the artemisinin derivatives [7]. This problem represents a major threat to the region and the rest of the world. Given the paucity of new drugs, the only alternative is to attempt elimination before the rebound of malaria that inevitably follows the spread of high-level drug resistant parasites. Between 2012 and 2014 a pilot Targeted Chemo-Elimination study (TCE) was conducted in four villages on the Thai-Myanmar border [1]. These villages were selected because a high proportion of the population was infected with malaria parasites but without symptoms. In each village, malaria posts with RDTs and ACTs were provided as well as long lasting insecticide-treated nets (LLIN). Community engagement (CE) activities were conducted and mass drug administration (MDA) was offered to the populations in this controlled environment. The safety and acceptability of this intervention were carefully evaluated. The impact was measured by detailed surveys using an ultra-sensitive and validated qPCR assay [2]. Detailed entomological evaluations were conducted throughout the 24 months of the TCE study [8]. The results show that the strategy is safe and effective in rapidly eliminating the sub-microscopic reservoir of malaria parasites, in reducing the transmission to mosquito vectors and is well accepted by the population. It also indicates that new vector control methods are needed because the majority of infections were not preventable by LLINs. These encouraging results motivated the METF project to attempt *P. falciparum* elimination on a larger scale using the same approach [27].

II. PROGRAMME COMPONENTS

A. Mapping and geographic information system (GIS)

As Kayin State has been in civil conflict for over half a century, there was no accurate census or map for most of the target area [9]. This information is essential for all further steps in the project (including logistics, sampling and data management). The data generated from field mapping are linked to all other data (survey dates and results, logistics, financial matters, malaria cases at malaria posts, etc.), so that all programme data are spatially referenced in a geographic information system (GIS) and can be analysed in a spatially explicit manner. Maps are useful only if they are accurate, complete and rapidly acquired.

Mapping strategy:

- The entire area must be mapped at the smallest geographic unit possible (preferably at least one point per village). Mapping relies on "ground-truth" data as opposed to assuming that existing maps are true or only using remote sensing.
- During mapping basic attributes of a village or other small geographic area are recorded (population estimate, existing health facility capabilities, cell phone service, etc.)
- The area is frequently re-mapped, both as a form of quality control and to capture changes in the geography and demography of the region.
- Unique identification codes are assigned to each of the geographic points (villages or hamlets) and this code is used in all other parts of the program.
- From a logistic and administrative standpoint it is then useful to create aggregate units (e.g. "zones" and "areas") from geographic points.

Mapping logistics:

The mapping team is composed of community members familiar with the region, an experienced geographer and several trained staff. Mapping begins with training of these community members, who are recruited via local leaders. The training occurs in a central location and generally lasts one to two days. The training introduces basic map reading concepts, the use of satellite-enabled georeferencing systems (such as GPS (Global Position System) and GLONASS (Globalnaya navigatsionnaya sputnikovaya Sistema)), and survey forms. Trainings usually occurred in resource-limited field settings. Marker or chalk boards and maps printed on vinyl were used as instructional aids. Mapping trainings always concluded with a practical exam whereby new mappers are required to visit three to four locations near the training site, take a GPS reading at those locations and record the required information about those locations on the survey form. The forms are checked for accuracy on site and if errors are discovered retraining immediately occurs. As soon as field mappers are deemed capable of carrying out the survey, logistic plans are developed through the aid of local community leaders. The plans include which regions will be covered by mapping teams (usually mappers go in groups of two), roughly how long the mapping should take and how to return the GPS units and survey forms to the

central location. Once the survey forms and GPS units are collected at the central location they are shipped back to SMRU office.

Geographic surveys:
The first surveys focused on whether or not malaria services existed in a community, whether or not they are properly staffed and stocked, names of villages, and the number of houses in a village. A second wave of surveys (conducted in 2014) aimed to correct any missing geographic points that were missing from the first wave, to fill in any gaps in the target area map, and to identify the locations of referral clinics. In 2015-2016 a third wave of mapping and surveys included a small set of economic indicators, including basic questions about agricultural development (whether or not there were tractors in a village), transportation capabilities, electricity and water sources.

Technical aspects of the GIS:
Data from the forms are entered into spread sheets that are merged with the geographic data downloaded from each GPS unit. These data form the basic architecture for METF's geographic information system (GIS) and also provide a baseline understanding of the target population.

R statistical software (https://cran.r-project.org/) and Python programming language (https://www.python.org/) are used for data tabulations and merging; mapping of the data has primarily been done using ArcGIS (http://www.esri.com/software/arcgis), especially ArcMap; and QGIS (http://www.qgis.org/) is used for creating and manipulating some spatial shape files. The core GIS data are stored in a file geodatabase (file type .gdb). Each mapped village is assigned an arbitrary identification code and all information relating to a village (blood surveys, weekly malaria post reports, financial reports, etc.) is labelled using this identification code. Such data come in on a continuous basis and are merged to the core data set which can be viewed as a spread sheet (e.g. as a comma separated value file) in a wide variety of software (Access, Excel, LibreOffice, etc.) Python is used to pull new data from various sources and to update the base spread sheet. The geodatabase, spreadsheets and resulting maps are stored on a secure centralized server and shared with METF supervisors and administrators weekly.

B. Community engagement (CE)

Community engagement (CE) is a process by which a dedicated CE team (usually consisting of five – 15 people from the programme team and the community) works with the community to build relations and trust to develop an understanding and to facilitate community ownership of the malaria elimination project. The CE team draws on long-term ties to the target community and uses a modified community-based participatory action research approach [10]. The malaria elimination project relies on widespread participation and cooperation within and between villages. The success (or potential failure) of the project is

therefore heavily dependent on the ability to properly interact with the people, making CE a cornerstone of the malaria elimination project.

Preparation with social scientists

The malaria-focused CE work started with four pilot villages as part of the Targeted Malaria Elimination study (TME) in 2013. Through the experiences gained and lessons learned a guiding set of key themes was established, including principles and methods that could be applied across a wide geographic range in the scale-up programme (i.e. METF). Three major themes emerging from this preliminary work were human behaviour, geography, and social structures.

Human behaviour

CE workers and other malaria elimination team members must work toward understanding community members' worldviews, the ways that they allocate their time and the motivations and desires that drive their decisions and decision-making processes. For example, CE and other malaria programme tasks must not conflict with villager needs to work at certain times of the year. Most rural villages in the METF area follow a basic calendar revolving around rice paddy farming and several other crops. Harvest seasons (September to December) are typically labour-intensive and require some farmers to spend up to several weeks away to protect the crops and harvest them.

Geography

The physical and social geographic attributes of a community have important correlates with regard to CE, public health and ultimately malaria elimination. The relative physical and/or social isolation of a village has a major impact on the knowledge and understanding of the population as well as the logistic constraints of health-related work. For example, people in remote locations are often poor and have had little understanding of malaria or other public health threats. Malaria in such settings may be worse than elsewhere and may also be more difficult to address because of the remoteness.

Social structures

It is crucial that CE team members understand and utilize some of the existing social, political and economic power structures in place. Such systems include local village heads, township health officers, important religious and other political and military actors. Furthermore, socio-political dynamics can dictate appropriate means of engaging with community members and rolling out health-focused projects. For example, Kayin state has many different political actors, some operating simultaneously in the same areas. This political complexity can make implementation of health programs very challenging. The malaria elimination project has been able to work despite these potential obstacles through the incorporation and help of important key contacts. It is often possible to directly go to upper level health officials and obtain permission to set up a malaria programme in an area. Without community acceptance, however, implementation at the ground level may flounder. In at least some places it is much better to work through locally influential people who are capable of drawing on pre-existing strong relationships with villagers and to help navigate complex political hierarchies.

Implementing CE in all aspects of the project

CE training for MPs
Malaria posts are typically established in batches. Prior to MPW training, the CE team asks for a meeting with local health workers, village headmen, and other leaders. During this initial meeting the programme, MP function and CE are explained to local leaders. CE training also takes place with the actual MPW during training workshops. MPWs are educated about malaria biology and ecology, how to prevent malaria and what to do in case of malaria symptoms. This training is valuable for the MPWs who will also convey this knowledge to community members. Thus, the MPW effectively becomes an extension of the CE team, an important component, as he/she is already part of the local community.

Malaria prevalence surveys
Before embarking on a survey, the project team meets to discuss the detailed planning. Township-level health care leaders and village headmen are then asked to attend a meeting at a central location so that the plan can be proposed and the CE team asks for permission to conduct the surveys. Survey planning relies heavily on village headmen, who notify and gather the participants on the specific day and time(s). The concept of submicroscopic or asymptomatic malaria can be difficult to explain. Several workshops are organised to train local leaders (health care workers and village headmen) who are already trusted by local villagers and can therefore aid in the dispersal of knowledge and information.

MDA preparation
Once a village is identified for MDA, plans begin for CE exercises aimed at community preparedness. The Area and Zone coordinators inform the village headmen. The CE team arrives two days prior to the beginning of MDA in order to organize and set up new meetings with leaders and villagers to explain the medication, the potential side effects, and the regimen that will be followed. The MDA team stays in a village for seven days per visit to document any side effects, to address any concerns and to treat other minor illnesses. In villages with MPs already in place feedback from villagers after the seven-day period will come via MPW, through MP coordinators, Zone coordinators, and Area coordinators.

CE as an iterative process
CE is not a short-lived process with successes or failures that can easily be measured. The trust and understanding upon which the project is built are based on dynamic relations with the community. Part of this relationship includes providing feedback to the community about the project and reacting to new developments in the community, including rumours that can be detrimental. The CE team must play a central role with regard to such rumours. Rumours act like forest fires, the CE team and other project collaborators must be watchful and catch them early or they will spread far and damage the project.

Tools and activities used for CE
- Workshops, trainings, and group discussions (focus groups)

- Demonstrations and hands-on activities-learning materials including handouts, manuals and posters.
- Capacity building activities aimed at youth, including children's songs and poems, drawing, school activities aimed at teaching scientific methods.
- Participation in monthly village meetings, celebrations, and community work activities (such as farming).
- Household visits.
- Village incentives (water supplies or systems, buildings for community activities, solar panels, some training opportunities for health workers, boosting existing medical capabilities, providing basic out-patient care while the team is in the field).

C. Malaria posts (MPs)

MPs are set up in all villages in order to provide early malaria diagnosis and treatment for every fever case occurring in the community. MP tasks include:

- Testing all fever or suspected malaria cases in the village using RDTs within 24 to 48 hours of symptoms.
- Administering quality-assured anti-malaria treatment to all confirmed malaria cases: ACT+primaquine for *P. falciparum* and chloroquine for *P. vivax.*

This activity not only provides treatment for malaria-infected patients but also helps to limit the ongoing transmission of *P. falciparum* since early treatment of symptomatic *P. falciparum* cases prevents the emergence of gametocytes [11]. The use of quality-assured antimalarials contributes to fighting drug resistance that may emerge through the use of low quality or substandard drugs.

MP minimal requirements:

- A clean place that could be the MPW's household or another location
- Storage room or shelves with proper lock
- Continuous supply of RDTs, ACTs, data forms
- Trained MP worker, available at all times
- Correct diagnosis of malaria
- Correct treatment of malaria
- Timely data return

Choice of antimalarial treatment for uncomplicated malaria

Treatment algorithms (Annex 1) follow the Myanmar National Malaria Control Programme, the World Health Organization (WHO) treatment guidelines and the SMRU malaria handbook. For *P. falciparum* infections, a fixed dose formulation of artemether - lumefantrine (AL) is given for three days. Pregnant women are treated with quinine clindamycin for seven days in first trimester and artemether -lumefantrine (AL) in the second and third trimesters of pregnancy. A single low dose of primaquine (0.25 mg/kg) is given to prevent further transmission except in pregnancy, children younger than six months and lactating mothers. For *P.*

vivax, chloroquine 25mg base/kg over three days is used for the treatment. The doses administered are determined by the patient's s body weight.

MP worker (MPW) selection and training

MPWs are selected by the village headman and the community. They must have basic literacy skills, interest in health-related activities and they should live in the village. After selection, the MPW undergoes a five-day training covering malaria case management, referral and reporting systems, CE, followed by a course completion test. The training curriculum includes hands-on training on how to use RDTs, dosing-tables to administer weight-based ACT, record patients in logbook and report weekly cases in a standard form. MPWs are provided a MPW manual in a Kayin language (S'gaw), which serves as a reference for their daily activities. Refresher trainings are given annually and include re-trainings on malaria biology, treatment protocols, as well as any programmatic revisions, feedback about technical problems or difficulties encountered in the field. Pre- and post-testing is again conducted to ensure the quality of malaria treatment knowledge of the MPWs.

Real-time data collection

It is essential that all elimination efforts are coordinated at the regional scale in order for the programme to be piloted according to the situation. It is also important that logistics information is available at all times to prevent any stock-outs. Data reports are sent on a weekly basis and reports have to be available to the programme management team in near-real time. Weekly data reports fit on a one-page form (Annex 2) and include:

- All cases of fever by age groups (0-4y, 5-14y and ≥ 15y)
- All RDT results (*P. falciparum* / *P. vivax*/ Negative / Invalid by gender and age groups
- The number of severe malaria cases referred and the number of pregnant women with malaria and the number of deaths attributable to malaria
- Remaining stocks of ACTs and RDTs

The hierarchical organization of the programme allows data to be crosschecked and validated by MP supervisors during transfer from the site to the data centre.

