YANGON UNIVERSITY OF ECONOMICS

MASTER OF PUBLIC ADMINISTRATION PROGRAMME

A STUDY ON PATIENT'S ADHERENCE ON ANTIMALARIAL TREATMENT PROVIDED BY COMMUNITY VOLUNTEER

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EMPA - 42 (15th Batch)

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Athesis submitted asapartial fulfillmenttowardstherequirement for thedegreeof Master of PublicAdministration (MPA)

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ABSTRACT

Treatment adherence to *Primaquine* is crucial for radical cure and interruption of *P. vivax* malaria transmission. This study was carried out to examine the associated conditions related with the treatment incompleteness of 8-week *Primaquine* regimen (0.75mg/kg once weekly for 8 weeks), which, together with a 3-day course of chloroquine, was prescribed for uncomplicated *P. vivax* cases by community-based village malaria workers (VMWs). This is a descriptive study using quantitative information obtained by interviewing a sample of 140 *P. vivax* positive patients from Hpa-An, Hlaingbwe, Kawkareik and Myawaddy townships of Kayin State. Out of the total 342 *P. vivax* cases detected and reported in the 4 Townships from October 2017 to September 2018 by the 71 VMWs, 140 patients could be interviewed by the study team with a semi-structured questionnaire in November-December 2018. The results of the interviews showed that 100 (71%) of them were male, 100 (71%) were migrant, 89 (64%) were farmers and forest workers, and 111 (79%) were Kayin ethnicity. Of the 140 cases who received *Primaquine* treatment from VMWs, 83 (60%) were considered as probably adherent (completed full course of 8-week course at the right dose and right interval) based on their self-reported behavior. Among the 57 cases (40%) considered as non-adherents, *Primaquine* treatment incompleteness was found to be associated with being migrant vs non-migrant and being forest worker vs non-forest worker. But, no significant association was found with male vs female and Kayin vs non-Kayin ethnicity. The main reasons reported for incompleteness were forgetfulness (29%), travelling (11%), busy work (13%), long treatment course (2%), and dizziness (1%). Therefore, migrant status and forest-related works were the main factors associated with incompleteness to the *Primaquine* 8-week regimen.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURE

LIST OF ABBREVIATIONS

ACT	Artemisinin-based Combination Therapy
APLMA	Asia Pacific Leaders Malaria Alliance
ARC	American Refugee Committee
BHS	Basic Health Staff
DOPH	Department of Public Health
DOT	Directly Observed Treatment
G6PD	Glucose- 6-Phosphate dehydrogenase Deficiency
INGO	International Non-Governmental Organization
IRS	Indoor Residual Spray
ITN	Insecticide Treated Net
LLIN	Long Lasting Insecticide Treated Net
M & E	Monitoring and Evaluation
MDR	Multi Drug Resistance
MHAA	Myanmar Health Assistant Association
MNMA	Myanmar Nurse and Midwife Association
MOHS	Ministry of Health and Sports
NMCP	National Malaria Control Program
NSA	Non State Actor
NSHPME	National Strategic Health Plan for Malaria Elimination
NSP	National Strategic Plan
TNTY	Tanintharyi
URC	University Research Co., LLC
VMW	Village Malaria Worker
WHO	World Health Organization

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This is to certify that this thesis entitled **"A Study on Patient's Adherence on Antimalarial Treatment Provided by Community Volunteer"**, submitted as a partial fulfillment towards the requirements for the degree of Master of Public Administration has been accepted by the Board of Examiners.

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CHAPTER I
INTRODUCTION

1.1 Rationale of the Study

Every place in the world has a certain potential for malaria transmission that is intrinsic to it at a given point in time, ranging from zero to some level above zero. This characteristic is often referred to as "receptivity", and indicates the extent to which conditions are favorable for malaria transmission in a specific location. The potential for malaria transmission is a function of many varied factors including; mosquito vector species, their abundance and behavior, the *Plasmodium* species, temperature and rainfall, geography and topography of the land, amount and type of agriculture or land-cover in that area, strength of the health system, quality of housing in which people live, how people spend their time for daily living in the places and times when vectors are feeding and together. These characteristics will lead to a specific level of malaria burden that would exist in a given place if no interventions are implemented to control it. Because of the number and variability of factors that influence malaria situation, it will vary both between and within countries; different areas within the same country may have different vectors, geographies, socioeconomics, and health system coverage.

Malaria programmes can reduce malaria through active measures. Protecting all or a particular fraction of the at-risk population with effective control measures, will reduce malaria by some level over a certain response time. The amount that malaria will be reduced in a given operational unit (area) is determined primarily by three key factors; 1) the pre-control baseline condition in general in which the higher the malaria baseline condition in a particular area, 2) the greater the fraction of the at-risk population that must be protected with control interventions in order to achieve a reduction in transmission to a specific threshold, the magnitude of the impact of specific interventions on transmission may vary by type of intervention and, 3) setting and the fraction of the at-risk population in the area that can be fully protected by effective control measures.

Globally, an estimated 219 million cases of malaria occurred worldwide each year and of these cases, 660, 000 people died (World Malaria Report 2018, WHO). The illness and burden is felt most severely in sub-Sahara Africa. Data indicates that in sub-Sahara Africa a child dies of malaria every minute. The region with the heaviest malaria burden is sub-Sahara Africa. Pregnant women and children under age five are the most susceptible. Sub-Sahara Africa reports 90% of the total malaria related deaths worldwide, and foreshadows what is happening globally. Despite important gains in some areas, malaria remains a major problem in most of the tropical world, and it continues to cause hundreds of millions of illnesses and hundreds of thousands of deaths each year.

In the past decade, Myanmar has made significant progress in reducing malaria morbidity and mortality. The number of malaria deaths has dropped steadily year by year from 1,707 in 2005 to just 37 in 2015 (about 98% reduction over 10 years) reflecting major improvements in access to early diagnosis and appropriate treatment (NMCP, 2016). Despite these recent advances, malaria remains a leading cause of morbidity and a cause of mortality in Myanmar, and in 2015 the country's malaria burden still accounted for around 70% of reported cases in the Greater Mekong Subregion (NMCP, 2016).

The malaria burden in a particular area may vary from year to year. It is due to varying weather patterns or unusual human movement and despite such complicating factors, it is important to take them into account through the process of making detailed, long-term strategic plans and for surveillance, monitoring, and evaluation of progress of malaria control. The intrinsic malaria transmission level of a region, is determined by environmental and socioeconomic factors that change only slowly and is usually not directly affected by malaria control measures. Thus, to change malaria condition of a region, it is important to carry out through long-term changes in environmental or socioeconomic factors, intervention with permanent effects and sustained malaria control.

Appropriate use of antimalarial drugs remains a cornerstone of malaria control. Antimalarial drugs have two key roles for malaria control. First, prompt and effective treatment of malaria prevents progression to severe disease and limits the transmission of malaria. Second, drugs can be used to prevent malaria in endemic populations, including various strategies of chemoprophylaxis, intermittent preventive therapy, and mass drug administration. Antimalarial drugs act principally to eliminate

the erythrocytic stages of malaria parasites that are responsible for human illness. Available antimalarial drugs can be divided into multiple classes.

Treatment adherence refers to the extent to which patients take their antimalarial drug as prescribed. The three key elements involve taking a medicine at the right dose, the correct dosing frequency and for the recommended treatment duration. Failure to take medicines as recommended has negative consequences; for some therapeutic areas, such as the treatment of uncomplicated malaria, the consequences can be far more serious.

In summary, incomplete adherence and serious long-term consequences of poor adherence to antimalarial treatment cannot be overstated. This applies not only at the individual patient level, but also at the global level. This study has focused on the requirement of adherence to Primaquine treatment to get radical cure of *P. vivax* parasite from the human body so that transmission to other people can be prevented. National Malaria Control Program, Myanmar (NMCP), Ministry of Health and Sports (MOHS) recommended Village Malaria Worker (VMW) to prescribe Primaquine 0.75 mg/kg orally one time per week for 8 weeks to *P. vivax* malaria patients. But, Basic Health Staffs (including in rural setting) are allowed to prescribe Primaquine 15 mg orally 14 days dosing schedule (0.25 mg base/kg/day for 14 days). This study aims to examine the associated conditions of poor adherence to 8-week Primaquine course and a survey will be conducted in Hpa-An, Hlaingbwe, Kawkareik and Myawaddy townships of Kayin State. So that, the study findings are expected to be able to suggest NMCP (MOHS) to change Primaquine treatment schedule guide for VMW as Basic Health Staff's guideline of 15 mg 14-days schedule instead of 8-weeks schedule (National Malaria Treatment Guideline, NMCP Myanmar, 2015).

1.2 Objective of the Study

The objective of study is to examine the associated conditions related with the incompleteness of 8-week Primaquine course in *P. vivax* malaria patients.

1.3 Method of Study

This study applied a primary data collection using a structured questionnaire at Hpa-An, Hlaingbwe, Kawkareik and Myawaddy townships of Kayin State. The descriptive method and random sampling method were used in this study. In order to fulfil the objectives of the study, both quantitative and qualitative study based on

primary data and secondary data were used in this study. Primary data were collected through interviewing to the (140) *P. vivax malaria* positive patients who took *Primaquine* treatment provided by village malaria workers of Defeat Malaria Project. Number of patients interviewed in each township were; (28) from Hpa-An, (8) from Hlaingbwe, (18) from Kawkareik and (86) from Myawaddy. Number of patients per township depended upon the number of *P. vivax* positive patients presented in concerned township between October 1, 2017 and September 30, 2018. The patients who were younger than 15-year were interviewed by the assistance of parent or a guardian of the patient's family. Key informant interviews were done to central level, township level and community level resource personnel (Malaria Technical Support Group, Project staff, Village Malaria Worker). Secondary data were gathered from "Defeat Malaria Project" annual report, published journals, internet websites, relevant texts and project report from malaria control projects. Secondary data were extracted from "Defeat Malaria Project" annual report only focused on Dawei, Palaw, Tanaintharyi and Palaw township data.

1.4 Scope and Limitations of the Study

This study focused only on Primaquine treatment adherence of malaria parasite *P. vivax* positive patients who took Primaquine treatment provided by community level volunteers between October 2017 and September 2018. There was limitation to study in details on the side-effect of Primaquine. Geographical coverage area of data collection was Hpa-An, Hlaingbwe, Kawkareik and Myawaddy townships of Kayin State.

1.5 Organization of the Study

This study was organized into five chapters. Chapter I is Introduction and it included Rationale of the Study, Objective of the Study, Scope and Limitations of the Study and Organization of the Study. Chapter II described the literature review including; Malaria Background Concept, Strategies and Interventions for Malaria Elimination, National Treatment Guideline for the treatment of Malaria, Barriers of Malaria treatment and Review on Previous Studies. Chapter III presented Malaria situation in Myanmar, Epidemiology profile of Malaria in Myanmar, Malaria and Mobile Populations, National Strategic Plan for Malaria Elimination, and Antimalarial Treatment Policy. Chapter IV was the Analysis of Surveyed Data in which included

field research, characteristics of respondents, assessment of Primaquine treatment adherence by surveyed population and review on Primaquine treatment adherence of secondary data, review of secondary data and Key Informant Interview. Chapter V consists of Finding and Suggestion.