All weekly forms are transmitted from the MPWs to the MP supervisor who controls them and sends them to the nearest data entry point. Data entry mode depends on location and access to a GSM (global system for mobile communications) network.

Paper transmission and online data entry is used for zones where no GSM network is available. Data collection in these zones relies on runners who collect the forms from the MP supervisors and transport them (using any convenient transportation means) to the nearest place where they can be entered in an online

data entry form and database developed using VooZaNoo®, an open-source form generator developed by EpiConcept[1].

In areas where access to a GSM network is available, individual weekly data reports are entered using a smartphone application and sent as SMS. Cheap (< $ 100) smartphones (Asus Zenfone 4) are used and are robust and reliable in most field conditions[2]. The data entry form has been developed from DroidDB, an android-based freeware[3]. All generated SMS reports (one per week / MP) are sent to dedicated phone numbers. One reception station is located in Hpa An office for areas relying on Myanmar GSM network and the other station is located in Mae Sot office for areas relying on Thai GSM network. They are extracted into Excel files and imported into the VooZaNoo database. During the week paper forms are collected by MP supervisors, transmitted to Zone coordinators and then to data centres to be filed for future reference.

Data quality and reporting

After aggregation, MP data completion and correctness is assessed regularly by searching for every duplicate and missing week of data in paper records and through integrated weekly GIS routines that link records to spatial references. A double entry is also performed on a subset of records. All errors that are recorded are transmitted to field staff in charge of data to provide key points during MP supervisor meetings and MPW refresher trainings. Regular cleaning of the database in search of duplicates and missing data is performed using paper records or other source data as necessary.

Reports on MP function, data quality and malaria indicators are produced weekly. Feedback information is provided to field teams for programme management and malaria surveillance. All weekly MP data are made available to partners and stakeholders on a secured internet portal and a monthly report on malaria indicators is generated and communicated to partners.

Monitoring of MPs

MPWs have weekly contact with their MP supervisors to aggregate individual patient data into weekly reporting forms. This allows for the follow-up of any event occurring during the previous week. During the initial months of the programme all used RDTs were sent to SMRU for a second reading. The activities of the MPs are continuously monitored via the weekly data reporting system. MPs that cease to transmit data, or report no activity or stock outs are visited by MP supervisors.

A team of six persons (two per area) was recruited for MP monitoring and evaluation (M&E) of the MP network (beginning in 2016). In an initial evaluation phase, 300 MPs (25% of total) were randomly selected to undergo an M&E visit. An M&E visit generally lasts half a day and involves extensive discussion,

[1] http://voozanoo.net

[2] In some places concentrating a lot (sometimes more than 50) malaria posts data for SMS transmission, smartphones have been replaced with 7" phablets (Asus fonepad 7), for more comfort. These phablets are available in Thailand at the price of THB 4,500 ($ 125).

[3] www.droiddb.com

observation of the MP environment and MPW skills (e.g. to perform RDT). During the visit, a standardised questionnaire is completed by the monitor, including observations (e.g. supplies, records) and answers to questions by the person in charge (Annex 3). All data collected are entered in an online database for subsequent analysis.

The M&E team also record geographic coordinates during their MP visits as a further check for concordance between MP identification numbers and the geographic coordinates in the METF data system.

In addition, systematic quality control of RDT is performed at central headquarters in Mae Sot. 15 MP are randomly selected each month and all RDTs from the selected MPs are assessed by experienced laboratory staff.

D. Malaria prevalence surveys:

Surveys are conducted at the village level to estimate the prevalence of *P. falciparum* and *P. vivax* malaria. An ultrasensitive high-volume qPCR assay (uPCR) is used so that low-density infections that would not be identified using microscopy (sub-microscopic infections) or RDTs are included in the prevalence estimates.

Sample size and randomization

To ensure that the selected villages are representative of the area a grid (with 20km wide by 30km long cells) was superimposed on a map of the target area and each cell of the grid was assigned a number of surveys, sufficient to reach roughly 25% survey coverage (from an original village count of 1000). Villages within each grid cell were then randomly selected. The within-village sample size is calculated taking into account feasibility constraints and the expected precision of estimates. The feasibility constraints are: small village populations, time and conservation of samples (cold chain and processing in Mae Sot within 48h of collection) and access and security of teams (in case of conflict areas or natural disasters). In order to estimate the prevalence of malaria infections of 40% with a precision of +/-10% and a 90% confidence level, the sample size required is between 41 samples for a village of 20 houses (~100 inhabitants) and 65 for larger communities (above 500 houses or 2500 inhabitants).

Surveys were planned in 250 randomly selected villages. As the deployment of the program progressed and more data on prevalence and incidence of malaria was available, it was possible to target an additional 50 surveys towards suspected hotspots: villages located in the vicinity of a hotspot, or villages presenting persisting incident clinical cases in spite of a functional MP for a long period of time.

Survey and laboratory analysis

Three survey teams conduct coordinated survey campaigns in selected villages within a defined sector, which are planned with and agreed by local health and political authorities. These campaigns can include up to 30 villages over several

weeks. The logistics are intensive as samples must be shipped to the lab within 48 hours of collection.

Before each survey CE activities are conducted to invite adult villagers to participate. Individuals are randomly selected and willing participants provide 2mL blood by venous puncture, after giving informed consent. Samples are collected on EDTA tubes, stored in an icebox and brought back to SMRU laboratory within 48h of collection. In the laboratory samples are centrifuged to collect packed red blood cells. DNA is extracted from 500µL and analysed by uPCR to detect malaria parasites. This method allows detection of parasitaemias as low as 20 parasites/mL [2]. It is estimated that >70% of the total population infected by *P. falciparum* can be detected by this method.

Monitoring of surveys

Monitoring occurs at the planning phase and when teams return since contact with the field is often difficult or impossible (little or no cell phone coverage in many areas). Reports include modifications of the number of samples collected to match the observed number of households in the target village and replacement of selected villages by neighbouring ones when surveys cannot be performed. Sample transportation is closely documented. Upon arrival, the samples, lists and consent forms are checked to ensure proper conservation, labelling and recording. In the laboratory a negative control is included for every 10 samples to detect potential contamination.

Hotspot definition criteria

A village is operationally classified as a "hotspot" when the 90% CI upper limit of the prevalence estimate is ≥ 40% and the corresponding value of the proportion of *P. falciparum* in the positive samples is ≥20%. This is an arbitrary definition and it is reviewed periodically using the data collected. Modelling work has suggested that malaria may more quickly be eliminated if these thresholds are lowered[1]. Surveys where an insufficient number of samples were collected are excluded from analysis.

Developing new tools for field detection of sub-microscopic malaria

In addition to the standard protocol, a specific component has been added to METF surveys to evaluate a new hypersensitive rapid diagnostic test (hsRDT) for *P. falciparum* developed by PATH (formerly Program for Appropriate Technology in Health: http://www.path.org). This hsRDT aims at a 10 times higher sensitivity compared to current RDTs and could be an important alternative to heavily constrained uPCR malaria detection [25] (low number of samples, time-sensitive processing, costly methods). Using already collected samples, our objectives are: to verify the intrinsic properties of this newly developed test (i.e. sensitivity and specificity, limits of detection) compared to currently available RDTs, microscopy and uPCR; and to compare the performance of different methods in the field to measure malaria prevalence

[1] There are practical limitations related to operational design, work load and other expenses associated with surveys and MDA

E. Mass drug administration

Choice of drugs for mass administration

In order to limit drug pressure MDA is conducted with different ACTs than those used in MPs. The regimen used in MDA consists of dihydro-artemisinin (7mg/kg) plus piperaquine (55 mg/kg) (DP) with a single low dose of primaquine (0.25mg/kg). DP remains highly efficacious against *P. falciparum* parasites in this region and is associated with a post-treatment prophylactic effect of around 30 days after one complete course. One treatment course (three days) is sufficient to eliminate the reservoir while three consecutive rounds of DP, one month apart are necessary to maximise the impact on transmission by preventing reinfection from infected mosquitoes.

MDA exclusion criteria

Women in the first trimester of a pregnancy, children under one year of age, individuals with previous drug allergies and villagers who refuse to participate are not included in MDA. Women within reproductive age (roughly 14 – 44 years old) and of unknown pregnancy status are screened with a urinary HCG test kit. Women in the second and third trimester of a pregnancy as well as breastfeeding mothers are eligible for DP treatment but are excluded from the single dose of primaquine.

Treatment administration

After obtaining informed consent, each eligible participant's medical history is briefly reviewed and a clinical examination is conducted. Those who meet the inclusion criteria are provided a three-day course of DP with a single low dose of primaquine on the first day and this is repeated over three consecutive months. Treatment is administered under supervision by the METF team to ensure participant adherence and to monitor the population for adverse events (AE). All AE that are reported by MDA participants within one week of taking an MDA course are carefully recorded and treated when necessary. (Figure 5)

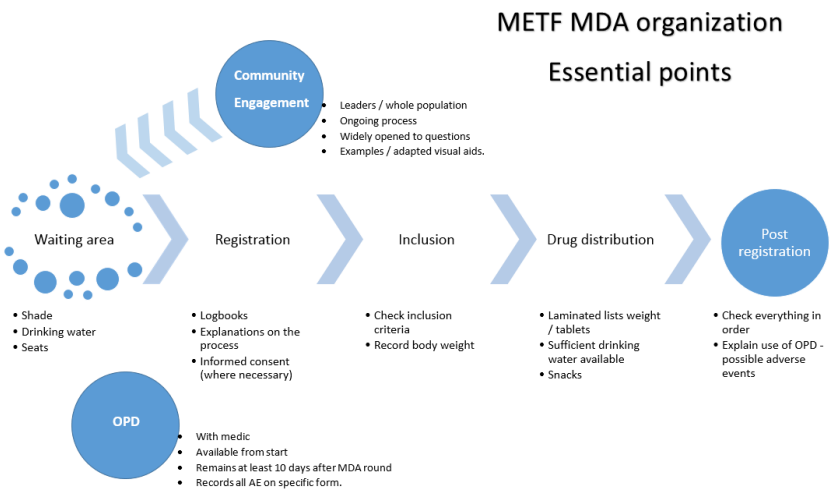


Figure 5 MDA flow chart

Monitoring of MDA

MDA activities are conducted in a stepwise process, with all steps documented and controlled. Teams of health staff are trained before each MDA. Consent forms and

MDA logbooks are used daily to record inclusion and to track participant presence and drug uptake. After each day some team members and their supervisor review the logbooks with the team supervisor to check for correctness of inclusion criteria, weight measurement, drug dosage and AEs. After each month of MDA data are transferred to spread sheets for field follow-up. At the end of the three-month period the logbooks are reviewed again and entered into an Access database. The medical team documents all complaints reported after taking the drug. A medical doctor reviews all symptoms reported to differentiate potential drug-related causes and non-drug related symptoms. The procedure for severe AEs involves alerting a medical doctor to conduct care and assessment of the case.

Assessment of MDA efficacy

MDA efficacy was assessed by prevalence surveys conducted 12 months after the start of MDA. The methods and analysis of these surveys are similar to baseline surveys, however, in order to have a more precise estimates the sample size is increased to roughly 80% of all adult village population for surveys. The sample size is increased so that statistically significant differences (from before and after MDA) can be detected, given that the original prevalence was relatively high. The number of required samples is calculated in order to measure a prevalence representing a 90% decrease of baseline PF prevalence, with a +/-50% precision, at the 95% confidence level.

F. Entomology

Entomological surveys

Mosquito collection was performed before (M0) and 12 months after (M12) the MDA. Mosquitoes were collected individually in 5mL plastic tubes for five consecutive nights from 06.00 pm to 06.00 am using both human landing catch (HLC) and cow bait collection (CBC) methods. A total of 70 surveys were conducted in 43 villages (43 M0 surveys and 27 M12 surveys) yielding a total of 2,972person-nights and 348 cow-nights of collection.

Identification of Anopheles

Anopheles mosquitoes were identified using the morphological key developed or the identification of *Anopheles* mosquitoes in Thailand [12]. Sibling species among the Funestus, Maculatus and Leucosphyrus Groups were identified using allele specific multiplex PCR [13], [14] and [15] respectively.

Plasmodium detection

The *Plasmodium*-infection rate of malaria vectors was assessed on whole mosquitoes using a quantitative real-time PCR (qrt-PCR) assay adapted from [16]. The limit of detection of this assay was estimated at 60 and 36 sporozoites per mosquito for *P. falciparum* and *P. vivax* respectively.

Entomological indexes of malaria transmission

The mean human biting rate (HBR) was calculated as the number of mosquitoes collected divided by the corresponding number of person-nights. The mean

sporozoite index (SI) was calculated for *P. falciparum* and *P. vivax* as the number of specimens positive in qrt-PCR *Plasmodium* divided by the total number of specimen analysed. The mean entomological inoculation rate (EIR) of *P. falciparum* and *P. vivax* was calculated as the number of specimen positive in qrt-PCR *Plasmodium* divided by the corresponding number of person-nights of collection.

G. Drug resistance in METF target area

Antimalarial resistance is monitored through clinical *P. falciparum* cases diagnosed and treated by MPs as well as through resistance markers. During an initial phase, *P. falciparum* positive RDTs were shipped back to the main METF office and stored in a dry, cool location. The RDTs were sorted by MP code (corresponding to the GIS) and sent to the laboratory for subsequent extraction of parasite DNA in order to monitor any major changes in the distribution of important drug resistance markers (markers for artemisinin, mefloquine, or piperaquine resistance) in parasite populations across the area [17–19]. The low amount of parasite genetic material on each RDT meant that this method yielded an interpretable result limited to K13 markers and for only 20% of processed RDTs. Beginning in 2015 MPWs were trained to collect DBS on filter paper from *P. falciparum* infected patients who had presented at an MP and were RDT positive. Since 2015 lab analysis also included mefloquine and piperaquine resistance markers (Pfmdr1 and plasmepsin 2 amplification).

III. RESULTS:

A. Mapping and geographic information system

Logistic results

Villages were aggregated into administrative units including malaria post coordinator areas (usually 5 – 15 MPs), Zones and Areas. There are 3 main Areas each with up to 12 Zones (FIG 3). The target area has now been completely re-mapped three times, each time carrying over a few survey questions as a quality control check for the data, and including new questions.

Geography, settlement demography and rough development indicators

Overall 1517 villages and hamlets have been mapped in the target area, spanning approximately 18002 km^2 divided into 3 areas (Area 1 = 6747 km^2; Area 2 = 6405 km^2; Area 3 = 4850 km^2). During the 3rd round of mapping some basic economic indicators were recorded. Survey coverage was extensive, though some small areas in the south of Area 1 and north of Area 2 were not covered because of armed conflict (Naing 2016). During 2017, 27 new villages were mapped (either non-accessed yet villages (20) or new villages created from internal displacements (7) linked to local insecurity).

A GIS database clean-up process was started, through a systematic review of all points corresponding to villages visited by the M&E team.

B. Community engagement

The CE team has conducted numerous workshops and meetings with community leaders and with the population most related to surveys and MDA, and also on the use of the malaria posts.

An overall good rapport between project implementers and targeted communities is evident through requests from community health leaders for further action to address *P. vivax* infections and by the ability of METF to cover to the target area (with the exception of small ongoing unrest zones) in only 2 years. From the community perspective, there is also a high demand of providing other health-related services at MPs.

MDA participation

Perhaps the best metric for measuring the success of community engagement (CE) efforts is participation in MDA. METF was regularly able to achieve greater than 90% participation in eligible villagers that were present in the village during a round of MDA. In a few cases, there were rumours of side effects or that the medicine could make villagers ill (see next section).

Rumour control

Rumours can have a major negative impact on any programme. Rumours that have emerged during the malaria project have typically been related to two main factors: 1) blood surveys (dangers or side effects related to sampling, fear of needles, fear of being tested for other conditions or that the blood will be sold, superstitious beliefs related to blood) and 2) MDA (concerns about side effects and fear of being poisoned). Seasonal illnesses sometimes overlap with timing of MDA or blood surveys, and this can result in rumours that the medication is causing illness. The CE team found that if community leaders and local village health workers understand and take ownership of the malaria program, people have more trust in the programme and rumours either do not start or are easily quelled. Focus groups have proven an effective tool to help elucidate potential trust problems, worries, doubts, or misperceptions about the malaria project.

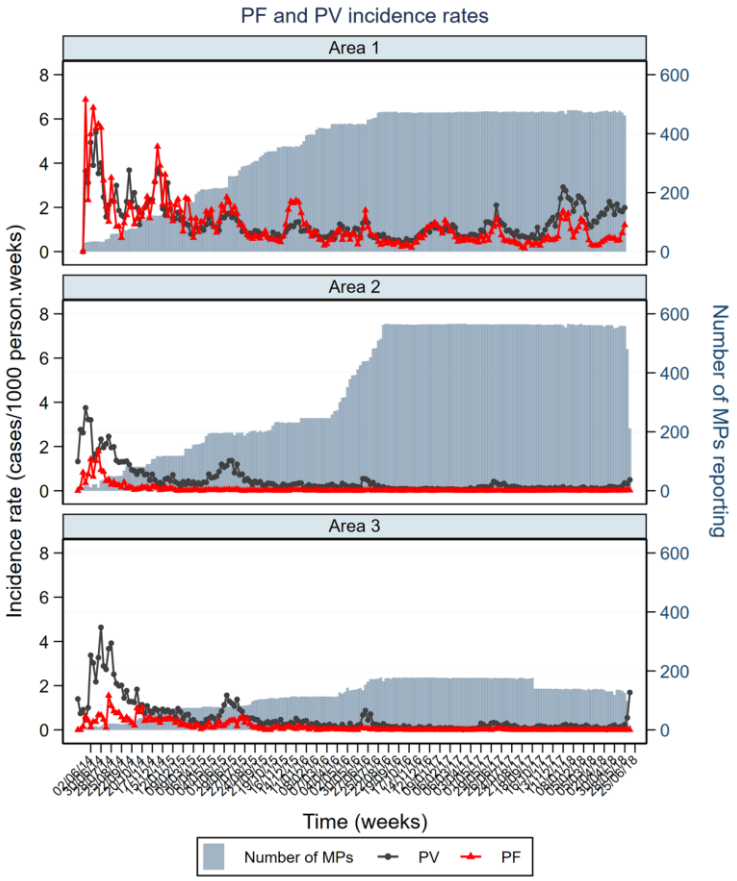
Filling in gaps in MP coverage

Some areas within the target area have been difficult to cover with MPs because of ongoing conflict. These areas have been drastically reduced in both size and number over the life of the project. The ability to open MPs in these areas is directly related to intensive efforts from the CE team to reach agreement with important actors on the ground and at higher levels. During 2017, precarious MP structures were set up in order to make sure approximately 10 villages that had to be evacuated due to continuous skirmishes still have access to malaria post services.

C. Malaria posts (MPs)

From 1 May 2014 to 30 March 2018, METF has trained 1,648 MPWs, 133 MP supervisors, 47 Zone coordinators and opened 1,226 MPs covering more than 80% of all villages mapped (FIG 1). Of these 1,226 MP, 1,183 were reporting in March 2018. Out of the 43 malaria posts not reporting, 37 MP located in places overlapping with another structure were reallocated to KDHW, and the 6 others are located in an area where conflict is sparking on and off , disrupting normal MP function.

During the 47 months of activities 341,808 fever cases were seen by MPWs and 343,344 RDTs were performed. RDT-positivity for malaria was 11.8%, with large seasonal and geographical variations (FIG 6). In total, 14,001 *P. falciparum* cases and 26,212 *P. vivax* cases were treated. Eight deaths related to malaria and 47 severe malaria cases were reported.



Malaria clinical case incidence follow-up

Incidence of RDT-confirmed clinical falciparum and vivax malaria cases was followed through weekly activity reports and showed strong differences between the three project areas. Area 1 had a higher incidence rate with pronounced malaria seasonality with one peak at the start of the rainy season (June-July) and one in the cold season (December). Areas 2 and 3 had generally lower incidence rates, higher proportions of *P. vivax* cases (Pf/Pv ratio<1) and one main malaria peak at the start of the rainy season (FIG 6). A strong decrease in malaria incidence was observed since the start of the program (see section E).

Real time data collection

The main indicators for success of real-time data collection are the level of data completion and the delay observed between the end of a reporting week and the availability of data in the database. Out of 1226 MPs opened by 30 March 2018, 686 sent data using smartphones, while paper data sheets were brought to online data entry points for 540. Among MPs transmitting by paper forms, 476 are located in Area 1 where no phone network coverage is available. Of these 1,226 MPs having reported during 2017, 1,089 (88%) presented no gap in their series

of data, while 143 (12%) had one or several gaps of one week. Only 15 MP (1.2%) presented gaps of more than one week.
Over the whole period since opening of the program, this translates into:

- No gap since opening: 860 (70%)
- 1 week gap only 202 (16%)
- Gap bigger than 1 week or more than 1 gap 167 (14%)

Many of these gaps result from transmission or entry errors and can be resolved *a posteriori* by checking the paper records. Across all available data, the median delay was 7 days (interquartile range (IQR)=1-9 days), but there is strong heterogeneity according to sending method. Gradual introduction of smartphones resulted in a steep decrease in delay where they were implemented: data transmitted by SMS is available after a median of 1 day (IQR=0-2 days), while data relying on porter carriage, mainly in Area 1, is available after a median of 8 days (IQR=8-9).

Quality control of data reporting and RDTs

Early in the project, the quality of the MP weekly data reports was assessed by double entry for 4,076 records (14% of all records) for 27 variables and 110,052 entries. Overall, the percentage of errors was 1%. Most of these errors (date format error, coding/spelling error, ambiguous handwriting) occurred within the first week of MP activity (111/4,076 2.7%). In the remaining 3,965 records the proportion of errors was 0.4%.

Systematic checking of reporting quality is now under implementation by comparison of real-time aggregated weekly reports to individual records (transmitted monthly and entered on a quarterly basis).

Central quality control (QC) of RDTs was conducted for 424 MPs for the period between December 2015 and December 2017, corresponding to 7,109 RDTs. RDT quality control performed over 1 month after the test was conducted present several challenges, especially when the tests are kept in harsh conditions that can alter the result. The most frequent problems are backflow of blood in test units (~30% of tests) and fading of control lines (~10%). From the 7,109 RDTs, 5,995 were read by a MPW as negative, 380 as *P. falciparum* positive, 7 as mixed infection (*P. falciparum + P. vivax)*, 634 as *P. vivax* positive, 12 as invalid, and 78 with unknown result. Of those *P. falciparum* 387 RDTs, 349 (90.2%) were confirmed by the control as *P. falciparum* positive, and 15 (3.9%) were rechecked as *P. falciparum* negative. Of 634 Pv RDTs, 400 (62.9%) were confirmed by control as *P. vivax* positive, and 51 (8.0%) were rechecked as *P. vivax* negative.

Monitoring and evaluation visits

Data was collected from 905 malaria posts visited since the beginning of the activity (August 2016 to 30 April 2018).
Each M&E visit consists of 2 persons visiting an MP which has been chosen randomly or selected based on suspected issues found in routinely collected data

from the METF program. During the visit the MP worker is surveyed by the M&E team to obtain information around MP stock management, training, supervisor visits, stipend received, MP closure and whether there was another MP in the area operated by another medical structure. Moreover, a 'treatment knowledge quiz' was passed to all MP workers and MP supervisors since January 2017.

Main trends revealed by M&E visits can be summarized as follows (Fig 7)

A vast majority of the MP are operated with at least 1 trained worker (86%). A majority of MP receive regular visits from their supervisor (More than 2 times in the 2 months prior to the visit 58%), but 34% declare not having had a Supervisors visit. As it seems that in these cases, the visit is done from the MP worker to the Supervisor, collection of this item has recently been modified.

Almost all do have the necessary forms and manual with them (98%) and receive their stipend regularly (98%).

In 18% of the cases (mostly in Area 2 and 3), the presence of another organization operating a MP has been reported. This issue will continue to be addressed at the Executive Committee level, in order to make sure there is no unnecessary overlap as this was already the case in Area 2, zones 5 and 7 where 37 MP were reallocated by KDHW,

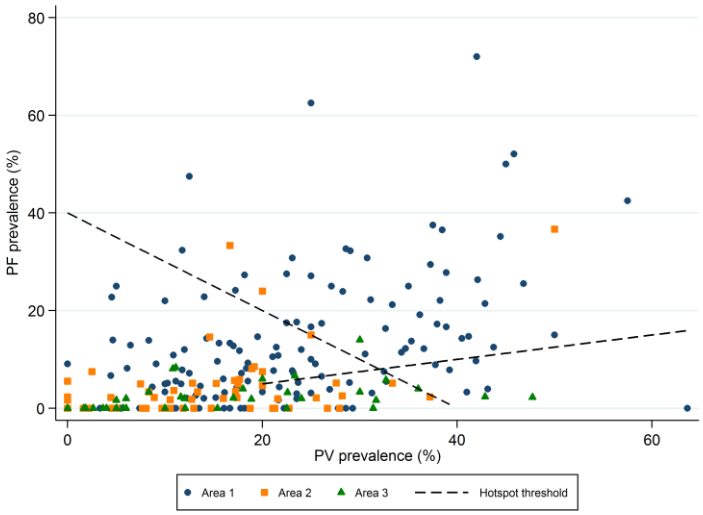
Indicator	Proportion	Percentage (%)
MP operated by at least 1 trained MP worker	493/573	86%
Supervisor visit frequency in past 2 months		
0	305/893	34.2%
1	105/893	11.8%
2 - 3	153/893	17.1%
≥4	308/893	34.5%
Forms on site	880/898	98.0%
Manual on site	878/898	97.8%
Regular salary received	866/886	97.7%
Another MP in village	166/889	18.7%
Observed stock outs		
ACT or RDT	78/897	8.7%
ACT and RDT	6/897	0.7%
Reported stock outs for >2 days in the past month	67/899	7.5%
MP closure for >24 hours in the past 2 months	219/901	24.3%

9% of the MP visited were having either ACT or RDT stock out, and less than 1% both in the same time. This shows logistics should be reinforced in some areas. 24% of the MP had closed for more than 24 hours in the previous 2 months, which needs also to be addressed through refresher training, as accessibility within 24 to 48 hours of fever onset is capital and a core element of the program.