CHAPTER II
LITERATURE REVIEW

2.1 Concept of Malaria

Malaria is caused by the protozoan parasite *Plasmodium*, which is transmitted by female Anopheles mosquitoes, which usually bite between sunset and sunrise (WHO, 2017). There are four human malaria parasite species; *P. falciparum, P. vivax, P. malariae and P. ovale*. Of the nonhuman malaria parasite species, *P. knowlesi* has recently been reported to infect humans in South-East Asia with increasing frequency, but there is no evidence so far of human-to-human transmission.1 Of the human malaria parasite species, *P. falciparum* and *P. vivax* pose the greatest threat. *P. falciparum* remains the most dangerous and is responsible for the majority of malaria-related deaths.

Outside sub-Saharan Africa, *P. vivax* malaria accounts for about half of malaria cases and predominates in countries that are prime candidates for elimination; the parasite accounts for more than 70% of malaria cases in countries with fewer than 5,000 cases each year (WHO, 2017). In contrast to *P. falciparum*, which does not cause persistent liver-stage infection, *P. vivax* can stay dormant in the liver for many months or even year after inoculation and can cause repeated relapses. Thus, the elimination of *P. vivax* malaria is particularly challenging and may in some settings require new tools and strategies.

Of about 515 Anopheles species, only 30 to 40 are considered important malaria vectors (WHO, 2017). Multiple species can coexist within one geographical area, each with its own biting and resting pattern and preferred human or animal host; thus, species vary widely in their transmission efficiency and in their susceptibility to existing or potential anti-mosquito interventions.

Malaria parasites are unicellular organisms belonging to the genus *Plasmodium*. Human malaria is due to four species that cause four types of malarial disease: *P. falciparum, P. malariae, P. ovale and P. vivax*. The four human malaria species are not evenly spread across the malaria-affected areas of the world, and their relative

importance varies between and within areas, by zoo-geographical region. *P. falciparum* is the most common species and predominates in Africa South of the Sahara. *P. vivax* predominates in the subtropics and coexists with *P. falciparum* in tropical Asia, the tropical Americas and the Horn of Africa. *P. ovale* is found in Africa and sporadically in South-East Asia and the western Pacific. *P. malariae* has a similar geographical distribution to *P. falciparum*, but its incidence is lower and its distribution is patchy.

P. vivax and *P. falciparum* infections cause low birth weight in neonates and are associated with anemia and splenomegaly, particularly in children and pregnant women. Unlike other *Plasmodium* species, *P. vivax and P. ovale* can remain dormant in the liver for up to several months or even years after inoculation and cause relapses. Forms of malaria due to *P. malariae* and *P. ovale* are less severe and are rarely life-threatening; unlike the other malaria parasites, *P. malariae* can remain undetected for decades and can lead to chronic immune-pathological sequelae.

The risk for contracting malaria is highly variable from country to country and even between areas in a country. The distribution of malaria in the world was widest in the late nineteenth century, since when, the area affected by malaria transmission has continued to contract. During the past decade, cases of zoonotic Plasmodium infection, first and foremost with *P. knowlesi*, have been reported with increasing frequency in South-East Asia, especially in Malaysia. The natural reservoirs of this species are several macaque species found in forests in South-East Asia. The main vectors belong to the Anopheles leucosphyrus group, which is also associated with forest environments.

Malaria parasites are transmitted by female mosquitoes belonging to the genus Anopheles. The development of malaria parasites in the vector, called sporogony, includes a number of stages in different organs of the insect. Male and female gametocytes mate after being ingested by an anopheline mosquito during blood feeding. The zygotes develop as ookinetes, which move across the mosquito stomach to form oocycsts, within which asexual multiplication leads to the production of up to thousands of sporozoites. The sporozoites migrate and accumulate in the salivary glands, from which they are injected when the infective mosquito bites a human or animal host for a blood-meal.

The speed of development of sporozoites depends on temperature and the parasite species. At the optimal temperature, 28 Degree Celsius, the duration of

sporogony is 9 to 10 days for *P. falciparum* and 8 to10 days for *P. vivax*. The time from ingestion of gametocytes to release of sporozoites is the extrinsic incubation period or duration of sporogony. Sporozoites injected by a mosquito enter the host's blood circulation; when they reach the liver, they invade hepatocytes. All *P. falciparum* sporozoites then undergo exoerythrocytic schizogony, in which the parasite nucleus divides repeatedly over several days; at the end, the schizont bursts, giving rise to thousands of merozoites, which are released into the bloodstream. The duration of exo-erythrocytic schizogony is 5.5 to 7 days for P. falciparum and 6 to 8 days for *P. vivax*. In *P. vivax* malaria, some sporozoites, after invading hepatocytes, become dormant as hypnozoites for periods lasting from 3 to 18 months and very rarely up to 5 years. The merozoites invade erythrocytes, where the great majority multiply asexually, undergoing repeated cycles of growth, rupture, release and reinvasion of fresh red cells. All clinical manifestations of malaria are due to this erythrocytic schizogony. The duration of each cycle of erythrocytic schizogony is about 48 hours for both *P. falciparum* and *P. vivax*. Some merozoites grow and develop into male or female gametocytes within erythrocytes. When mature, they do not develop further, unless they are ingested by a mosquito vector. The immature gametocytes (stages 1 to 4) of *P. falciparum* are sequestered in the bone marrow and other deep tissues; only mature gametocytes (stage 5) circulate in the blood. In contrast, all stages of gametocytes of the three other species are present in the peripheral circulation (WHO, 2017).

The duration of the biological processes mentioned above is not observed directly in clinical or public health practice. It is, however, possible to define a number of critical, observable intervals that depend on these elementary processes. For example, the clinical incubation period is equal to the duration of exo-erythrocytic schizogony plus the time required for a build-up of the parasite density above the pyrogenic threshold, which may take one or more cycles of erythrocytic schizogony. These observable intervals are of great importance for determining from a patient's history whether the case was imported or contracted locally and for how many days it may have been infective to vectors in a given area.

Infection with malaria parasites may result in a wide variety of symptoms, ranging from absent or very mild symptoms to severe disease and even death. Malaria disease can be categorized as uncomplicated or severe (complicated). In general, malaria is a curable disease if diagnosed and treated promptly and correctly.

In uncomplicated malaria, the classical (but rarely observed) malaria attack lasts 6–10 hours (WHO, 2017). It consists of, a cold stage (sensation of cold, shivering), a hot stage (fever, headaches, vomiting; seizures in young children); and finally, a sweating stage (sweats, return to normal temperature, tiredness). Classically (but infrequently observed) the attacks occur every second day with the "tertian" parasites (*P. falciparum*, *P. vivax*, and *P. ovale*) and every third day with the "quartan" parasite (*P. malariae*). More commonly, the patient presents with a combination of the following symptoms; fever, chills, sweats, headaches, nausea and vomiting, body aches and general malaise. In countries where malaria is frequent, residents often recognize the symptoms as malaria and treat themselves without seeking diagnostic confirmation ("presumptive treatment"). Physical examination findings of malaria patient include; elevated temperatures, perspiration, weakness, enlarged spleen, mild jaundice, enlargement of the liver and increased respiratory rate. Diagnosis of malaria depends on the demonstration of parasites in the blood, usually by microscopy or Rapid Diagnostic Test. Additional laboratory findings may include mild anemia, mild decrease in blood platelets (thrombocytopenia), elevation of bilirubin, and elevation of aminotransferases. Severe malaria occurs when infections are complicated by serious organ failures or abnormalities in the patient's blood or metabolism.

The manifestations of severe malaria include:

(i) Cerebral malaria, with abnormal behavior, impairment of consciousness, seizures, coma, or other neurologic abnormalities
(ii) Severe anemia due to hemolysis (destruction of the red blood cells)
(iii) Hemoglobinuria (hemoglobin in the urine) due to hemolysis
(iv) Acute respiratory distress syndrome (ARDS), an inflammatory reaction in the lungs that inhibits oxygen exchange, which may occur even after the parasite counts have decreased in response to treatment
(v) Abnormalities in blood coagulation
(vi) Low blood pressure caused by cardiovascular collapse
(vii) Acute kidney injury
(viii) Hyperparasitemia, where more than 5% of the red blood cells are infected by malaria parasites
(ix) Metabolic acidosis (excessive acidity in the blood and tissue fluids), often in association with hypoglycemia

(x) Hypoglycemia (low blood glucose). Hypoglycemia may also occur in pregnant women with uncomplicated malaria, or after treatment with quinine.

(xi) Severe malaria is a medical emergency and should be treated urgently and aggressively.

In case of malaria relapses (repeated malaria fever) with *P. vivax* and *P. ovale* infections, patients having recovered from the first episode of illness may suffer several additional attacks ("relapses") after months or even years without symptoms. Relapses occur because *P. vivax* and *P. ovale* have dormant liver stage parasites ("hypnozoites") that may reactivate. Treatment to reduce the chance of such relapses is available and should follow treatment of the first attack.

Other Manifestations of Malaria are;

(i) Neurologic defects may occasionally persist following cerebral malaria, especially in children. Such defects include trouble with movements (ataxia), palsies, speech difficulties, deafness, and blindness.

(ii) Recurrent infections with *P. falciparum* may result in severe anemia. This occurs especially in young children in tropical Africa with frequent infections that are inadequately treated.

(iii) Malaria during pregnancy (especially *P. falciparum*) may cause severe disease in the mother, and may lead to premature delivery or delivery of a low-birth-weight baby.

(iv) On rare occasions, *P. vivax* malaria can cause rupture of the spleen.

(v) Nephrotic syndrome (a chronic, severe kidney disease) can result from chronic or repeated infections with *P. malariae*.

(vi) Hyper reactive malarial splenomegaly (also called "tropical splenomegaly syndrome") occurs infrequently and is attributed to an abnormal immune response to repeated malarial infections. The disease is marked by a very enlarged spleen and liver, abnormal immunologic findings, anemia, and a susceptibility to other infections (such as skin or respiratory infections). (World Health Organization, 2017)

2.2 Strategies and Interventions for Malaria Elimination

Most countries have diverse transmission intensity, and factors such as ecology, immunity, vector behavior, social factors and health system characteristics influence both the diversity of transmission and the effectiveness of tools, intervention packages and strategies in each locality. To manage the inherent complexity of addressing transmission intensities in different geographical areas, malaria programmes should stratify their national maps of malaria distribution into discrete area.

Stratification should, if possible to differentiate receptive from non-receptive areas; to identify receptive areas in which malaria transmission has already been curtailed by current interventions; to distinguish between areas with widespread transmission and those in which transmission occurs only in discrete foci, to differentiate strata by transmission intensity, particularly if different intensities are being addressed by different sets of interventions; and to determine geographical variations and population characteristics that are associated with vulnerability.

Stratification allows better targeting and efficiency, with assignment of specific packages of interventions and deployment strategies to designated strata. Stratification packages may include; further enhancement and optimization of vector control, further strengthening of timely detection, high-quality diagnosis (confirmation) and management and tracking of cases, strategies to accelerate clearance of parasites or vectors in order to reduce transmission rapidly when possible and information, detection and response systems to identify, investigate and clear remaining malaria foci.

For prevention of transmission, optimal coverage of ITNs/LLINs or IRS should be ensured and maintained in strata that are both receptive and vulnerable to malaria transmission. Vector control interventions should be conducted in addition to ITNs/LLINs and/or IRS according to the principles of integrated vector management and evidence-based, WHO-recommended strategies.