As the treatment quiz is concerned, data entry is ongoing. A majority of MP workers replied correctly to 15 out of 20 questions (average 62% [min 40% Max 92%]), where the Supervisors to 18/20 (average 69% [min 39% Max 96%]). In all but 2 questions out of 20, supervisor's performance was higher than MP workers.

D. Surveys and Mass Drug Administration

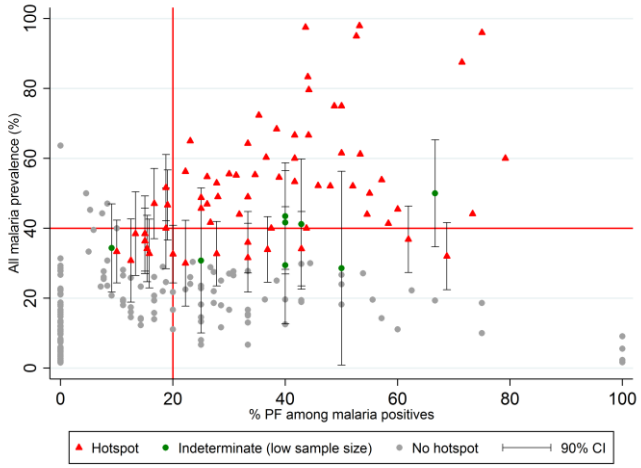
Survey progress and results



From April 2014 to December 2017, 272 baseline prevalence surveys were completed. Malaria prevalence was heterogeneous across the target area (FIG 8)

Baseline prevalence (proportions) of Plasmodium infection measured by qPCR at village level was heterogeneous, in median 21% (IQR=8-35%, n=272 villages). The median *P. falciparum* infection prevalence was 3% (IQR=0-11%), while *P. vivax* was 15% (IQR=5-25).

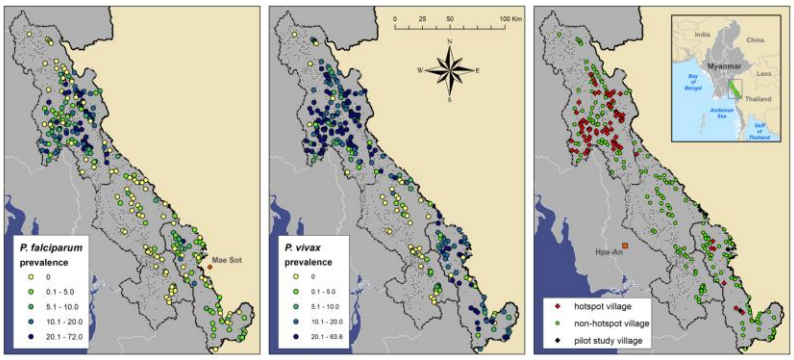
Detection of hotspots



Out of the 272 villages which have undergone qPCR surveys, 69 villages meeting hotspot criteria were identified (FIG 9). A large majority of these villages was located in Area 1 (FIG 10), also characterized by higher incidence of *P. falciparum* clinical episodes.

Spatial analysis of survey results

Hotspot villages tend to spatially cluster across the target area landscape (FIG 10).



Most hotspots were discovered in the northernmost region despite roughly proportional testing in all three major regions. Out of 272 villages that were randomly selected for malaria surveys, 69 were identified as hotspots, 21 (30%)

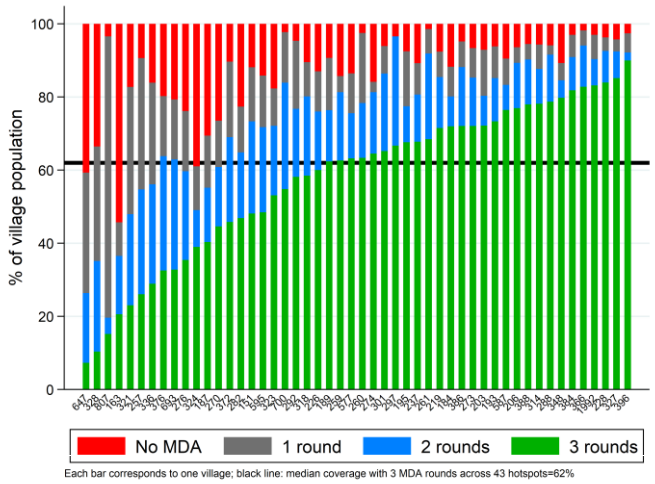
were located within 5 km from another hotspot and 33 (48%) were located within 10 km of one another.

Strong clustering of villages by malaria prevalence is also evident when analysing the quantitative prevalence estimates for *P. falciparum* or *P. vivax* rather than the binary hotspot/not data. Spatial clustering was most strong among villages in close proximity and decreased linearly. At 50 km distance there was no correlation between pairs of villages and by 75 km distance there was a significant negative correlation, indicating strong differences between villages that are geographically distal. This pattern of clustering is largely driven by the surveys in Area 1. When the data are stratified by Area the clustering pattern remains in Area 1 (though the overall pattern is less strong) but not in Areas 2 and 3. This suggests that there are no strong spatial patterns in prevalence in Areas 2 and 3, either of high prevalence or low prevalence villages.

These data and analyses suggest that malaria prevalence is the result of ecological patterns that exist on a scale larger than a village. This finding has strong implications with regard to estimating prevalence and their confidence intervals, as well as to mass drug administration, which relies on high proportions of participation among the target community. Well-connected villages or hamlets may behave as a single population unit or community. If only a small portion of a given unit is targeted with MDA, the overall proportion of carriers who participate will necessarily be low (i.e. surrounding villages with high prevalences won't be covered by the MDA).

MDA

MDA was conducted in the 61 out of 69 detected hotspots in five phases over two years. In 2015, 11 villages were treated in the first quarter, two villages in the second quarter and 16 in the third quarter. In 2016, 14 villages were addressed during the first quarter and 7 during the third quarter, and 11 were addressed in 2017. Data from participation was available for 61 villages for this report; and M12 prevalence was available for 46 hotspots out of 61 addressed for 1 year or more.



Monthly participation and population stability

The population of hotspot villages was generally small (mean=165 inhabitants, range=45-873). MDA targeted a total population of 13,687 persons (approximately 3% of the target area population). The median proportion of village populations taking ≥1 MDA round was 92% (IQR=86-95%, n=61 villages), and taking 3 rounds was 64% (IQR=50-78%) (FIG 11).

MDA coverage was measured by the proportion of the population that received 0, 1, 2 or 3 complete 3-day curative courses, over the 3 months of intervention. In villages with higher magnitudes of population movement, only part of the village population could be reached during each round. Population stability was estimated as the percentage of people present in the village during the 3 months of activity. This stability was lower in Areas 2 and 3 (median 80%) compared to Area 1 (median 87%). At the end of the 3-month intervention the complete coverage (i.e. the proportion of people that received 3 times the treatment course) was 62%, (IQR=49-72) and was significantly correlated with population stability (FIG 11).

Safety of MDA with DHA-piperaquine and single low-dose primaquine

Reported adverse events were analysed for 22 addressed hotspots. Among 14,182 delivered curative course of DP and PQ, the most frequently reported symptoms were dizziness (2%), nausea (2%) and headache (2%), followed by minor gastrointestinal adverse events (1%), anorexia (1%) and sleep problems (1%). Less than 1% reported fatigue and palpitations.

Reasons for non-participation

On average, 19% of individuals present in a village during a given month of intervention did not receive a curative course. These individuals can be grouped into 3 main categories: 13% who refused, stayed at home, or who could not be reached; 4.5% not meeting inclusion criteria; and 1.3% who initiated a treatment but didn't complete it. Among people refusing or staying at home, the main reason given was not wanting to take medicine, mostly because villagers did not feel sick, did not trust "western" medicine, or because they did not see malaria as a problem. Some participants already had other conditions, or felt weak and did not want to take another drug. Overall these results show that MDA intervention is feasible, and well-accepted by the population.

E. Impact on malaria

MP impact on Malaria incidence

The massive increase in access to early diagnosis and treatment (EDT) via MPs led to significant decrease of *P. falciparum* incidence at the village and the regional level. The number of *P. falciparum* cases recorded was usually highest during the first weeks of opening a MP in a village, and during the first malaria season. On average across all METF villages, the incidence was 2.5 cases per 1,000 people per month, during the first month of an MP opening. Afterwards the incidence rate of clinical falciparum malaria followed a decreasing trend, falling below 0.5 cases per 1,000 people per month after 2 years of MP activity (FIG 2). This decrease was specific to falciparum malaria, with lower reductions in vivax incidence related to MP inability to provide radical cure (requiring 7 – 14 days of primaquine which can be harmful in patients with G6PD deficiency). This decreasing trend was more evident in non-hotspot villages compared to hotspot villages.

The occurrence of *P. falciparum* cases at the village level also decreased. The probability of an MP declaring at least one *P. falciparum* case was 20% during the first months after opening in a village, similar to the probability of declaring one *P. vivax* case. After 24 months the corresponding figure was ≤10% for *P. falciparum* while that of *P. vivax* showed an increasing trend. This translated into a decrease in the Pf/Pv ratio according to duration of MP activity (FIG12).

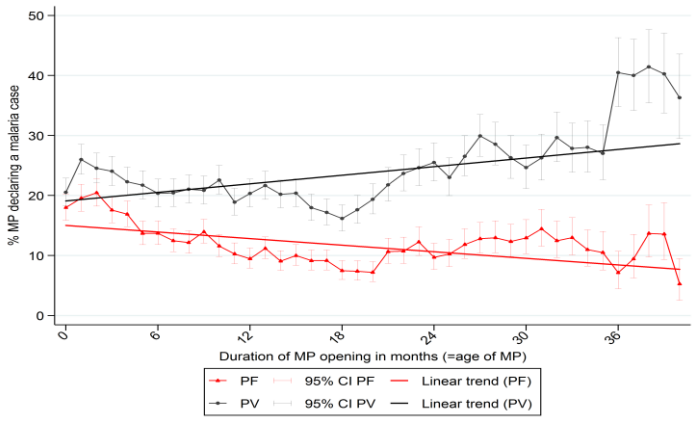


Figure 12 proportion of MP declaring a malaria case according to the age of the MP

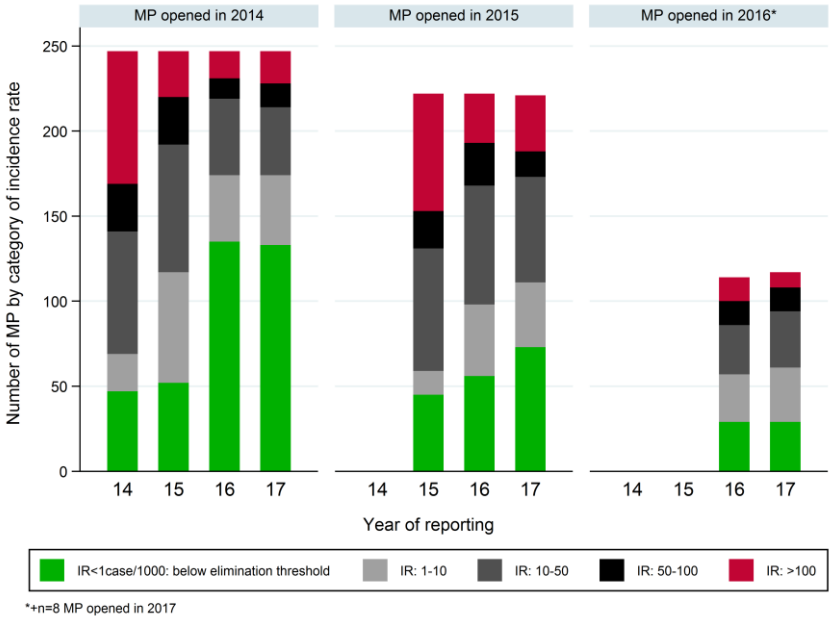
A statistical model was used to quantify the contribution of the different interventions and parameters to the evolution of the incidence rate of *P. falciparum* cases in METF target area. A negative binomial generalised additive multilevel model (GAMM) was used to quantify the impact of MPs, adjusting for seasonality in transmission, the geographic location of villages, elevation, and coverage of neighbouring villages with MP.

Results indicate that, on average, functioning MPs led to a 20% decrease in *P. falciparum* incidence rate for every 3 months of activity in a village (incidence rate ratio (IRR) for 10 additional weeks of activity=0.80; 95% Confidence interval (95%CI)=0.78-0.83). In addition, an increase of 10% in the proportion of villages equipped with an MP within a village tract resulted in a 5% decrease in incidence rate at the village level, indicating that there is a protective effect of being surrounded by MPs. Finally, this analysis also suggested that MDA had a significant impact on *P. falciparum* incidence in hotspot villages when compared to non-hotspot villages, beyond the effect of the MP itself. Before MDA, hotspot villages had a 3 times higher incidence when compared to non-hotspot villages (IRR [95%CI]=3.5 [2.4-5.3]), and their incidence decreased slower (IRR [95%CI]=0.85 [0.80-0.90] for 10 additional weeks of activity). After MDA there was no difference between hotspot and non-hotspot villages (IRR=0.8 [0.4-1.4]). Further data collection and analysis is warranted to understand if the impact of MP is similar in hotspot and non-hotspot villages.

Progress towards elimination at village level

Throughout the 47 months of the METF program there were an increasing number of villages with incidence rates under the WHO elimination threshold of < 1 case per 1,000 people per year. Many villages equipped with MPs reported no falciparum malaria cases (70% in 2016, 71% in 2017 and 78% during 2018 1st quarter). These posts were mainly located in Area 2 and Area 3, West of the Downa Range near the towns of Kawkareik and Hlaingbwe and opened in 2016. These low malaria prevalence territories are well-connected to high prevalence areas and surveillance is necessary across the entire target region.

Limiting the analysis to villages where MPs declared at least one falciparum malaria case since opening (n=604), the proportion of MPs below the elimination threshold went from 17% in 2014 to 41% in March 2018. The contribution of MP activity to falciparum malaria elimination is evident when looking at yearly incidence rate of MP by year of opening (FIG13).



Overall, 78% of MP in METF target region had a cumulative incidence rate below the elimination threshold for 2018 quarter 1. In Area 2, 90% of MPs haven't experienced a single falciparum malaria case for more than one year and in Area 3, 90% of MP haven't experienced a case during last rainy season (since April 2017). In Area 1, 40% of MP haven't experienced a falciparum case since the last rainy season (since April 2017).

MDA efficacy

The impact of MDA on the *P. falciparum* was strong. The long-term efficacy of MDA at reducing the asymptomatic and submicroscopic reservoir of *P. falciparum* was assessed by a prevalence survey conducted 12 months after the start of MDA. As of the 30th of March 2018, 46 hotspots had completed over 12 months of follow-up and were surveyed. At month 12, the prevalence of *P. falciparum* infection was around 0% in 14 villages and between >0 and 2.5% for 11 villages. 17 were between 2.5 and 10% and 4 above 10%. (FIG14)

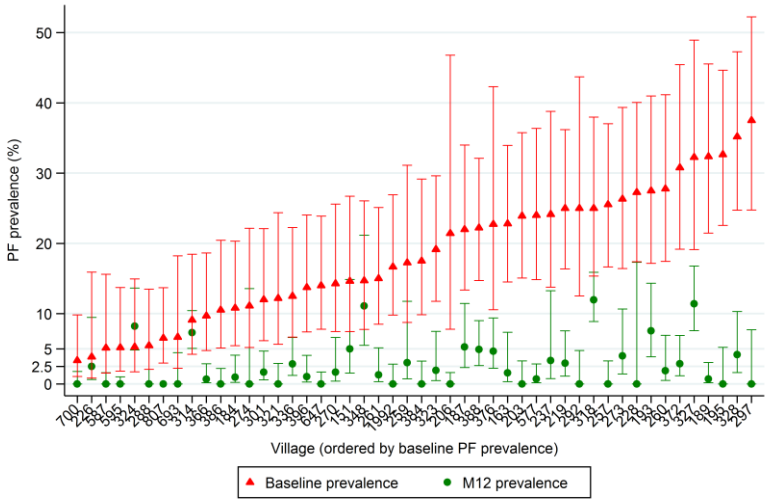
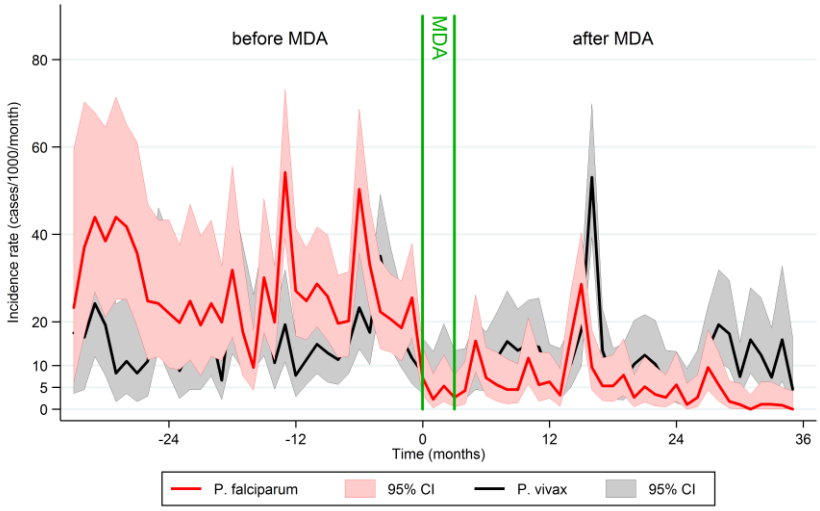


Figure 14 Pf prevalence at baseline and 12 months after MDA

The incidence of Pf clinical cases was also reduced during the period after MDA compared to the period before MDA (FIG15). In hotspot villages before MDA, 2,684 clinical cases of Pf were diagnosed and treated diagnosed 826 cases (6% of all cases) were recorded in hotspot villages after MDA.



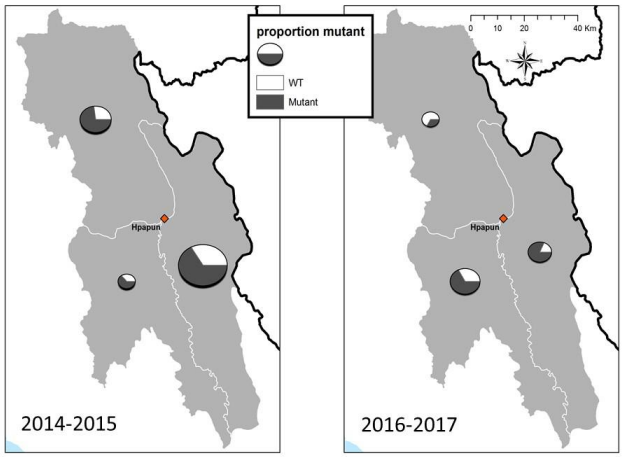
Modelling work suggests that MDA alone will not be sufficient to achieve elimination in the target area, but that through pairing MDA with a dense MP network elimination can be achieved. Our results show that in combination with MP activity, MDA proved successful at quickly eliminating the sub-microscopic reservoir of *P. falciparum* and accelerating the decline in incidence of clinical cases.

Drug resistance in METF target area

The drastic reduction in falciparum cases throughout the target area has made it difficult to collect and analyse samples from a single field site before and after MDA. Resistance markers are here reported by year.

Molecular marker of artemisinin resistance: Kelch 13 alleles distribution

The proportion of all analysed samples that were K13 wild-type in 3 area was 39% (101/258) in 2014, 37% (30/100) in 2015, 43% (221/516) in 2016 and 41% (119/288) in 2017. Prevalence of wild-type K13 alleles remained stable around 40% (95%CI=36-43).



There is evidence of changes in the proportions of certain K13 alleles (FIG 16) but not in the overall percentage of parasites with mutations (Annex 4)

Molecular markers of partner drug resistance: Pfmdr1 and plasmepsin 2 amplification

From 2015 onwards, samples were analysed for copy number variations in Pfmdr1 and plasmepsin 2, associated with mefloquine and piperaquine resistance respectively.

Prior to the beginning of METF there were high proportions of Pfmdr1 copy number variants in samples collected from SMRU border clinics. For example, between 1995 and 2003 there were 890 samples with Pfmdr1 multiple copy number out of 2284 total analysed (39%). All samples from 2015 that were analysed for Pfmdr1 copy number repeats (63) were single copy number variants. In 2016 eleven samples (out of a total of 554; 2%) and in 2017 thirteen samples (out of a total 243, 5%) had multiple copy number variants. There is slight increase in proportion of multiple pfmdr1 CNV. All samples that were analysed for plasmepsin 2 amplification (51 in 2015, 693 in 2016 and 247 in 2017) are single copy number variants (FIG 17).

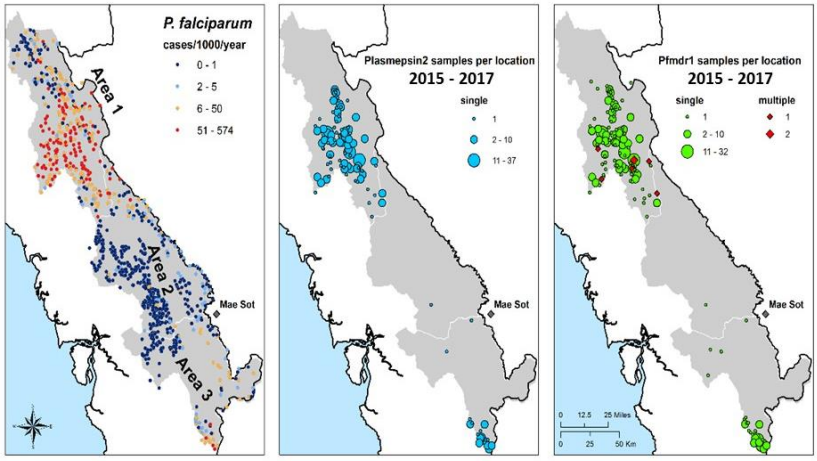
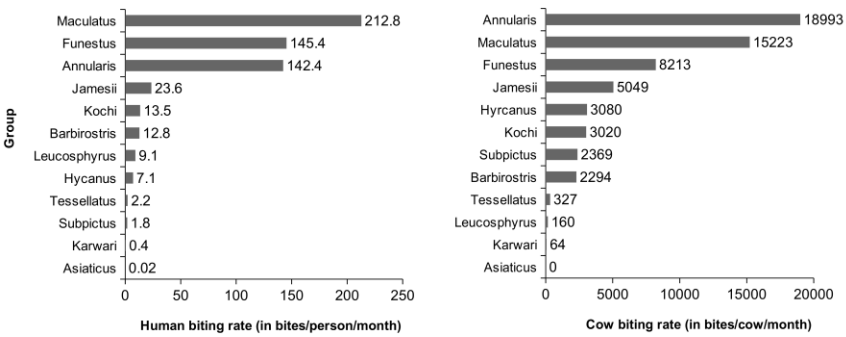


Figure 17 Distribution of partner drug resistance markers over time.

F. Entomology

Biodiversity of Anopheles entomo-fauna

A total of 57,560 and 58,793 *Anopheles* mosquitoes were collected by HLC and CBT during 2,972 person-nights and 348 cow-nights of collection, respectively. By morphology, it was possible to identify only 3 species *sensu stricto* (*An. karwari*, *An. kochi* and *An. tessellatus*). Other specimens belonged to 9 Groups of closely related species that are often difficult to discriminate by morphology. Five Complex of sibling species (*i.e.* species



that are not distinguishable by morphology yet being genetically different) were also detected, adding another layer of complexity to the taxonomy of *Anopheles* mosquitoes in this area: Minimus Complex (Funestus Group), Dirus and Leucosphyrus Complex (Leucosphyrus Group) and Annularis Complex (Annularis Group). The Maculatus, Annularis and Funestus Groups were the most abundant taxa collected by both HLC and CBC collection methods (FIG. 18).

Specific diversity in the Funestus, Maculatus and Leucosphyrus Groups was assessed by molecular identification methods on a subsample of 5,211 and 4,325 specimens collected by HLC and CBC, respectively (Tables 1 and 2). *Anopheles minimus s.s.* was the main species detected in the Funestus Group yet members from the Culicifacies and Aconitus Subgroups represented 7-17% of the remaining, according to the collection method. *Anopheles maculatus s.s.*, *An. sawadwongporni* and *An. pseudowillmori* accounted for 99% of the specimens from the Maculatus group. As expected, the Leucosphyrus Group was almost exclusively composed of two members from the Dirus Complex (*An. baimaii* and *An. dirus s.s.*). So far, the specific diversity in other Groups of *Anopheles* remains elusive.

Table 1. Specific diversity in the Funestus, Maculatus and Leucosphyrus Group collected by HLC, determined by molecular identification methods.

Group	Species	N	Percentage
Funestus (2,325/14,400=16%)	*An. minimus s.s.**	2160	93
	An. harrisoni	9	0.3
	An. culicifacies A***	11	0.5
	An. culicifacies B	85	3.7
	An. culicifacies C***	1	<0.1
	*An. jeyporiensis****	54	2.3
	*An. aconitus***	4	0.2%
	An. varuna	1	<0.1
Maculatus (2,107/21,083=10%)	*An. maculatus s.s.**	1259	60
	*An. pseudowillmori***	626	30
	*An. sawadwongporni**	210	9.5
	An. rampae	7	0.3
	An. dispar	3	0.1
	An. dravidicus	2	0.1
Leucosphyrus (706/902=78%)	*An. baimaii**	667	94
	*An. dirus s.s.**	37	5
	An. introlatus	2	<1

Table 2. Specific diversity in the Funestus, Maculatus and Leucosphyrus Group collected by CBC, determined by molecular identification methods.