National malaria programmes have tools (e.g. insecticides to kill vectors, methods to prevent vector–human contact, diagnostics to detect infections and document clearance of infections, a variety of medicines to kill parasites in humans) and strategies to use those tools (e.g. spraying insecticides on walls or distributing ITNs/ LLINs, managing clinical illness or proactively seeking infected people or at-risk populations to ensure clearance or prophylaxis of malaria infections). New tools and strategies will become available in the future, nevertheless, even current

tools and strategies can dramatically reduce the malaria disease burden and transmission, many countries have already eliminated malaria with existing tools.

In order to define optimal intervention packages, current and evolving transmission intensities and the ecological and epidemiological features of the areas of a country must be understood.(World Health Organization, 2017)

2.3 Malaria Treatment

Malaria treatment guidelines were updated from mono therapy use of drugs such as Chloroquine, Amodiaquine and Sulphadoxine-Pyrimethamine (SP) to the currently recommended Artemisinin based Combination Therapies (ACT). The ACTs are generally highly effective and well tolerated. This has contributed substantially reduction in global morbidity and mortality from malaria. The below table summarized the current treatment guideline of malaria. (American Journal of Tropical Medicine and Hygiene, 2015).

Table (2.1) Currently Used Antimalarial Drugs

Class	Drug	Use
4-Aminoquinoline	Chloroquine	Treatment of non-falciparum malaria
	Amodiaquine	Partner drug for ACT
	Piperaquine	ACT partner drug with dihydroartemisinin as ACT
8-Aminoquinoline	*Primaquine*	Radical cure and terminal prophylaxis of *P. vivax* and *Plasmodium ovale*; gameto-cytocidal drug for *Plasmodium falciparum*
	Quinine	Treatment of *P. falciparum* and severe malaria
Arylamino alcohol	Mefloquine	Prophylaxis and partner drug for ACT for treatment of falciparum
	Lumefantrine	Combination with artemether as ACT
Sesquiterpene lactone endoperoxides	Artemether	ACT: combination with lumefantrine
	Artesunate	ACT; treatment of severe malaria
	Dihydroartemisinin	ACT: combination with piperaquine
Mannich base	Pyronaridine	Combination with artesunate as ACT
Antifolate	Pyrimetham-ine/sulfadoxine	Treatment of some chloroquine-resistant parasites; Combination with artesunate as ACT
Naphthoqui-none/antifolate	Atovaquone/proguanil	Combination for prophylaxis and treat-ment of *P. falciparum* (Malarone)
Antibiotic	Doxycycline	Chemoprophylaxis; treatment of *P. falci-parum*
	Clindamycin	Treatment of *P. falciparum*

(ACT = artemisinin-based combination therapy)

Source: American Journal of Tropical Medicine and Hygiene, 2015

2.3.1 Treatment of Uncomplicated Malaria Caused by *P. vivax*

P. vivax causes significant morbidity and mortality, and poses unique challenges for malaria control and elimination. *P. vivax* tolerates a wider range of environmental conditions and can be transmitted from infected humans to human through the vector (malaria parasite carrier) mosquitoes (World Health Organization, 2015). Therefore, prompt and effective treatment is one of the important interventions in malaria control activities. Moreover, the human reservoir of latent hypnozoite (*P. vivax* malaria parasite in the liver form), which are responsible for an appreciable proportion of morbidity. *P. vivax* malaria. Hence, there may be a large reservoir of infected people who are unaware of their condition and are only diagnosed when they relapse (repeated malaria fevers again after first infection). The elimination of *P. vivax* liver-stage parasites requires a 14-day course of Primaquine (in some case such as community volunteer level malaria service provider are prescribing weekly dose for 8 weeks course of Primaquine). Despite there is side-effects (hemolytic anemia) in patients who have severe forms of glucose- 6-phosphate dehydrogenase (G6PD) deficiency, Primaquine is most effective medicine to eliminate the *P. vivax* malaria parasites from human body. Prevention, controlling and eliminating *P. vivax* malaria is therefore a development challenge one that is inextricably linked with health system strengthening, poverty reduction and equity. This study will examine patients' adherence status to Primaquine weekly dose for 8 weeks dosing schedule and the associated reasons of low adherence of the treatment.

P. vivax malaria parasite positive patient's adherence to antimalarial treatment can affect the malaria control activities in a particular region or country. *P. vivax*is generally still sensitive to Chloroquine, although resistance is prevalent and increasing in some areas (notably Indonesia, Peru and Oceania). The details of guidelines are (NMCP, Ministry of Health and Sports, 2015);

1. Chloroquine (total dose of 25mg base/kg)
2. *Plasmodium vivax* requires radical curative treatment with Primaquine on the last day of Chloroquine
    (a) Health staffs to prescribe Primaquine 0.25 mg base/kg/day for 14 days for radical treatment
    (b) Volunteers (Village Malaria Worker) to prescribe Primaquine 0.75 mg/kg once weekly for 8 weeks

When Primaquine is given, patient must be informed to stop the drug as soon as urine color becomes red. The only drugs with significant activity against the hypnozoites are the 8-aminoquinolines (Buloquine, Primaquine, Tafenoquine).

2.3.2 *P. vivax* Treatment by Community Malaria Volunteer

Treatment of *P. vivax* infection in the community level is either prescribed by community level Village Malaria Worker (volunteer) with 8-week dosing schedule of 45 mg once in a week or by Basic Health Staff(BHS) with daily dose of 15 mg *Primaquine* for 14-day course (Village Malaria Worker Manual, NMCP, Ministry of Health and Sports, October 2015). But, in practice the treatment compliance is controversial with the unstable work nature of the rural community whose livelihood rely onto mobile works such as forest going, migrant works and other temporary works which make them frequent departure from their home. As result, low adherence to the treatment occur and relapse (repeatedly suffering from malaria fever) for many years and therefore, it will have critical implication to malaria elimination goal 2030. There were also pilot projects under Defeat Malaria Project in Tanintharyi region where Village Malaria Workers are providing 14 days (daily dose for 2 weeks) course of 15 mg Primaquine tablets to the *P. vivax* positive patients (Defeat Malaria Project, 2018).

2.3.3 Control and Elimination of *P. vivax* Malaria

Complete treatment of *P. vivax* malaria requires treatment of both blood and liver stages, to achieve clinical cure, and to prevent relapses, onward transmission and progression to severe disease (World Health Organization, 2015). Primaquine is currently available for attacking the liver stages of *P. vivax* malaria. For radical cure, WHO recommends a 14-daytreatment course or weekly dose of 8-week treatment course of Primaquine. Asexual stages of *P. vivax* are susceptible to Primaquine; thus, chloroquine plus Primaquine can be considered as a combination treatment for blood-stage infections, in addition to providing radical cure. But, there is challenge that Primaquine causes mild to severe hemolysis in patients with G6PD deficiency. Current tests for G6PD deficiency are not suitable for use in most clinical settings because they require laboratories and skilled workers, or are too expensive. In settings where G6PD-deficiency testing is not available and deficiency prevalence is high, the risk of hemolysis may be prohibitive, especially in South and South-East Asia where severe variants commonly occur. Current guidelines recommend that Primaquine

should not be given to pregnant or lactating women with children aged under 6 months, or to children aged under 6 months because of safety concerns. Weekly dosing of Primaquine (0.75 mg/kg) may mitigate the risk of hemolysis in G6PD-deficient patients, close medical supervision is still required and adherence to the 8-week regimen of a single weekly dose can be challenging to enforce.

2.3.4 Primaquine Use in *P. vivax* Malaria Elimination

Primaquine is also effective against all exoerythrocytic forms of the parasite and is used in conjunction with other anti-malarial for the treatment of *P. vivax* and *P.ovale* malaria. However, Primaquine is often associated with serious adverse effects, in consequence of its toxic metabolites. Over the last two decades, medicinal chemists have battled against Primaquine's disadvantages, while keeping or even improving its unequalled performance as an anti-malarial. The European Journal of Medicinal Chemistry (2009) informed that at the present time, Primaquine and its properties have the path towards the development of effective and safe Primaquine-based anti-malarial. But at the same time, there were challenges to Primaquine use is treatment adherence in both daily course of 14-day regimen and once a week dosing of 8-week regimen. According to Ernest Beutler (2015), the consequence of G6PD enzyme deficiency in some patients was drug-induced hemolysis and Primaquine is one of many drugs that shortens RBC lifespan in G6PD-deficient persons. When hemolysis is severe, the urine turns dark and the patient may complain of back pain. When G6PD deficiency is relatively mild, the hemolytic anemia is "self-limited". In patients with more severe forms of enzyme deficiency such as G6PD Mediterranean, hemolysis continues until well after the administration of drug is stopped. The fact that Primaquine was only one of many drugs that precipitated hemolysis in G6PD-deficient individuals was recognized early in studies.

2.4 Barriers to Malaria Diagnosis and Treatment

The barriers to malaria diagnosis and treatment include; (a) Malaria control strategies, policies, and guidelines, (b) Patient awareness, demand, and behaviors, (c) Provision of quality services, (d) Quality assurance, quality control, and regulation, (e) Availability of supplies, funding, and procurement and (f) Monitoring, evaluation, and surveillance (Scott Wittet, 2014). Addressing these issues will require interven-

tions at global and national levels because many of the issues are associated with broader health systems, beyond malaria and febrile disease.

Issues related to malaria control strategies, policies, and guidelines; it is imperative to refresh malaria control strategies at all levels of the health care system and to move beyond presumptive diagnosis. This is crucial in both public and private sector programs. Updated diagnostic policies at the national level may not be implemented at regional/local levels. Some national malaria strategic plans and policies are out of date. In many countries, policies are updated only every five to ten years and have not yet incorporated the new strategies. Even if countries cannot update now, they should prepare for updating as soon as possible. There is a shortage of clear national guidelines for implementing universal diagnosis and treatment.

Issues related to patient awareness, demand, and behaviors; Patients and caregivers often do not request/demand specific malaria diagnosis. Patients do not comply with malaria treatment, do not understand how to comply, do not know what to ask for, are afraid of malaria drugs, and/or discontinue treatment early rather than completing all doses. This results in treatment-seeking at the community level, where some complications cannot be properly managed.

Issues related to provision of quality services; Some health services providers do not educate their patients about malaria diagnosis and treatment compliance. There can be a disconnect between staff who run diagnostic tests and those who prescribe treatment. Universal diagnosis and treatment should be incorporated into all relevant pre-service and in-service training curricula for clinicians and laboratory technicians.
Issues related to quality assurance, quality control, and regulation; Without continuing quality assurance for malaria services including diagnostics, quality could slip and confidence in the tests could erode.

Issues related to availability of supplies, funding, and procurement; More funding, and more stable funding, is needed for malaria diagnosis, treatment, and tracking. External funding for training and scale-up often is erratic or not sustainable. It is crucial to build coordination mechanisms to deal with this challenge.

Issues related to monitoring, evaluation, and surveillance; Health management information systems may not have been updated to include data on who has been tested for malaria, who was treated, etc. Systems must add malaria indicators to surveillance tools and must differentiate between confirmed malaria and presumptive

diagnosis of malaria. Most governments do not gather data from private-sector providers.

2.5 Review on Previous Studies

The previous studies related to this study's scopes of interest were reviewed and referenced facts were extracted in this section. The previous studies focused areas were related to *P. vivax* treatment, adherence to malaria treatment, Primaquine side effect in G6PD deficiency patients and community engagement in malaria elimination. Literature review on previous studies explored the facts that which were supporting the rationale of this study proving that other studies were indicating the need of this study area.