Group	Species	N	Percentage
Maculatus (1,994/15,223=13%)	*An. maculatus s.s.* *	1208	60.6
	An. pseudowillmori **	478	24.0
	An. sawadwongporni *	285	14.3
	An. rampae	14	0.7
	An. dravidicus	8	0.4
	An. dispar	1	0.1
Leucosphyrus (133/160=83%)	*An. baimaii* *	124	93.2
	An. dirus s.s. *	9	6.8
Funestus (2,037/8,213=25%)	*An. minimus s.s.* *	1690	83.0
	An. culicifacies B	256	12.6
	An. jeyporiensis ***	46	2.3
	An. aconitus s.s. **	41	2.0
	An. varuna	4	0.2

* Primary malaria vectors
** Secondary malaria vectors
*** Suspected malaria vectors (role in transmission elsewhere)

Malaria vectors

The known primary malaria vectors on the border are *An. minimus s.s.* (Funestus Group, Minimus Complex), *An. maculatus s.s.*, *An. sawadwongporni* (Maculatus Group), *An. dirus s.s.* and *An. baimaii* (Leucosphyrus Group, Dirus Complex). *Anopheles barbirostris s.l.*, *An. annularis s.l.*, *An. aconitus s.s.* and *An. pseudowillmori* play a secondary role in the transmission. Several other species are suspected to contribute to the transmission because they have been incriminated as malaria vectors elsewhere: *An. culicifacies* A and C, *An. jeyporiensis*, *An. tessellatus* and some members of the Subpictus and Hyrcanus Groups.

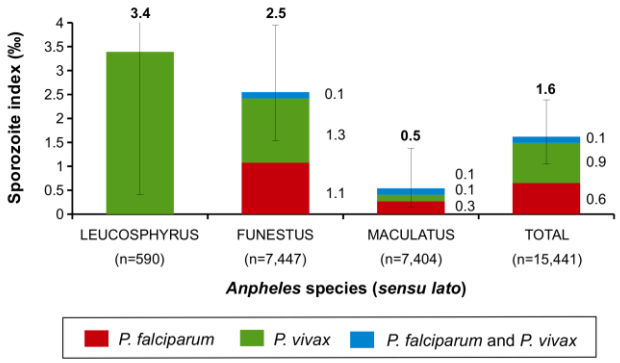


Figure 19 *Plasmodium* infection rate in naturally infected population of malaria vectors.

A total of 15,441 specimens from the Funestus, Maculatus and Leucosphyrus Groups collected by HLC were analysed by qPCR *Plasmodium*. Twenty-five specimens were positive (13 *P. vivax*, 10 *P. falciparum* and 2 co-infected with both *Plasmodium* species), yielding sporozoite index of 0.8 /1,000 (95%CI= 0.4-1.3) and 1.0 /1,000 (95%CI= 0.5-1.6) for *P. falciparum* and *P. vivax* respectively (FIG 19). The contribution of other *Anopheles* species to the transmission remains to determine.

Host seeking behaviour of Anopheles mosquitoes

Anopheles mosquitoes preferentially fed out of doors and an important proportion of the bites happened during the early evening (before 09:00pm) and during the early morning (after 05:00 am). Moreover, all *Anopheles* species were preferentially zoophagic (with the exception of some species in the Funestus Group, detected at very low frequencies). Members from the Maculatus Group were the most exophagic and zoophagic primary malaria vectors (*An. maculatus s.s.*, *An. sawadwongporni*), whereas members from the Dirus Complex were the least exophagic and zoophagic (*An. dirus s.s.* and *An. baimaii*). *Anopheles minimus* appeared to be very opportunistic, feeding equally on cow or humans, indoors or outdoors (Annex 5-8).

This early and outdoor biting pattern is an important determinant of LLINs efficacy. The proportion of malaria vectors that were collected indoors between 09:00pm and 05:00 am ranged between 16% and 41% according to the species, and only 28% (7/25) of the infected mosquitoes were collected indoors, between 09:00 pm and 05:00 am (FIG 20). The night biting pattern of anopheles mosquitoes suggests that exposure to malaria vectors and transmission may extend before 06:00 pm and after 06:00 am, hence minimizing even more the impact of mosquito bed-nets on the disease . More investigations are needed in order to quantify more accurately the part of the transmission that is not prevented by mosquito-bed nets. This would require to collect more data on the

diurnal activity of *Anopheles* mosquitoes, and to take into account the sleeping habits and movement of the population in the estimation

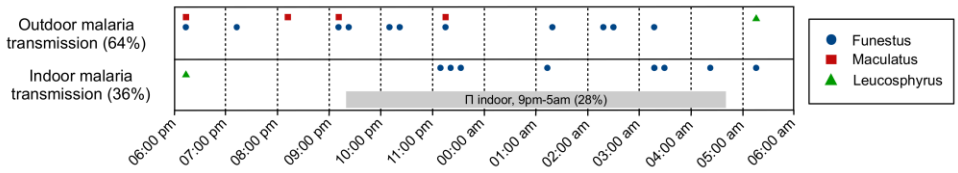


Figure 20 Distribution in space and time of the potential infective bites

Impact of elimination strategy on the entomological indices

Mean values of the entomological indices of malaria transmission determined before and one year after MDA campaigns are presented in the table 3. Our data confirm previous observations that high biting rate compensate for low infection rate in naturally infected populations of malaria vectors, yielding entomological inoculation rate of 6.8 and 8.4 infective bites /person /year for *P. falciparum* and *P. vivax*, respectively (M0 survey). Twelve months after MDA campaign, entomological inoculation rate of both *P. falciparum* and *P. vivax* was divided by five while HBR remained remarkably stable over the follow-up period.

Table 3. Evolution of the entomological indices between M0 and M12 surveys

	Value of the indice during the indicated survey	
Indice	**M0**	**M12**
HBR bites/person/month	*22,914/1,852* 371 (366 - 376)	*13,471/1,120* 361 (355 - 367)
Pf-SI /1000	*9/5,869* 1.5 (0.7 - 2.9)	*3/9,572* 0.3 (0.01 - 0.9)
Pv-SI /1000	*11/5,869* 1.9 (0.9 - 3.3)	*4/9,572* 0.3 (0.06 – 0.9)
Pf-EIR infective bites/person/month	*9/1,852*5,869/22,914* 0.57 (0.26 - 1.08)	*3/1,120*9,572 /13,471* 0.11 (0.02 – 0.33)
Pv-EIR infective bites/person/month	*11/1,852*5,869/22,914* 0.70 (0.35 - 1.25)	*4/1,120*9,572 /13,471* 0.15 (0.04 – 0.39)

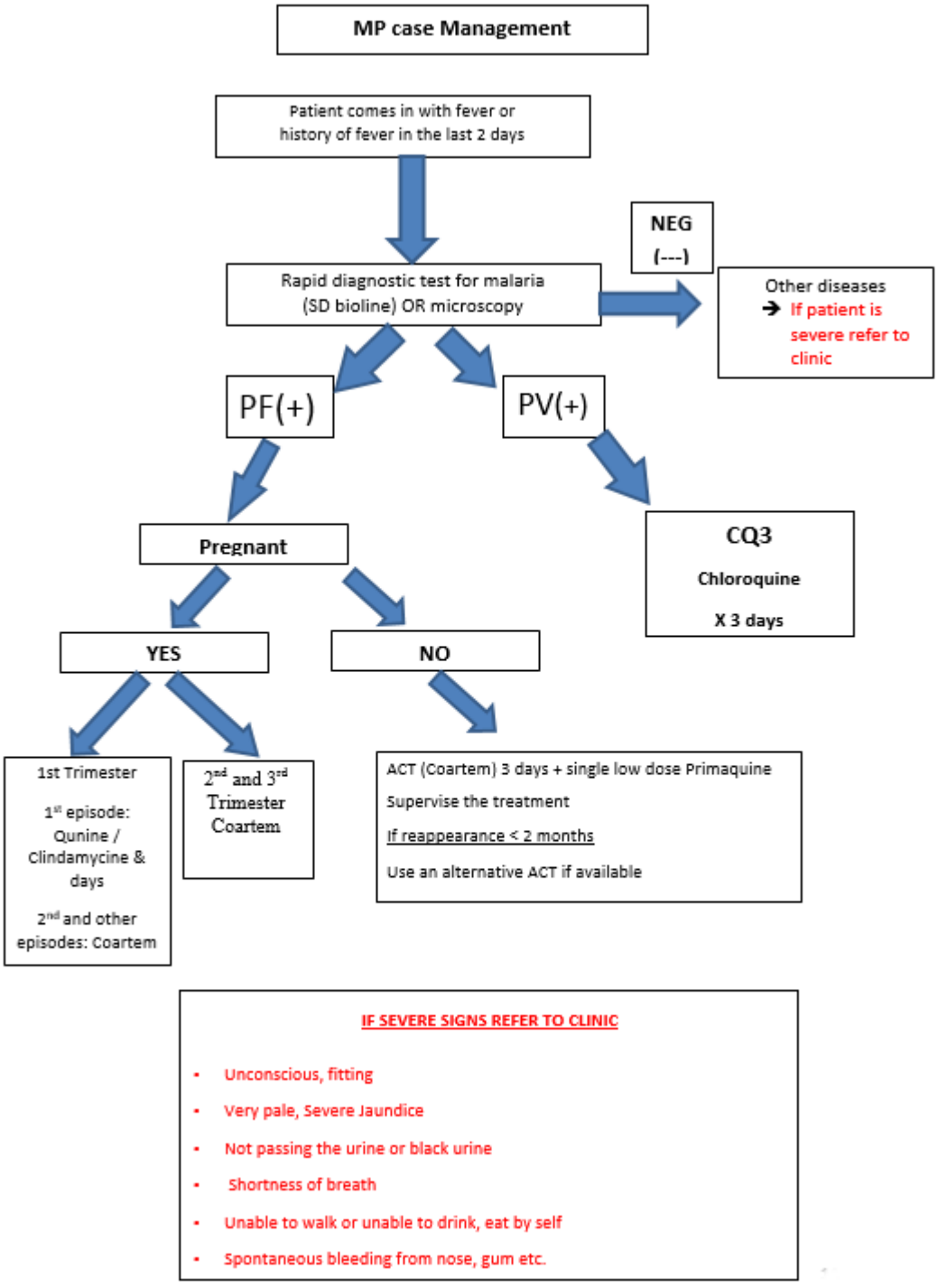
IV. DISCUSSION AND PERSPECTIVES:

The METF activities have shown considerable progress in the rapid elimination of *P. falciparum*. The strategy used for **elimination** complements that used for the **control** of malaria. In a malaria **control** programme the focus is on the people: preventing infections and treating clinical cases. In the **elimination** strategy the focus is on the parasite: treating patients **before** their parasites are transmitted to the vectors, searching and eliminating **the sub-microscopic reservoirs** because they maintain transmission and preventing new infections by using long acting drugs and adapted vector control measures. The detailed geographic knowledge (mapping), the strict terms of reference of the MPs (detect and treat within 24-48 hours), the real-time data and intelligence gathering and analysis (weekly), the search and treatment of sub-microscopic reservoirs (MDA) are all essential components of this elimination programme. The quality of CE is key to ensure community participation. At a programmatic level the involvement of all health-related Karen organizations (CBO, NGO) is essential to success, within a robust structure to ensure proper management and supervision. The results presented here are all very significant. Participation of the communities has exceeded expectations largely because of the trust built by the CE team, the MPWs have done a fantastic job (even if improvement is possible) and the number of *P. falciparum* cases has been drastically reduced and continues to decline. All operations are going smoothly because of the dedication of the supervisors, coordinators, trainers and surveys and logistic teams, despite operating under difficult circumstances. While the project is going in the right direction, care must be taken in order to not become complacent. Time is of the essence in the elimination of falciparum malaria. Parasite resistance to artemisinin, its derivatives and combination therapies is increasing in the area and new drugs are years away. While we have not detected any decline in the efficacy of piperaquine or the existence of piperaquine resistance markers in the target area, resistance to this drug has emerged in Cambodia and Vietnam [22, 23]. However the presence of parasites with multiple copies of Pfmdr1 in the Area1 could signal the emergence of resistance to lumefantrine. In addition there is a growing demand from the population to also tackle *P. vivax* malaria and this is an even greater challenge. As *P. falciparum* is disappearing from this part of Karen State, the *P. vivax* caseload becomes more visible. As Myanmar should be 'malaria-free by 2030' as indicated in Myanmar National Strategic plan [26], we also will assess the feasibility of using our dense EDT network to tackle *P. vivax* elimination, using primaquine radical cure, as G6PD point-of-care testing devices are now available [28, 29].
Finally, the transition from MP to health post to ensure that the surveillance system remains effective will need to be addressed in the coming months.