According to Cindy S. Chu (2015), repeated attack (relapse) of fever by P. vivaxmalaria are important contributors to illness and morbidity in *P. vivax*. Relapse prevention with Primaquine is required for optimal management, control and ultimately elimination of *P. vivax* malaria. May Myo Thwin (2015) stated that the community engagement efforts for a pilot malaria elimination project, the challenges encountered and lessons learnt were related with seasonal tasks of the villagers and included logistical, scientific and political difficulties. An approach that is tailored to the local population is key. Toby Leslie (2008) stated that *P. vivax* malaria remains a major cause of morbidity in the subtropics. Safe and effective use of Primaquine without the need for G6PD testing would be ideal. Widespread use of the 8-week regimen could make an important contribution to reservoir reduction or regional elimination where G6PD testing is not available. But, the evidence about the adherence to complete course of the 8-week Primaquine in right interval and right duration was missing in the study.

Mohammad Abdur (2004) stated that the potential problem with long course chemotherapy is the issue of compliance after clinical symptoms have subsided. The presumed problem of poor compliance may be overcome with simple health messages even when the majority of individuals are illiterate and without formal education. Unsupervised treatment with 14-day Primaquine when combined with simple instruction can avert a significant amount of the morbidity associated with relapse in populations. Nardlada Khantikul (2009) indicated that the treatment adherence of the patients was associated with knowledge scores of malaria and access to drug

prescription. But, other associated conditions related to the treatment adherence are missing in the study.

Christine Luxemburger (1999) stated that Chloroquine remains highly effective on the western border of Thailand and the use of strictly supervised Primaquine effectively prevents relapse. The introduction of Primaquine on a large scale in an endemic area still requires a long-term risk-benefit assessment which must take into account potential toxicity, low compliance and reductions in the incidence.

Myo Myo Zin (2009) studied on malaria prevention and control programme in Rakhine State. This study found that the reasons of malaria diseases still remain unchanged in Rakhine State. The reasons include lack of knowledge on malaria, occupations at risk to malaria, counterfeit drug, access to malaria health services, migration status, climate condition of Rakhine State, forest related economic activities, weak health system and funding issues. Moe Thu Zar (2003) studied on situation of mortality and morbidity from malaria and socio economic loss due to malaria. This study found that malaria burden was high in Myanmar around the year 1990's and 2000. There were technical problems, administrative problems and operational problems in National Malaria Control Programme in Myanmar. Malaria was recognized as a socio economic issue. May Aung Lin (2011) studied on community based malaria control interventions. This study found that voluntary health workers had performed well in malaria control activities and community's perception on these volunteers was highly satisfactory. Involvement of voluntary health workers should be assumed as a good approach for community mobilization in malaria control programs.

CHAPTER III
MALARIA CONTROL ACTIVITIES IN MYANMAR

3.1 Malaria Control in Myanmar

Malaria remains a leading cause of morbidity and mortality in the Republic of the Union of Myanmar. Considerable progress has been made over the past 10 to 15 years in reducing the burden. However, the disease is still a priority public health problem in the country (NMCP, 2016). It occurs mainly in or near forests, but also in some coastal areas and plantations. Because of these environmental determinants, the malaria burden is particularly high among national races in remote areas and migrants, who seek economic opportunities in rural economic frontier areas, and the economic development activities such as forestry, mining, plantations and road-building. The significant reduction of malaria morbidity and mortality so far made in Myanmar is threatened by evolving complexity of the problem, especially multiple resistance of the parasites to antimalarial medications and the uncertainty about the financial basis for continued malaria control. The epidemiology of malaria, biology of vectors, socio-behavioral characteristics of the communities and geographical areas also present a challenge to achieve further progress in the implementation of malaria control interventions, making it necessary to develop and validate new implementation strategies. Compared to other countries in the South-East Asia and the Greater Mekong Sub-Region (GMS), malaria situation of Myanmar ranked third in the WHO South-East Asia Region, and first in the GMS countries.

National Malaria Control Programme (NMCP Myanmar) had developed National Malaria Treatment Policy and guideline since 2002 and it was updated in 2008 and minor modifications were made in 2011. Malaria case management remains a vital component of the malaria control strategies. This entails early diagnosis and prompt treatment with effective antimalarial medicines. Now a day, the scope of malaria treatment expands not only to reduce malaria morbidity and mortality but also to prevent transmission. Although this guideline is aiming mainly for all medical personnel who treat the patients, it also intends for the public and private sectors

concerning antimalarial drugs quality assurance and quality control. Without understanding the malaria treatment policy and updated regimes, availability of obsolete and substandard antimalarials in the market may hinder the adherence of treatment guideline by private sector and community. Banning of oral artemisinin monotherpy also should be smoothly encountered by collaborative effort of respective departments and companies after recognition of this national guideline. As National Malaria Programme (Myanmar) is preparing to move from malaria "Control" to "Elimination", the treatment policy and guideline on malaria is also transforming especially at community level. However, this guideline tries to encompass all aspects of malaria treatment at all levels in every stage (i.e. uncomplicated or severe & complicated) of any species infection of *Plasmodiae*.

Table (3.1) Malaria Incidence and Malaria Mortality (per 100,000 population) by Region/State of Myanmar 2005 - 2014

Year	Malaria Incidence (per 100,000 population)	Malaria Mortality (per 100,000 population)
2005	1341.8	3.79
2006	1415.4	3.86
2007	1192.9	2.27
2008	1226.5	2.37
2009	1327.3	2.24
2010	1420.0	1.73
2011	1085.2	1.17
2012	686.0	0.73
2013	438.3	0.50
2014	253.3	0.25

Source: NMCP, Department of Public Health, Ministry of Health and Sports, 2015

Myanmar has made significant progress in reducing malaria morbidity and mortality. The incidence of reported malaria has dropped by about 37% since 2012 (from 686.0 in 2012 to 253.3 in 2014 per 100,000 population) (NMCP, 2015). The goal of the previous National Strategic Plan (2010-2016) was to reduce malaria morbidity and mortality by at least 60% by 2016 relative to 2007 figures. Despite these recent advances, malaria remains a leading cause of morbidity and a cause of mortali-

ty in Myanmar, and in 2015 the country's malaria burden still accounted for around 70% of reported cases in the Greater Mekong Sub-region (GMS). Compounding this issue and threatening recent progress is the independent emergence and geographical spread of multi-drug resistant malaria throughout the country. Recent evidence suggests that elimination of *P. falciparum* from the GMS is likely to be the only way to halt the spread of multi-drug resistance and prevent the emergence of untreatable malaria. The WHO Malaria Policy Advisory Group has recommended that the elimination of *P. falciparum* malaria in the GMS by 2030 is technically, operationally and financially feasible and at the 9th East Asia Summit in November 2014 all Asia Pacific leaders committed to a region free of Malaria by 2030 (APLMA, 2014). With high-level political commitment now in place, Myanmar is well positioned to pursue an elimination agenda.

3.2 Epidemiological Profile of Malaria in Myanmar

As one of the leading causes of morbidity and mortality, malaria is a major public health problem in Myanmar (WHO, 2016). The majority of malaria cases and deaths in the GMS occur in this country, which accounts for approximately one-fifth of the Sub-region's population. In 2006, Myanmar had 200,679 confirmed cases and 1,647 deaths due to malaria. Historically, malaria morbidity and mortality in Myanmar peaked between1988 and 1991 as a result of epidemics, widespread population mobility and drug resistance, particularly along the border with Thailand (WHO, 2016). From 1992 onwards, efforts to improve the coverage of health services by installing more hospitals, rural health centers and sub-rural health centers led to an improvement in the overall malaria situation.

Myanmar continued to suffer from outbreaks, having experienced a total of malaria outbreaks between 1991 and 2000, most of which were sparked by migration. Since 2000, the frequency of malaria outbreaks has decreased. More recently, the number of confirmed cases has risen between 1998 and 2006, while the annual number of deaths attributed to malaria was almost halved over the same period, from 3,182 to 1,647deaths. The drop in malaria mortality may be partially attributed to greater private sector provision of artemisinin derivatives. As of 2006, the estimated malaria mortality rate in Myanmar was 2.9 deaths per 100,000 populations (down from 6.7 in 1998), while the incidence of confirmed malaria was 3.6 cases per 1,000 populations (WHO, 2016). Possible explanations for the increase in the number of

malaria cases are improvements in case finding and reporting systems, as well as the greater movement of migrant workers. Malaria is endemic in 284 out of 324 townships (WHO, 2016). About 60% of the total malaria cases occur in forest or forest fringe areas where the main vectors are present. Population groups at high risk of malaria are internal migrants, people who resettle in malaria endemic areas, subsistence farmers in forests and on the forest fringes, and forest workers (loggers, gem-miners etc.), particularly non-immune migrants working in forested areas. Within the country, the malaria burden is particularly high in the border areas. The highest morbidity rates were recorded in 2006 in Rakhine state on the west coast (54.6 clinical suspected malaria cases per1,000 population). The other provinces that also recorded a high rate of malaria cases per 1,000 persons are Chin state which borders Bangladesh, Kachin and Northern Shan states on the border with China, and Tanintharyi Region which borders Thailand. Rakhine and Shan states, which accounted for the highest number of suspected malaria cases in 2006, also had the most epidemics between 1991 and 2006 (nine and ten epidemics respectively). The highest mortality rates were recorded in Kaya (on the Thai border) and Kachin states, with 9.4 and 7.8 deaths respectively per 1,000 populations in 2005. Factors contributing to high morbidity and mortality in the border areas are the topography and climate conditions that facilitate malaria transmission, compounded by difficult communication in these remote areas, low literacy rates of ethnic minorities, difficult access to health services, high population mobility and the prevalence of multidrug-resistant P. *falciparum*. The malaria burden maybe even greater than these figures suggest, as only approximately 25% to 40% of fever cases utilize public health facilities, and self-treatment or treatment by the private sector are not reported (WHO, 2016).

Continued high malaria burden in hot spots and among vulnerable populations can be attributed to a combination of the following factors:

(i) A relatively large portion of the population live in or near forested areas or have occasional exposure to forested areas.

(ii) Specific malaria control investments have been inadequate, leaving large gaps in finance and service delivery areas.

(iii) Topography and climatic conditions are favorable for transmission of malaria, and presence of difference species of efficient vectors also enhances transmission.

Areas controlled by non-state actors (NSA) are not accessible by the NMCP to provide services, and thus information on malaria conditions is limited for these areas. Service delivery is further complicated by differing languages and beliefs related to health. Traditional slash-and-burn and paddy field farming communities visiting their forest farms, seasonal agricultural laborers, defense services, non-state actors, forest workers in the formal sector (police, border guards, forest/wildlife protection services), forest workers in the informal sector (hunters, small-scale gem/gold miners, people gathering forest products (timber, construction timber, rattan/bamboo), transient or mobile camps associated with commercial projects (road/pipeline construction, large-scale logging, deep sea port projects), formal and informal cross-border migrant workers (legal and illegal workforces) groups are at risk of malaria in endemic areas of Myanmar (NMCP, 2015).

3.3 Malaria and Mobile Populations

Many ethnic minority groups have large communal villages that are left all but empty for much of the year as families spend months away tending their crops in small farms scattered through the nearby forest. In addition, individuals (usually young men) may spend short periods away from their homes or forest farms, hunting or collecting forest products. Access to healthcare is often made even more difficult as a result. Forest goers and seasonal workers. People involved in forest-based activities in both the formal and informal sectors are at high risk Migrants. Migrants may be found in most of the situations described above, working for large private companies, living in unauthorized housing developments, working as seasonal agricultural laborers or as informal forest workers. Migrants, both national and international, are a particular concern in that they could potentially contribute to the spread of artemisinin resistant malaria parasites. Myanmar has a well-established free community based case management service for malaria delivered by village malaria workers (volunteers), work site volunteers and backpacked (mobile)volunteers. Coverage however is still sub-optimal. Technically the community service providers are part of public sector health services, but the providers themselves are volunteers, who depend on the support of an INGO or the National Programme. The volunteers substantially complement and extend the reach of public health services, particularly in rural and remote areas including to reach mobile and migrants, where health infrastructure tends to be weak or absent and malaria transmission tends to be highest. In order to

maximize the efficiency of the intervention, in future efforts will be made to reach the optimal solution of only one implementing partner managing community based services in each Township (DOPH, 2016).

3.4 National Strategic Plan for Malaria Elimination

The Republic of the Union of Myanmar has signed APLMA declaration to eliminate malaria by 2030 in 9th East Asia Summit in 2014. The National Malaria Control Programme is also committed to pursue malaria elimination by 2030. "National Malaria Strategic Plan (NSP) for Intensifying Malaria Control and Accelerating Progress towards Malaria Elimination 2016-2020" has been developed and finalized which is in alignment with the "Global Technical Strategy for Malaria (2016-2030)" and "Strategy for Malaria Elimination in the Greater Mekong Sub-Region (GMS) (2015-2030)". The "National Plan for Malaria Elimination-NPME in Myanmar 2016-2030" has been developed with the vision of *Plasmodium falciparum* elimination by 2025 and malaria elimination by 2030. Development of the plan is in line with the commitment made by the Ministry of Health and Sports to eliminate malaria by 2030 in the 9th East Asian Summit (APLMA, 2014).

Over recent years Myanmar has made a significant progress in reducing malaria morbidity and mortality. However, despite these recent advances, malaria remains a major public health issue in the country accounting for about 56% of all reported cases in the GMS. The malaria situation in Myanmar is rather complicated, because of its heterogeneity and parasite resistance, and the declared elimination goal is still distant because the rapidity in achieving the goal is influenced by the relatively high burden of malaria, a suboptimal national health systems and technical/ operational constraints. The presence of multi-drug resistance (MDR), in Myanmar call for urgent actions at national and regional levels. The best strategy for coping with the problem of MDR in Myanmar is to aim for the elimination of P. falciparum. The NPME 2016-2030 has been developed in line with the WHO Global Technical Strategy for Malaria 2016-2030, the Strategy for Malaria Elimination in the GMS 2015-2030 and the National Strategic Plan (NSP) for Intensifying Malaria Control and Accelerating Progress towards Malaria Elimination 2016-2020.

The WHO Malaria Policy and Advisory Committee recommended that the elimination of P. falciparum in the GMS by 2030 is technically, operationally and

financially feasible and at the 9th East Asia Summit in November 2014 all Asia Pacific leaders committed to a region free of malaria by 2030. The initial concept of NPME was prepared by WHO and discussed with NMCP on 26 August 2016 and the first draft was discussed thoroughly with Central and State/Regional level staff on 16 September 2016 and was further refined with the support of WHO. The draft document was presented by NMCP to the TSG-Malaria on 19 September 2016 and was finalized. The ultimate goal of the NSHPME in Myanmar 2016-2030 is to interrupt transmission of and eliminate indigenous malaria throughout the entire country by 2030; and maintain malaria-free status in areas where malaria transmission has been interrupted and prevent re-establishment of local transmission. The proposed NSHPME emphasizes massive scaling up of existing disease management and preventive approaches and interventions to reduce the burden of malaria in high transmission areas in a short run where elimination of malaria does not appear to be feasible at present. This may form a transitional stage on the path to elimination. Wherever malaria elimination has good prospects it should be pursued with vigor towards the defined goal. The NSHPME highlights the necessity of a conductive policy environment and support from the highest level of the State to ensure effective multi-sectoral engagement (APLMA, 2014).

NMCP needs to address human resources requirements for malaria elimination at all levels. National leadership and governance, including stakeholder coordination needs to be assured. Curative and preventive services including community based approaches should be in place to provide full access to effective case management and disease prevention for everyone at risk of malaria. Malaria in border areas of Myanmar and neighboring GMS countries also becomes a major problem that requires special attention because of the intense population movements within as well as across national borders.

The NMCP of the Ministry of Health and Sports of the Government of Myanmar aims to achieve malaria elimination by ensuring equitable and universal access to effective curative and preventive services to everyone at risk of malaria, in close coordination with all communities, national and international non-government organizations, private sector stakeholders, United Nations agencies and financial partners. Achieving the vision of “A Malaria free Myanmar by 2030” will contribute significantly to poverty alleviation as malaria is most prevalent in the poorest segment

of the population, those living or spending time in remote forested areas including mobile and migrant population (DOPH, 2016).

3.5 Antimalarial Treatment Policy

The main determinant of antimalarial treatment policy is the therapeutic efficacy of the antimalarial medicines in use. Therapeutic efficacy monitoring involves the assessment of clinical and parasitological outcomes of treatment over at least 28 days following the start of adequate treatment to monitor for the reappearance of parasites in the blood. Reappearance of the same genotype indicates reduced parasite sensitivity to the treatment drug. The current recommended duration of follow-up is a minimum of 28 days for all antimalarial medicines, while it is extended for longer periods of time depending on elimination half-life of medicines. Other important determinants include, changing patterns of malaria-associated morbidity and mortality; consumer and provider dissatisfaction with the current policy; and the availability of alternative medicines, strategies and approaches.

A change of an antimalarial medicine recommended in the national malaria treatment policy should be initiated if the total treatment failure proportion is ≥ 10%, as assessed through in vivo monitoring of therapeutic efficacy. The selection of a new and/or alternative antimalarial medicine for use at public health level within the context of national treatment guidelines, should be based on an average cure rate of > 95%, as assessed in clinical trials. Current situation of therapeutic efficacy study results showed that although day 3 parasitaemia is ≥ 10% in some areas, there is no evidence of treatment failure which means that partner drugs are still effective. Therefore, it is no need to change existing ACT combinations. But Artesunate plus Mefloquine combination must be “fixed-dose combination” rather than co-blistered or loose single agent formulations tablet because of banning oral monotherapy of Artemisinin in Myanmar (DOPH, 2015).

CHAPTER IV
SURVEY ANALYSIS

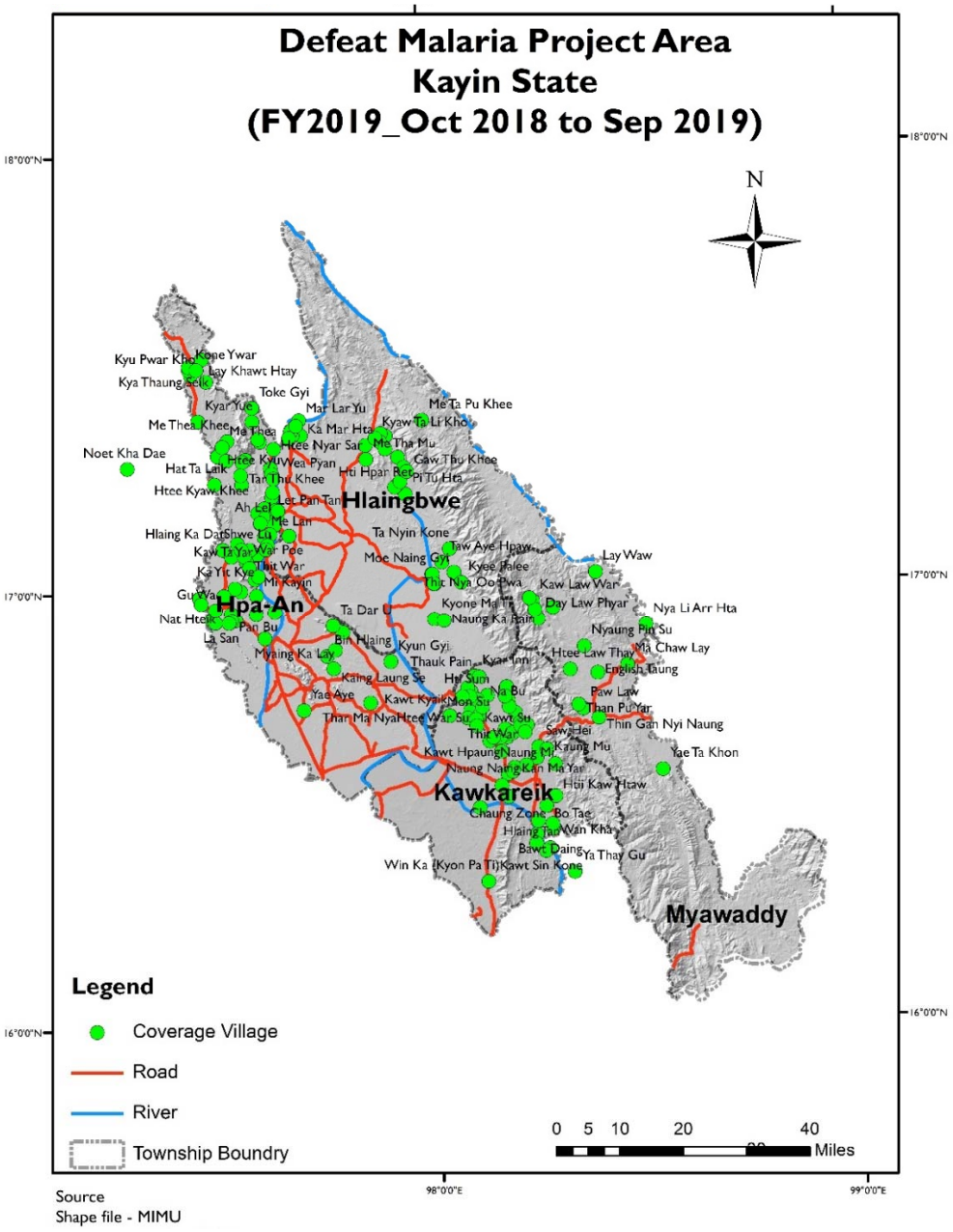
4.1 Survey Profile

This study surveyed to (140) *P. vivax* malaria positive cases who were treated according to National Treatment Guideline for Malaria (NMCP) by village malaria workers of "Defeat Malaria Project" in Hpa-An, Hlaingbwe, Kawkareik and Myawaddy townships of Kayin State. Number of patients interviewed in each township were; (28) from Hpa-An, (8) from Hlaingbwe, (18) from Kawkareik and (86) from Myawaddy. This number of patients interviewed in each township depended upon the number of *P. vivax* positive patients presented in concerned township between October 1, 2017 and September 30, 2018. Under Defeat Malaria project implementation, Village Malaria Worker prescribed weekly dose of Primaquine tablets 45 mg for 8-week dosing schedule to treat *P. vivax* infection in these 4 project townships of Kayin State. "Defeat Malaria Project" was implemented by the partner organizations; "URC, ARC, Jhpiego, MNMA, MHAA and University of Marylands" (International Non-Government Organizations) under funding of USAID in total 33 townships of Kayin State, Tanintharyi Region, Rakhine State and Sagaing Region. This study selected aforementioned 4 townships of Kayin state for primary data collection. For secondary data review, "Dawei, Palaw, Tanintharyi and Thayetchaung townships where Primaquine tablets 15 mg for 14 days dosing schedule prescribed by VMW was piloted" were selected for reviewing secondary data extracted from project annual report. The patients participated in the survey were selected by random sampling method.