MSAT to replace MDA to complete elimination in hotspots
In spite of its success, the MDA strategy is considered difficult to scale up due to numerous constraints and was finally not retained by the Myanmar NMCP. However, the successful decrease in case incidence obtained by treating the reservoir of asymptomatic carriers sparks interest for a simpler and faster intervention, relying on mass screening and treatment (MSAT) rather than MDA. Such approach was previously impossible due to the lack of sensitivity of standard

RDT to detect asymptomatic infections. A newly available ultrasensitive RDT (URDT) shows a 50% sensitivity and 99% specificity compared to uPCR [24, 25]. This sensitivity is sufficiently high to allow accurate detection of high prevalence villages, and to warrant evaluation of the impact of a URDT-based screening and treatment intervention. MSAT is a method approved by the Myanmar NMCP and recommended by the WHO.

Annex 1: Malaria case management at the malaria post.



Annex 2: Weekly cases reporting form used in all malaria posts.

MP Worker Name:	(Village barcode)
|_________________________|	Report by: |___________________| name

Malaria Elimination Task Force weekly report form (SD BIOLINE)

*From date:|___|___| |___|___| |___|___| to date: :|___|___| |___|___| |___|___|

*Please count from **MONDAY** to **SUNDAY** always:
စးထီၣ်ဂံၢ်နၢ်လါမုၢ်ဆၢနံၤတုၤလါမုၢ်ဆဲၣ်ဖှိၣ်ထီဘိ/း

Table 1: Total fever cases ပှၤဆါတၢ်ကိၢ်ထိၣ်(Number of cases of **FEVER** တၢ်ကိၢ်ထိၣ်အနီၣ်ဂံၢ်)

	Total
<5 years	
5 to 15 years	
Older than 15 years (>15)	
TOTAL	

Table 2: Laboratory results တၢ်မၤကွၢ်အစၢတဖၣ် SD BIOLINE

	Pf	Pv	Neg	Invalid	Total
<5 years					
5 to 15 years					
Older than 15 years (>15)					
Total					

Table 3: Number of patients **TREATED** for malaria. ပှၤဆါလၢအဒိးန့ၢ်တၢ်ညၣ်ဂံၢ်ကသံၣ်နီၣ်ဂံၢ်

	Pf		Pv		Total
	Male	Female	Male	Female	
<5 years					
5 to 15 years					
Older than 15 years (>15)					
Total					

A. **Severe cases** within reporting week: ပှၤဆါလၢအနးဖဲတနွံအံၤတၢ်ဟ်ဖျါ |______|cases

B. **Death due to Malaria or suspected of Malaria** within reporting week: |______|cases
ပှၤဆါသံလၢတၢ်ညၣ်ဂံၢ်(မ့)ဆိမိၣ်လၢတၢ်ညါဂံၢ်အယိဖဲတနွံအံၤတၢ်ဟ်ဖျါ//း

C. Total pregnant women within reporting week: Neg |____| Pf |____| Pv|____|
ပှၤမိၢ်ဒၢနီၣ်ဂံၢ်လၢတနွံအံၤတၢ်ဟ်ဖျါ

Remaining number of SD BIOLINE tests in stock: တၢ်မၤကွၢ် SD BIOLINE လၢအအိၣ်တ့ၢ် |______|

Remaining number of COARTEM boxes for Pf treatment: ကသံၣ်လၢတၢ်ညၣ်ဂံၢ်ယၢ် Pf အဂၢ်အိၣ်တ့ၢ် |_____________| boxes

တၢ်ဂ့ၢ်တၢ်ကျိၤအဂုၤအဂၤတဖၣ်အဂိၢ်ကွဲးအီၤလၢအချၢတကပၤ.

Annex 3: Monitoring and evaluation form.

Malaria Post Assessment

Village Name ____________ Township ____________ District ____________ State ____________

[1]Malaria Post Code ____________ HH number[2]: ____________

Village GPS coordinates: LAT: ____________ LONG: ____________

Name of [3]Malaria post worker (1) ____________ (2) ____________

TRAINING : Yes ☐ No☐

RETRAINING: Yes ☐ No☐

Name of MP Supervisor ____________

MP worker not present ☐ Number of days since MPW away: .... Number of days until back: ....

If not at post, where did the MPW go ? ....

Assessment questions to MP workers (Ask to malaria workers directly)

		Condition	Comment/remark
1	Was the MP closed for > 24 hours in last 2 months? If MPW was available even if MP was closed, mention in remark	☐ YES ☐NO	
2	Are there valid ACTs in the MP? ([4]ACTs)	☐ YES ☐NO	
3	Are there vaild RDTs in the MP ? ([5]RDTs)	☐ YES ☐NO	
4	Were there >2 days out of stocks (RDTs or ACTs) in the past 4 weeks? (RDTs) (ACTs) Adequate or sufficient medication and supplies(observe and check carefully) SD biolines = tests ACT= tabs CQ = tabs PMQ = tabs Clindamycin	☐ YES ☐NO	If no, ask why
5	How are the results reported? ☐ SMS ☐ Paper ☐ Other (.................)		
6	Does the MPW receive regular financial incentive?	☐ YES ☐NO	
7	Is there another MP in the village?	☐ YES ☐NO	

[1] Malaria Post =
[2] House that are inhabitated =
[3] Malaria Post Worker =
[4] ACT =
[5] RDT = Rapid Diagnosis Test

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8	If YES, specify the supporting organization	____________
8b	: If Yes, do you receive malaria data from them?	☐ YES ☐ NO
9	How often did you receive the visit of your MP supervisor in the last 2 months? .... time(s) (supervisor)	☐ 1 Per Month ☐ <1 Per Month ☐ > 1 Per Month

Assessment by Evaluator (Check - List)

1	Is there a Malaria Post Manual in the MP?	☐ YES ☐NO
2	Are there reporting forms in the MP? (forms)	☐ YES ☐NO
3	Is there a logbook (daily recording of individual patients) in the MP?	☐ YES ☐NO
4	Are the "Days of fever" recorded for each patient? (Review the daily record sheets)	☐ YES ☐NO
5	Are there more than 5 consecutive days without activity[6] in the logbook?	☐ YES ☐NO

1. Comment or suggestions from malaria post worker.

____

2. Comments or suggestion from the observer.

____

Name : ____________

Signature : ____________

Date : ____________

[6] Activity = (case of fever)

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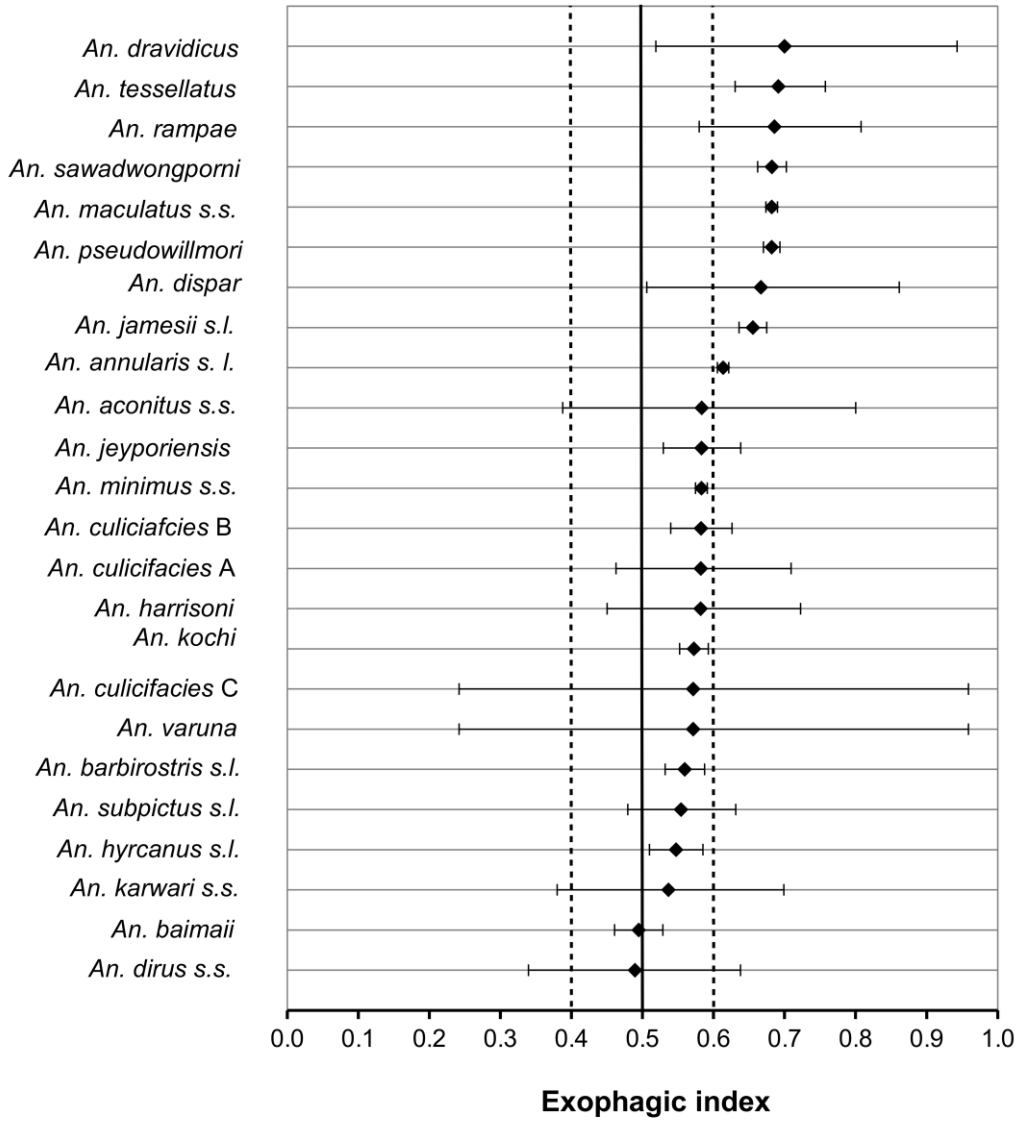
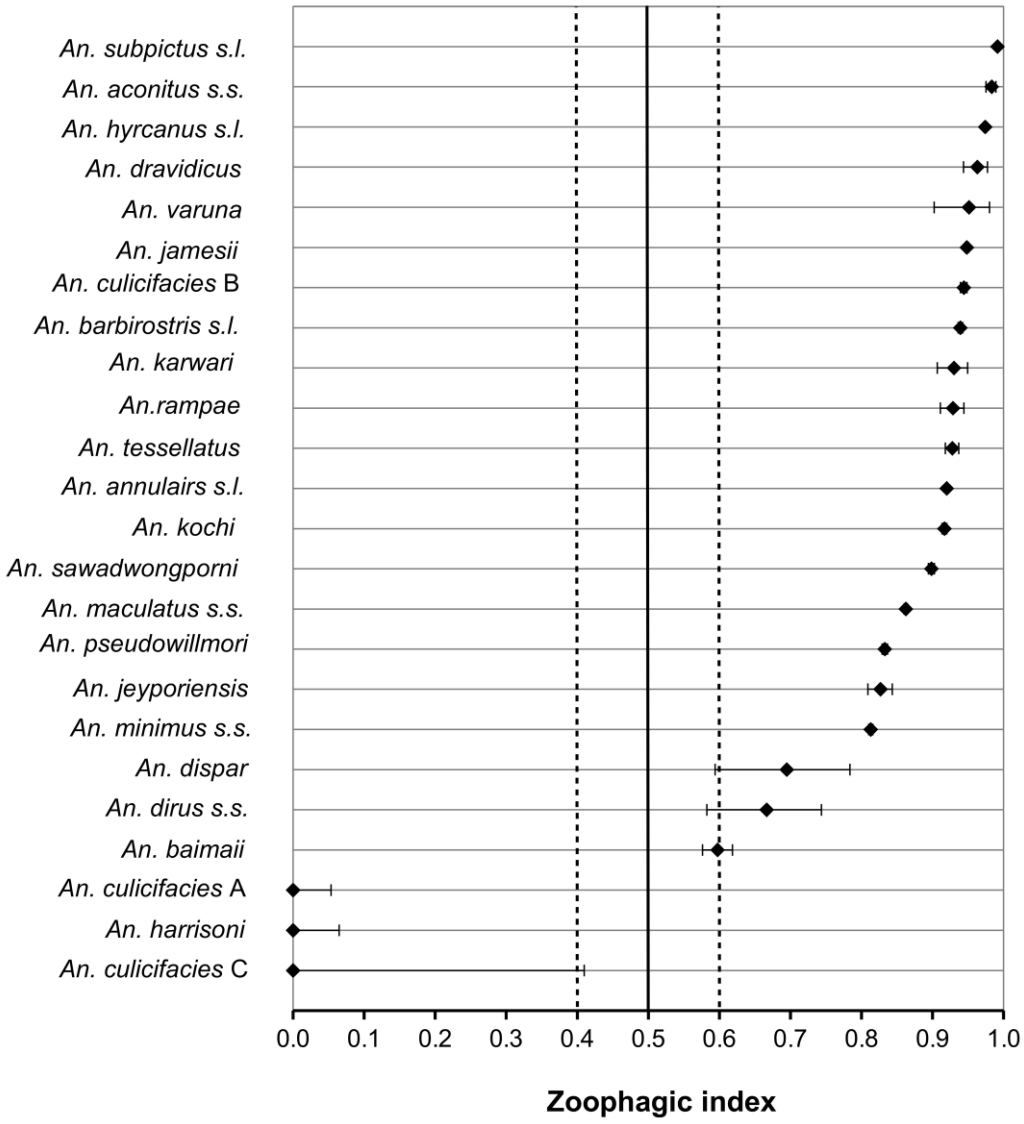
Annex 4: K13 alleles distribution 2014, 2015, 2016