Survey was conducted in Hpa-An, Hlaingbwe, Kawkareik and Myawaddy townships in Kayin State where surveyed *P. vivax* positive patients were residing. Hpa-An township covers the area of 2,903.13 Sq. Km. It has population of total 397,526 (2017) with Urban population 62,824 and Rural population 334,702. Hpa-An has 483 villages in the township. Hlaingbwe township covers area of 1607.7 Sq. Km. Total population is 338,593(2017) with Urban population 15,587 and Rural

population 323,006. Hlaingbwe township has 432 villages in the township. Kawkareik township covers 303,85.49 Sq. Km. It has total population 255,558 (2017) with Urban population 36,570 and Rural population 218,988. Kawkareik has 234 villages. Myawaddy township covers total population 169,376(2017) with Urban population 74,405 and Rural population 94,971. Myawaddy has 98 villages.

Figure (4.1) Defeat Malaria Project Area in Kayin State



Source: MIMU

Survey participants were selected by random sampling from *P. vivax* positive patients who were treated by village malaria workers of "Defeat Malaria project" between the period of October 1, 2017 to September 30, 2018. A training on "survey methodology and data collection technique" was conducted in Hpa-An Township on 13 November, 2018 to selected enumerators including township level Defeat Malaria project township staffs. A pilot survey was conducted in "Wei Pyan Chaung Wa" village on December 3, 2018. Data collection was done from 4 to 24 December, 2018 with pre-entry data verification, double entry, post-entry data verification and cross-checking of source documents were done in the last week of December, 2018. Data analysis and report development was done in January, 2019.

4.2 Survey Design

Quantitative data were collected through delivering a structured questionnaire to the respondents. SPSS version 24 and Microsoft Excel applications were used as research tools in this study. SPSS version 24 was mainly used to data entry and analysis of frequencies, percentage, mean scores, cross tabulations and Microsoft Excel was mainly used to prepare the relevant table, charts and organized data.

4.2.1 Sampling Method and Sample Size

A random sampling method was applied to the *P. vivax* positive patients who were treated during the period of October 1, 2017 and September 30, 2018 in four Defeat Malaria project townships (Hpa-An, Hlaingbwe, Kawkareik and Myawady townships) in Kayin State. Total 140 *P. vivax* positive patients among 342 *P. vivax* positive patients from these four townships were selected by random sampling method. Number of patients selected from each township were; (28) from Hpa-An, (8) from Hlaingbwe, (18) from Kawkareik and (86) from Myawaddy and they were invited for interview. The selected patients included *P. vivax* positive children under 15-year old and they were interviewed by the assistance of parents or guardian in the family.

4.2.2 Data Collection Method

The questionnaire was developed with the well-structured questionnaire with coding for common response categories and the inclusion of open-ended responses for unexpected answers was used. Open-ended responses were coded in the data analysis

phase. Question types included single and multiple responses. Some questions were needed for probing while some were spontaneous with a full description provided in the tool (See Appendices). There were four survey teams each composed of one supervisor and 4 enumerators who were staffs from "Defeat Malaria" project. Supervisors checked and verified all questionnaires prior to leaving villages. Performance of enumerators was closely supervised and overall quality assurance was provided.

4.2.3 Data Management and Analysis

Before data collection, survey team members and supervisors were on all variables in the questionnaire, appropriate utilization of codes, interview techniques for valid data capture, and validation/data cross-checking. Pre-entry data verification was done by supervisors and data was entered into SPSS via a double entry method. Post-entry data verification was done by supervisors for discordant data and then verified against source documents. Data analysis was done using SPSS Software application version 24.

4.3 Survey Results

Survey results from analyzing collected data were presented and explained its finding as per related questionnaire topics.

4.3.1 Demographic Characteristics of Respondents

According to the questionnaire, demographic characteristics of the respondents were presented by age, gender, education level, occupation, migration status and ethnicity. Detailed distribution of the demographic characteristic of the respondents were shown in the table (4.1).

Table (4.1) Demographic Characteristics of Respondents

Demographic characteristics	No. of Respondents	Percent
Age (Completed year) **Mean Age = 25 years; Minimum = 5 years; Maximum = 64 years**		
<15	28	20%
15-39	86	61.4%
40-59	24	17.2%
60+	2	1.4%
Total	**140**	**100%**
Education Level		
Illiterate	54	38.6%
Below Primary (Read & Write)	26	18.6%
Primary (1st – 4th Grade)	27	19.3%
Middle (5th - 8th Grade)	26	18.6%
High (9th – 10th Grade)	7	5%
Higher Education (Graduate)	0	0%
Total	**140**	**100%**
Occupation (Main income source)		
Dependent (Housewife & Student)	32	22.9%
Farmer	73	52.1%
Forest related works	16	11.4%
Casual work (domestic, various non-specific jobs)	15	10.7%
Other jobs	4	2.9%
Total	**140**	**100%**
Types of migrant		
Local	40	28.6%
Outbound migrants	87	62.1%
Inbound migrants	13	9.3%
Total	**140**	**100%**
Gender		
Male	100	71%
Female	40	29%
Total	**140**	**100%**
Ethnic group		
Kayin (Sakaw)	88	62.9%
Kayin (Poe)	23	16.4%
Bamar	27	19.3%
Mon	2	1.4%
Total	**140**	**100%**

Source: Survey data

The minimum age of the respondents was 5-year, maximum age was 64-year and the mean age was 25-year. Most frequency age group falls between 15 to 39 year. This age group is commonly known as in the range of working age group and shared the largest with (61.4%) among the respondents. More than (75%) of the respondents' education level was not higher than a primary education. Therefore, most of the respondents' education level reflected the knowledge status of the people living in the rural area. The main occupations were farmers who works in the farming places which are located near forested area (52.1%), forest related work (11.4%), and casual work (10.7%), dependent including housewife and student (22.9%) and other jobs category was (2.9%). Therefore, the distribution of occupation among the most of respondents fell in farming and forest related work. It reflects the respondents' low socioeconomic status in the rural area. Regarding with the migration status, (62.1%) respondents were outbound migrants who were migrating out from the village for their work. (9.3%) respondents were inbound migrants who migrated into the village from different geographical area and their stay in the village was not longer than one year. (28.6%) respondents were local to the respective village. Migration status showed that more than (70%) of the respondents were either type of outbound or inbound migrant; Outbound migrant is defined as the villager who has permanent resident in the village but temporarily living and working at outside of the village, for example, farmer who lives and works at farm and, logger at logging site in the forest. Inbound migrant is the villager who migrated from other area into the village and residing in the village since less than 1 year ago.

4.3.2 Malaria Knowledge of Respondents

(a) Knowledge on Cause of Malaria

Table (4.2) Knowledge on Cause of Malaria (N =140, Multiple Responses)

Specified Cause	No. of Respondents	Percent
Mosquito bite	116	82.86%
Drinking stream water	9	6%
Drinking unsafe water	7	5%
Going to forest	41	29.29%
Wrong behavior in forest	2	1.43%
Poor hygiene	1	1%
Bath in stream/river	1	1%
Eating banana	0	0%
Other causes	1	1%
Don't know	21	17.64%

Source: Survey data

Knowledge that mosquito bite causes malaria was high (83%). The most of the respondents had correct knowledge of cause of malaria as mosquito bite. The most common incorrect responses included drinking stream water (6%), drinking unsafe water (5%), and (18%) did not know the cause. Forest goers were assumed to be high risk because (29%) of respondents revealed that going to the forest was a causes of malaria. According to findings, knowledge on cause of malaria was high among the respondents it can be due to health education activities provided by Defeat Malaria project to the community.

(b) Knowledge on Symptoms of Malaria

Table (4.3) Knowledge on Symptoms of Malaria (N=140, Multiple Responses)

Specified Symptoms	No. of Respondents	Percent
Fever	110	78.60%
Chill & rigor	88	63%
Headache	63	45.00%
Body ache	29	20.70%
Sweating	27	19.30%
Fatigue	11	8%
Loss of appetite	12	8.20%
Loose motion	3	2.10%
Others	2	1.40%
Don't know	14	10.00%

Source: Survey data

Regarding with the symptoms of malaria, the most of the respondents shared (79%) and (63%) respectively knowing that fever and chill and rigor were symptoms of malaria. Headache and body ache were also common responses (45%) and (21%) respectively. (19%) of participants responded sweating as symptom of malaria, it was also one of the common symptoms of malaria. Therefore, most of the respondents commonly had knowledge about symptom of malaria.

(c) Knowledge of Malaria Prevention

Table (4.4) Knowledge of Malaria Prevention (N=140, Multiple Responses)

Knowledge of malaria prevention	No. of Respondents	Percent
Sleeping under mosquito nets (ordinary nets)	103	73.6%
Sleeping under insecticide treated nets	45	32.1%
Using mosquito coil	13	9.3%
Using mosquito repellent	13	9.3%
Insecticide spray	5	3.6%
Burning leaves	11	7.9%
Cleaning bushes around the house	22	15.7%
Using long sleeve clothes	14	10.0%
Staying out of the forest	6	4.3%
Malaria chemoprophylaxis	1	0.7%
Earth-filling of mosquito breeding place	11	7.9%
Drinking boiled water	2	1.4%
Other	1	0.7%
Don't know	21	15.0%

Source: Survey data

Regarding knowledge of malaria prevention, (73.6%) of participants responded sleeping under a mosquito net while only (32.1%) responded to sleeping under insecticide treated nets. Other preventive knowledge to reduce man-mosquito contact were cleaning bushes around the house (15.7%) and using mosquito coils (9.3%). Preventive methods not appropriate for malaria control included drinking boiled water by (1.4%) of respondents. Therefore, most of the respondents knew that sleeping under mosquito net can prevent malaria and it can be due to health education activities provided by the project to the community.

4.3.3 Respondents' Recall on Primaquine Treatment

The respondents were interviewed to feedback by their self-reported behavior of if taken right drug (Primaquine) with right dose, right interval and right course duration (8- week) of Primaquine when he/ she had *P. vivax* malaria fever during surveyed period.

(a) Right Drug for *P. vivax* malaria

Table (4.5) Respondents' Recall on Right Drug

Respondents' recall on right drug taken	No. of Respondents	Percent
White color tablet (Chloroquine)	78	55.7%
Brown color tablet (Primaquine)	88	62.9%
Others	1	0.7%
Don't know	33	23.6%
Total	**140**	**100%**

Source: Survey data

There were (55.7%) of respondents who could have reported about if he/ she has taken malaria medicines, Chloroquine tablet as white color, and (62.9%) of respondents recalled Primaquine tablet as brown color tablet. Some of respondents (23.6%) could not have recalled their memory about malaria medicines they have taken. Therefore, most of the respondents could have recalled that they have taken Primaquine (study's interest) as one of malaria medicines they have taken for *P. vivax* malaria. In this study, the respondents were selected from the *P. vivax* positive patients who were treated as per National Treatment Guideline for malaria and therefore, the questionnaire included question to confirm if the respondent has taken right drug (Primaquine) with right dose, right interval and right course of Primaquine.

(b) Right Dose of Primaquine at Each Time

Table (4.6) Respondent's Recall on Right Dose

Respondents' recall on right dose	No. of Respondents	Percent
Correct dose of Primaquine taken per week	87	62.1%
Incorrect dose of Primaquine taken per week	4	2.9%
Don't know	49	35%
Total	**140**	**100%**

Source: Survey data

There were (62.1%) of respondents who could have reported about right dose of Primaquine (in proportion to age) as per National Treatment Guideline of malaria.

But, (4%) could not have recalled right dose of Primaquine and (35%) of respondents were not able to recall their memory about right dose of Priaquine he/ she had taken.

(c) Right Interval of Primaquine

Table (4.7) Respondent's Recall on Right Interval

Respondents' recall on right interval	No. of Respondents	Percent
7-days	118	84.3%
Don't know	22	15.7%
Total	**140**	**100%**

Source: Survey data

There were (84.3%) of respondents who could have reported on right interval (one time per week) of Primaquine as per National Treatment Guideline of malaria. But, (15.7%) of respondents were not able to recall their memory on right interval of Priaquine he/ she had taken.

(d) Respondents' Different Completeness of Primaquine for 8-Week Course

Table (4.8) Different Completeness of Primaquine 8-Week Course

Different completeness of Primaquine course	No. of Respondents	Percent
Completed with right interval	83	59.3%
Completed but with varying interval	38	27.1%
Incomplete	19	13.6%
Total	**140**	**100%**

Source: Survey data

Regarding with the completeness of Primaquine that the respondents had taken, (59.3%) of the respondents completed right course (for 8-weeks) with right interval, (27.1%) of respondents completed 8-weeks course with varying interval and (13.6%) were incomplete. Therefore, there were total (40.7%) of respondents (57 out of 140 respondents) including two groups of incompleteness; 1) who didn't complete 8-week course and 2) who completed 8-week but not in right interval. This percentage showed that malaria parasite *P. vivax* would not have been eliminated from human

body if the treatment was not completely taken in right interval (one time per week) and right course (8-week).

Table (4.9) Combined Completeness and Incompleteness

Completeness of 8 week with both right interval and right course	No. of Respondents	Percent
Completed with right interval	83	59.3%
Incomplete (sum of both completed but with varying interval and incomplete)	57	40.7%
Total	**140**	**100%**

Source: Survey data

Combined data of total number of patients who completed Primaquine 8-week course with right interval was 83 (59-.3%) and number of patients who were incomplete (sum of incomplete patients and varying interval incomplete patients) was 57 (40.7%).

4.3.4 Relationship between Type of Migrant and Primaquine Course Completeness

Table (4.10) Primaquine Course Completeness by Type of Migrant

Course Completeness	Local	Outbound Migrant	Inbound Migrant
Complete	80%	51%	54%
Incomplete	20%	49%	46%

Source: Survey data

In terms of relationship between type of migrant and Primaquine treatment course completeness, (80%) of local residents completed Primaquine treatment course, and (20%) of them were incomplete. (50.6%) of outbound migrant type respondents completed treatment course but (49.4%) of them were incomplete. (53.8%) of inbound migrant type respondents completed and (46.2%) of them were incomplete. Therefore, there were relatively more association between either outbound or inbound migrant type with incompleteness of Primaquine course than local resident type respondents.

4.3.5 Relationship between Primaquine Treatment Course Completeness and Types of Occupation

Table (4.11) Primaquine Course Completeness by Type of Occupation

Course Completeness	Dependent	Farmer	Forest Work	Casual	Other Jobs
Complete	78.1%	57.5%	31.2%	60%	50%
Incomplete	21.9%	42.5%	68.8%	40%	50%

Source: Survey data

In terms of relationship between different types of occupation and Primaquine treatment course completeness, (78.1%) of respondents within dependent group completed and (21.9%) of them were incomplete. (57.5%) of farmer respondents were complete but (42.5%) of them were incomplete. (31.2%) of forest related occupation type respondents were complete but (68.8%) of them were incomplete. Casual work type respondents (domestic and non-specific jobs) were (60%) complete and (40%) of them were incomplete and within other jobs category respondents had (50%) complete and (50%) incomplete. Therefore, it was found that the respondents who work in forest related occupations had more than 68% incompleteness within their type of occupation while dependents were more than 78% complete.

4.3.6 Relationship between Primaquine Course Completeness and Forest Related and Non-Forest Related Occupation

Table (4.12) Primaquine Course Completeness and Forest Related Occupation

Course Completeness	Forest Related	Forest not-related
Complete	26.70%	63.20%
Incomplete	73.30%	36.80%

Source: Survey data

Respondents in forest related occupation had (26.7%) completeness of the Primaquine treatment course but (73.3%) of them with forest related occupation were incomplete. In case of non-forest related occupation respondents, (63.2%) of them were complete and (36.8%) were incomplete. The result showed that forest related

occupation had more association with treatment incompleteness either by right interval or right course.

4.3.7 Reasons of Incompleteness of Primaquine Course

Table (4.13) Reasons of Incompleteness of Primaquine Course (N-140, Multiple Responses)

Reasons for incompleteness of Primaquine course	No. of Respondents	Percent
Long duration of treatment course	3	2.1%
Forgot because of weekly treatment	40	28.6%
Because of travelling	15	10.7%
Because busy with the work	18	12.9%
Schooling	0	0%
Dizziness	1	0.7%
Other	3	2.1%
Don't know	0	0%

Source: Survey data

The reason for incompleteness of Primaquine course were found as; (2.1%) of respondents were due to long duration of treatment course, (28.6%) responded that they forgot to take medicine because of weekly treatment, (10.7%) were because of travelling, and (12.9%) were because of busy with the work. Dizziness and other were responded as (0.7%) and (2.1%) respectively. Therefore, some of the respondents' reason of incompleteness was they forgot to take right interval and right course of Primaquine tablets.

4.3.8 Occurrence of Black Urination

The occurrence of black urination was not responded by the all participants. This question was asked to exclude if there was occurrence of side effect of Primaquine (Primaquine can cause black urination due to breakdown of red blood cells) to the patients who took Primaquine for malaria treatment. It was found that all (140) respondents didn't experience Primaquine side effect after they had taken for *P. vivax* malaria treatment.

4.3.9 Preference of Primaquine Treatment Schedule

The preference of the respondents to Primaquine treatment schedule to daily for 2-week course instead of taking weekly dose of 8-week course schedule was (100%). All respondents preferred that Primaquine daily dosing for 2 week course instead of taking 8 weeks with weekly interval. The most of the respondents expressed that they would not forget if they take daily dose.

4.3.10 Review on Secondary Data

Table (4.14) Primaquine Course Completeness in Secondary Data Review

Sr. No.	Township	No. of *P. vivax* cases	No. of *P. vivax* cases who completed Primaquine treatment with daily for 2 week course	% of Completeness
1	Dawei	97	96	99%
2	Palaw	81	81	100%
3	Tanintharyi	34	32	94%
4	Thayetchaung	85	83	98%
	Total	**297**	**292**	**98%**

Source: Defeat Malaria project annual report, FY 2018

Secondary data of the Defeat Malaria project annual report of FY 2018 was retrieved from project monitoring archives and reviewed on Primaquine treatment completeness of P. vivax positive patients from "Dawei, Palaw, Tanintharyi and Thayetchaung" townships. "Defeat Malaria Project" conducted pilot trail on "Daily dose for 2 weeks course of Primaquine" for P. vivax positive patients in that 4 townships in Tanintharyi region and the treatment was prescribed by village malaria workers (VMW). The review on secondary data found that Primaquine course completeness were; Dawei (99%, N = 97), Palaw (100%, N = 81), Tanintharyi (94%, N = 32), and Thayetchaung (98%, N=85). Overall completeness of Primaquine daily for 2 week treatment course was (98%).

4.4 Key Informant Interview

Table (4.15) List of Key Informant Interviewees

Sr. No.	Designation/ Occupation	Date of Interview
1	Saw Lwin, Core Technical Support Group (CTSG) member, National Malaria Control Program, Ministry of Health and Sports, Myanmar	12 November, 2018
2	Thandar Lwin, Deputy Director General, Disease Control, Ministry of Health and Sports, Myanmar	13 November, 2018
3	Wai Lin Aung, Township Coordinator, Defeat Malaria project, Kawkareik township, Kayin state	19 November, 2018
4	Nant Htay Htay Aung, Village Malaria Worker, Defeat Malaria project, Htee War Galay village, Hpa-An township, Kayin state	20 November, 2018

Source: Survey data

Key informant interviews were done at central level (Malaria Technical Support Group), township level (Defeat Malaria Project Staff) and community level resource personnel (Village Malaria Worker). The purpose of interview was to get technically related information supportive to adherence of Primaquine treatment prescribed by community volunteer in rural setting. In line with malaria treatment guideline of WHO, National Malaria Control Program, Myanmar (NMCP) recommended on the treatment for uncomplicated *P. vivax malaria as;*

1. Chloroquine (total dose of 25mg base/kg) divided into 3-days course
2. For radical curative treatment of *P. vivax* malaria, Primaquine is required to prescribe starting from the last day of chloroquine (on 3rd day of chloroquine course) as:
    - Health staffs are asked to give Primaquine 0.25mg base/kg/day for 14 days for radical treatment
    - Volunteers and Village Malaria Worker (VMW) are asked to prescribe Primaquine 0.75mg/kg once weekly for 8 weeks because of the requirement on recognition of Primaquine side-effect causing red color urine

Both regimens are effective for radical cure of *P. vivax* malaria and when Primaquine is given, patient must be informed to stop the drug as soon as urine color becomes red.

4.4.1 Questions and answers from key informant interviews

Questions and answers from key informant interviews making with were;

Question 1: What is the strategic point of view on 8-week Primaquine dosing schedule in *P. vivax* malaria treatment prescribed by malaria volunteer?

Answer: Saw Lwin, Core Technical Support Group member (CTSG) of National Malaria Control Program explained that the VMW level Primaquine treatment guideline of once a week for 8-week dosing schedule was reviewed and CTSG was looking forward to revise the guideline as daily for 2-week regime because of occasional treatment adherence issues in 8-week Primaquine dosing schedule. To get well planned change from 8-week scheduling to 2-week scheduling, the actions required were; 1) To find more evidences proving that 8-week scheduling has adherence issues, 2) Advocacy to CTSG (NMCP) to change guideline, 3) Basic Health Staffs were needed to be trained on managing adverse event of Primaquine treatment, 4) To improve awareness by the community on the rare events of Primaquine adverse event and its management including notification of incidence of adverse event if it happens, and the importance of the interruption of malaria transmission while Myanmar is going to malaria elimination effort, the advocacy processes were needed through different ways including by social media how to manage.

Question 2: What is the important role of Primaquine treatment of *P. vivax* malaria in Myanmar malaria elimination goal?

Answer: Thandar Lwin, Deputy Director General of Disease Control, Ministry of Health and Sports (MOHS) mentioned that, the malaria burden is still high in Myanmar and MOHS called for malaria elimination before 2030 in line with GMS countries' strategy. It is important to strengthen malaria surveillance system given that there were experiences of malaria drug resistance in Cambodia, Thailand and Laos in GMS region. National Strategic Plan for Malaria Elimination has been already launched in country and elimination plan in Myanmar is to be launched in low malaria townships. Regarding with the Primaquine treatment of *P. vivax* malaria, effective

treatment is important in contributing malaria elimination goal. Treatment adherence is crucial for preventing malaria drug resistance.

Question 3: What are the challenges regarding with Primaquine 8-week treatment for *P. vivax* malaria patients?

Answer: Wai Lin Aung, Township Coordinator, Kawkareik township Defeat Malaria project, shared his experience that there were mobile migrant populations in the project villages and most of them were forest related workers. Township project staffs had challenges with the mobile population in prescribing Primaquine 8-week course treatment if they were infected by malaria including *P. vivax*. Township project staffs were not able to monitor if the malaria infected patients of mobile work nature were to be treated with longer duration of Primaquine.