2014			2015			2016			2017		
K13 Alleles	Frequency	Percentage	K13 Alleles	Frequency	Percentage	K13 Alleles	Frequency	Percentage	K13 Alleles	Frequency	Percentage
A626S/A	1	0.4	C469F	3	3.7	C469F	3	0.6	C469F	3	1.0
C469F	1	0.4	C469Y	1	1.2	C469Y	2	0.4	C580Y	13	4.5
C469Y	1	0.4	C580Y	9	11.0	C580Y	15	2.9	F446I	21	7.3
C542Y	1	0.4	G533S	8	9.8	C580Y/WT	2	0.4	F446I/WT	3	1.0
C580Y	14	5.4	K189T	2	2.4	F446I	62	12.0	G449A	22	7.6
E252Q	26	10.1	M476I	1	1.2	F446I/WT	2	0.4	G533S	1	0.3
F446I	27	10.5	N525Y	1	1.2	G449A	35	6.8	G538V	5	1.7
G449A	9	3.5	N537I	11	13.4	G449A/WT	1	0.2	M476I	19	6.6
G533S	22	8.5	P441L	8	9.8	G533S	4	0.8	P441L	55	19.1
G538V	1	0.4	P574L	6	7.3	G538V	4	0.8	R561H	23	8.0
K189T	2	0.8	R561H	2	2.4	M476I	18	3.5	WT	119	41.3
M476I	16	6.2	WT	30	36.6	M476I/WT	3	0.6	T535M/WT	1	0.3
P441L	6	2.3	Total	82	100.0	M562I	40	7.7	P667T	1	0.3
P574L	4	1.6				M562I/WT	1	0.2	C580F	1	0.3
R265P	1	0.4				P441L	58	11.2	N458Y	1	0.3
R539T	1	0.4				P441L/WT	7	1.4	Total	288	100.0
R561H	24	9.3				R561H	34	6.6			
WT	101	39.1				WT	222	42.9			
Total	258	100.0				G533S/WT	2	0.4			
						P553S/WT	1	0.2			
						R561H/WT	1	0.2			
						Total	517	100.0			

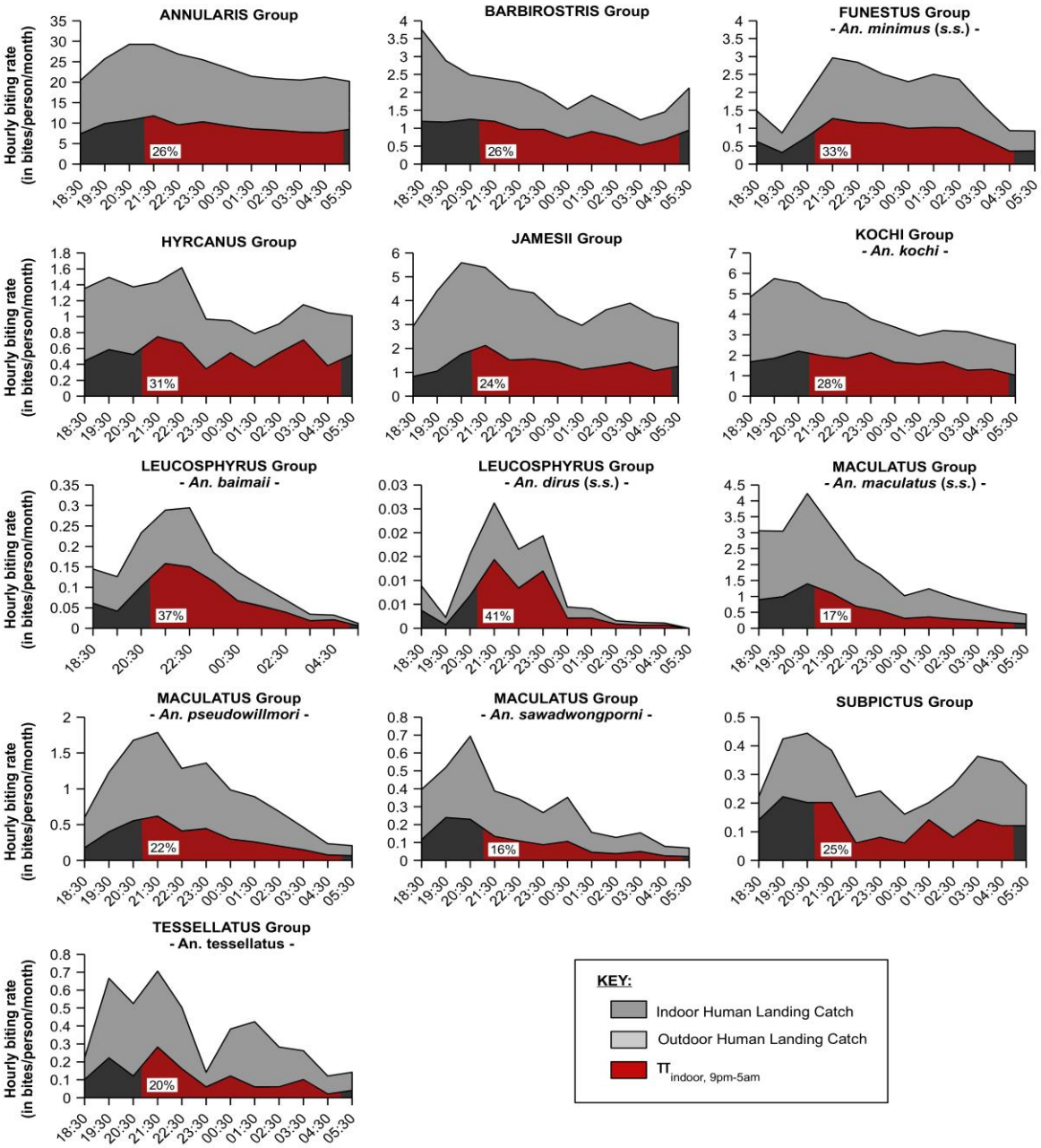
Annex 5. Exophagic index of Anopheles mosquitoes



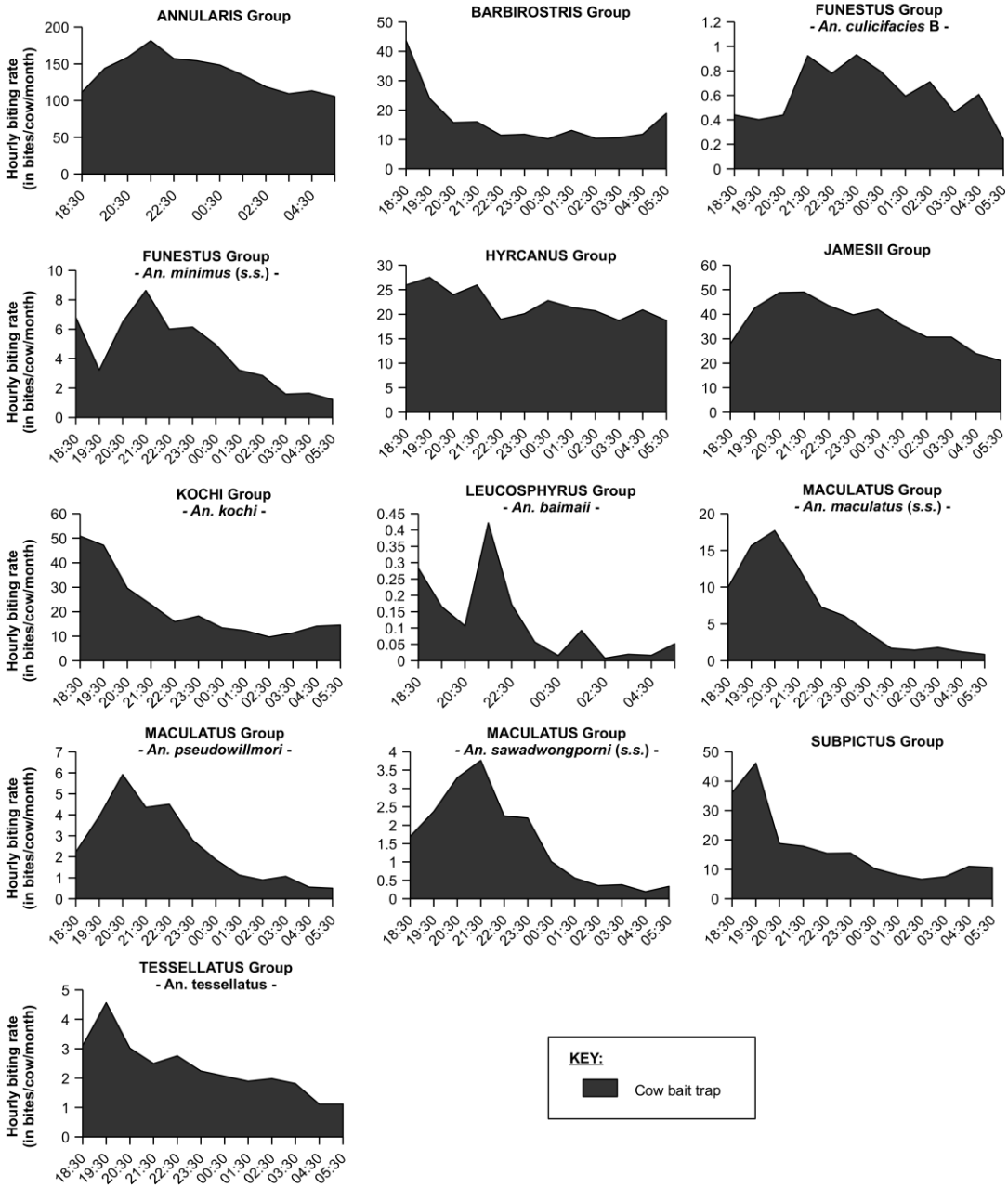
Annex 6. Zoophagic index of Anopheles mosquitoes



Annex 7. Night biting pattern of Anopheles mosquitoes collected by HLC



Annex 8. Night biting pattern of Anopheles mosquitoes collected by CBC



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GLOSSARY

AE : Adverse event

BMA: Burma Medical Association

BMGF: Bill and Melinda Gates Foundation

BPHWT: Back Pack Health Workers Team

CE: Community engagement

CPI: Community Partners International

EC: Executive Committee of the METF

EDT: Early Diagnostic and Treatment

EI: Exophagy index

EIR: entomological inoculation rate

G6PD: glucose-6-phosphate dehydrogenase

GFATM: Global Fund against Aids, Tuberculosis and Malaria

GIS: Geographic information system

GPS: Global positioning system. For our purposes this includes the use of GLONASS (global navigation satellite system). This is a system of recording geographic coordinates (such as latitude and longitude) using satellite technology.

HBR: human biting rate (bites per person per month)

HLC: human landing catch

Hotspot: Our operational definition of a hotspot comes from the results of village-level malaria surveys. Villages are classified as "hotspots" when the 90% CI upper limit of the prevalence estimate is ≥ 40% and the corresponding value of the proportion of *P. falciparum* in the positive samples is ≥20%

Incidence: cases per unit of population per unit of time (a rate)

Karen: Former name of Kayin State up to 1989.

Kayin: State of the Union of Myanmar (also referred to until 1989 as Karen State)

KBGF: Karen Border Guard Force

KDHW: Karen Department of Health and Welfare

KKO: Klohtoobaw Karen Organization

KPC: Karen Peace Council

K13: Kelch 13 mutations

Malaria survey: Blood screenings using an ultrasensitive high-volume qPCR assay (uPCR) to identify infections among survey participants, including those with low-density (submicroscopic) parasitemia which that would be undetectable by conventional methods (microscopy or RDT)

Mapping: for our purposes, mapping includes physically going to a location, taking a recording with a satellite enabled GPS unit and recording some basic information on a survey form.

MAM: Medical Action Myanmar

Mass drug administration: treatment of an entire community/population regardless of symptoms

MDA: Mass drug administration

METF: Malaria Elimination Task Force

MP: Malaria post

MPW: Malaria Post Worker

MTC: Mae Tao Clinic

NMCP: National Malaria Control Program

Pfmdr1 : Plasmodium falciparum multidrug resistance gene

Prevalence: proportion of people carrying an infection at a specific point in time

qrtPCR: quantitative real-time polymerase chain reaction

RDT: Rapid Diagnostic Test

SI: Sporozoite index

SMRU: Shoklo Malaria Research Unit

SMS: short message service or “text messages” sent via mobile telephone system

uPCR: ultrasensitive high-volume quantitative polymerase chain reaction

WHO: World Health Organization

ZI: Zoophagy index