Question 4: What was your experience about Primaquine 8-week treatment for *P. vivax* malaria patient?

Answer: Nant Htay Htay Aung, she is a VMW of Defeat Malaria project and she is a resident of "Htee War Galay" village of Hpa-An township. She had experience of treating to mobile population with malaria. According to her experience sharing, there were two mobile workers (both were loggers) who were infected by *P. vivax* malaria in last few months in 2018. In that case, she had given Primaquine tablets for 8-week course but she was not able to monitor their adherence to the Primaquine treatment because their occupation is mobile and forest related nature.

CHAPTER V
CONCLUSION

5.1 Findings

This study examined *P. vivax* positive patients' adherence to 8-week schedule of Primaquine treatment which is provided by Village Malaria Worker (VMW). The analysis of primary data was done on "8-weeks Primaquine treatment adherence by 140 patients" (N = 140) who were infected by *P. vivax* infection and treated by VMWs of Defeat Malaria project between period of October 1, 2017 and September 30, 2018. The analysis of secondary data has used report on treatment completion of 297 *P. vivax* infected patients from Dawei, Palaw, Tanintharyi and Thayetchaung townships of Tanintharyi region where Defeat Malaria project has been piloting Primaquine dosing schedule by VMW as daily for 2 weeks course. The key informant interview was made to focal persons from different levels of actors on malaria prevention and control services including from 1) central level; National Malaria Control Program (NMCP) and National Technical Advisor (Malaria Technical Support Group-TSG), 2) from township level; Township Project Coordinator of Defeat Malaria project, and 3) from village level; Village Malaria Worker (VMW).

The analytical findings of the study supported to answer the questions of the study objective; to identify the associated conditions related with the incompleteness of 8-week Primaquine course. In terms of completeness of Primaquine course with both right interval and right course, the results found that there were low adherences to 8-week Primaquine dosing schedule either by totally incomplete or complete with varying interval. This finding supported that there would be controversial implication to full effectiveness of Primaquine in *P. vivax* treatment. More than 40% of studied *P. vivax* positive patients were poorly adhering to the treatment of malaria and as consequences, there would be high risk of persistent transmission of malaria in the region.

There was relationship between migrant type of the patients and treatment course completeness. While majority of the locally resident patient completed

Primaquine treatment course, outbound migrant type patients and inbound migrant type patients were found as incomplete in treatment course. The result was supporting that mobile migrant populations were at risk of continued illness and favoring to onward transmission of malaria to others.

Relationship between Primaquine treatment course completeness and forest related occupation was found by analyzed data. Respondents in forest related occupation had (26.7%) completeness of the Primaquine treatment course but (73.3%) of them with forest related occupation were incomplete. In case of non-forest related occupation respondents, (63.2%) of them were complete and (36.8%) were incomplete. Forest related works such as logging, charcoal making and cattle transportation were mobile in nature and the low socioeconomic situation of the patients was forcing them to return to their work place before completing 8-week time to get weekly for 8 week Primaquine treatment complete. Therefore, this study intended to suggest NMCP to revise *P. vivax* treatment by VMWs as Primaquine 2-week dosing schedule.

The common reasons of treatment incompleteness were long duration of treatment course, the patient forgot to take medicine because of once in a week treatment, mobile works required travelling and therefore missed to take Primaquine during travelling and busy with the work. Therefore, this study would be suggesting that if the treatment was provided in daily dosing schedule with shorter course for 2-week, the patients awareness to take medicine in daily basis can be better than weekly interval and longer course.

The study result showed that all studied population didn't suffer from adverse reaction of Primaquine (Black Urination due to red blood cell breakdown caused by Primaquine). There were association between Primaquine side effect in G6PD enzyme deficient patients. According to this study, Primaquine side effect was not found in all respondents. But, health care provider (government health staffs and community level volunteer) must have awareness on side effect of the Primaquine in treating malaria patient to take necessary action if happen.

The analysis of secondary data from the Defeat Malaria project annual report of FY 2018 for "Dawei, Palaw, Tanintharyi and Thayetchaung" townships, found that Primaquine completeness of *P. vivax* positive patients were more than (98%) in that reviewed townships of the Tanintharyi region. According to the Defeat Malaria Project annual report, there was only one case reported as mild form of adverse effect due

to Primaquine but it was not fatal to that patient. Despite of side effect case was reported, the completeness of the treatment outweighed the impact on interruption of malaria in country. This finding was supporting to revise Primaquine dosing schedule from 8-week course to 2-week daily course to be prescribed by VMW.

Key informant interviews with the focal persons of different levels; strategic level, implementation level and community level including mobile and forest related worker informed that 8-week treatment course of Primaquine was found to be low adherence and recommended to shorter treatment course to get effective clearance of malaria parasite from human body. The respondents from Key Informant Interview informed that treatment adherence to longer course of Primaquine would be low particularly in patients with mobile and forest related work nature.

5.2 Suggestion

Risk of Malaria transmission by low adherence to 8-week Primaquine treatment was learned that it can lead to persistent transmission of malaria, drug resistance, increased morbidity among the vulnerable communities. The study questioned the adherence of patients with the 8weeks Primaquine treatment at the community level (rural setting) in which if the treatment time frame is a matter of poor adherence to complete the full course. The study findings were supporting that the weekly dosing of Primaquine for 8-week treatment course had low adherence in the rural setting in Myanmar.

The study findings were supporting the fact that Primaquine 8-week dosing schedule had risk of prolonged and repeated illness from malaria and more importantly there was the risk of persistent transmission of malaria in the community. The interruption of human malaria transmission is mandatory advancement required for country's strategic plan of malaria elimination.

Given that Myanmar has a well-established free community based case management service for malaria delivered by village health volunteers (VHVs) or village malaria worker (VMWs). Technically the community service providers are a part of public sector health services, but the providers themselves are volunteers. The volunteers substantially complement and extend the reach of public health services, particularly in rural and remote areas, where health infrastructure tends to be weak or absent and malaria transmission tends to be highest. The effective treatment guideline for volunteer's malaria treatment at the community level is therefore requirement to

fulfill the national malaria strategy implementation to interrupt malaria transmission among at risk population.

Based on the study finding, the factual evidences were withdrawn to support the suggestion as;

(i) Village Malaria Worker (VMW) treatment guideline of Primaquine treatment course for *P. vivax* patients, is to be revised as shorter dosing schedule of 15 mg daily for 14 days (2-weeks) schedule

(ii) Proper pharmacological vigilance mechanism is required to be in place including at the community level so that the adverse events of the Primaquine would be detected early for timely correctness

(iii) Prevalence of Primaquine adverse effect (due to G6PD enzyme deficiency) among the patients who took 2 week Primaquine course should be continuously studied

(iv) The community awareness to be improved on importance of interruption of human malaria linked to country goal of malaria elimination in 2030.

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APPENDIX

Questionnaire to study patient's demographic characteristics, blood test history, treatment provider, treatment adherence and reason of failure to adherence with 8-weeks full course of PQ treatment

(Ask question to patient who had been RDT tested by VMW with P. v positive result between October 1, 2017 and September 30, 2018 according to township monthly report data; No need to ask if patient was under 5-year and pregnant in last year between October 1, 2017 and September 30, 2018. Ask parent or guardian if the patient is below 15 year).

Village: ---------- Township: ---------- State/ Region ----------

Patient Name: ---------- Date: ----------

To assist in our review, please answer the following questions and provide a brief explanation where applicable.

To check if patient was *P. vivax* positive patient in the last year				
A	Did you have blood test for malaria in last 1 year? Select one;	Yes No Other Advise if other Not remember	1 2 77 99	No need to continue if answer is 2
b	Did you know if malaria is positive at that time? Select one;	Positive Negative Not remember	1 2 99	No need to continue if answer is (2)

Demographic Characteristics	
1.1 Patient age group (year)	
1.2 Gender (Select one)	1. Male 2. Female
1.3 Ethnicity (Select one)	1. Kayin (Sakaw) 2. Kayin (Poe) 3. Bamar 4. Mon 77. Other (Please specify) ☐
1.4 Education	
1.5 Occupation	
1.6 Type of Migrant Select one	1. Local (usually reside in village) 2. Outbound migrant 3. Inbound migrant
1.7 Number of family member	
1.8 Family monthly income (Average)	
1.8 Is there VMW in your village	
Malaria Knowledge	

2.1	Malaria is caused by (Multiple response) (Answer can be more than one, don't read the answer, just refer it by enumerator)	Mosquito bite Drinking stream water Not drinking boiled water Going to forest Wrong behavior in forest Dirtiness Bath in river Eating banana Other Please specify [ ] Don't know	1 2 3 4 5 6 7 8 77 99	
2.2	What are malaria symptoms? (Multiple response) (Answer can be more than one, don't read the answer, just refer it by enumerator)	Fever Chill & rigor Headache Body ache Sweating Tiredness Loss of appetite Loose motion Other Pease specify [ ] Don't know	1 2 3 4 5 6 7 8 77 99	
2.3	How to prevent from malaria? (Multiple response) (Answer can be more than one, don't read the answer, just refer it by enumerator)	Sleep with bed net Sleep in Insecticide Treated Net Use mosquito coil Use mosquito repellent Spray Burning leaves Clean around the house Wear long sleeve shirt Stay away from forest Chemoprophlaxis Fill water pools of mosquito	1 2 3 4 5 6 7 8 9 10 11	

		breed		
		Drink boiled water	12	
		Other	77	
		Please specify		
		Don't know	99	
2.4	What happen if malaria medicine is not taken in full course (Select one)	Nothing	1	
		Not cured	2	
		Fever again	3	
		Drug resistant malaria	4	
		Other	77	
		Please specify		
		Don't know	99	
Taking full course of 8- week Primaquine				
3.1	What was color of malaria medicine you have taken when you had fever and blood test done? (Note as respondent answered)			
		White	1	
		Brown	2	
		Other	77	
		Please specify		
		Don't know	99	
3.2	How many tablet taken per one time when you took brown color malaria medicine? (Select one)			
		2 Tablet	1	
		4 Tablet	2	
		6 Tablet	3	
		Other	77	
		Please specify		
		Don't know	99	

3.3	What was interval of taking malaria medicine when you have taken? (Select one)	7 days Other Please specify [ ] Don't know	1 77 99	
3.4	Did you take full course (8-week duration) of malaria medicine which you have taken with once a week interval? (Select one)	Completed for 8-week with right interval Completed for 8-week but not in regular interval Not completed 8-week	1 2 3	Do not ask 3-5 and 3-6 if answer is (1) Continue ask 3-6 if answer is (2) Continue ask 3-5 if answer is (3)
3.5	If not completed 8-week course, how many weeks you have taken? (Select one)	1-week 2-week 3-week 4-week 5-week 6-week 7-week	1 2 3 4 5 6 7	
3-6	What are the reasons of not taking full course (8-week) of malaria medicine (Multiple responses) (Answer can be more than one, don't read the answer, just refer it by enumerator)	Long duration of taking medicine Forgot due to weekly not daily Travelling With work Schooling Dizziness Other Please specify [ ] Don't know	1 2 3 4 5 6 77 99	

3.7	Did you experience black urination after taking that malaria medicine?	No Yes (If answer (2), continue ask at how many days after taking medicine, black urination occurred)	1 2	
3.8	What is preferred and easier between the courses of weekly for 8-week and daily for 14 days (2-week) taking that brown colored malaria medicine (Select one)	2-week course 8-week course (If answer (1) please specify reason)	1 2	