Factors associated with delayed treatment among malaria cases in Thailand

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Factors associated with delayed treatment among malaria cases in Thailand

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Master of Science in Public Health

By

Suravadee Kitchakarn

Declaration:

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Abbreviations

CSMBS	Civil Servant Medical Benefits Scheme
DDC	Department of Disease Control
DVBD	Division of Vector-Borne Diseases
FY	Fiscal Year
GDP	Gross Domestic Product
GMS	Greater Mekong Subregion
GNI	Gross National Income
GTS	Global Technical Strategy
HPH	Health Promoting Hospital
MC	Malaria Clinics
MMP	Mobile Migrant Population
MOPH	Ministry of Public Health
MP	Malaria post
P. falciparum	*Plasmodium falciparum*
P. knowlesi	*Plasmodium knowlesi*
P. malariae	*Plasmodium malariae*
P. ovale	*Plasmodium ovale*
P. vivax	*Plasmodium vivax*
SHI	Social Health Insurance
UCS	Universal Coverage Scheme
WHO	World Health Organization

Key terms

Delayed malaria treatment	=	The period from onset date to treatment date is more than 1-30 days
Malaria elimination	=	Interruption of local transmission of a specified malaria parasites in a defined geographical area as a result of deliberate activities
High-risk area/active foci	=	Area with an indigenous case in the current year
Low-risk area/residual nonactive foci	=	Area with no indigenous case <3 consecutive years
Potential area/ cleared foci with receptive	=	Area with no indigenous case ≥ 3 consecutive years and with main malaria vectors
Malaria-free area/cleared foci without receptive	=	Area with no indigenous case ≥ 3 consecutive years and with or without main malaria vectors
Migrant1/long stay foreigner	=	Foreigners who were living in Thailand for more than 6-months
Migrant2/short stay foreigner	=	Foreigners who have been living in Thailand for less than 6 months

Abstract

Introduction: Malaria in Thailand is still a challenge in terms of elimination. Thailand's ultimate goal is to be a malaria-free country in 2024. Delay in malaria treatment can increase the disease severity and onward transmission.

Methodology: A mix-method study using secondary data analysis and literature review was used to identify and analyse factors associated with delayed treatment among malaria cases. Data was collected from a routine surveillance system and analysed using logistic regression. Literature explores other factors and reviews current strategies and interventions related to delayed management.

Results: Among 44,900 eligible confirmed malaria records, during the fiscal year 2015-2021, 80.79% were found to have delayed treatment. The trend of the delays slightly decreased during the Covid-19 pandemic period. The study presented, that malaria patients who are infected with mixed parasite species (OR_{adj} = 1.92, 95%CI: 1.26-2.93), worked in a rubber plantation (OR_{adj} = 2.41, 95%CI: 2.11-2.76), lived at Thai-Malaysia border (OR_{adj} = 1.64, 95%CI: 1.34-2.01) and in potential areas (OR_{adj} = 1.22, 95%CI: 1.08-1.39), were more likely to receive delayed treatment than their reference. Whereas other factors (under 15 years old, *P. vivax* infection, short-stay migrants, agriculture occupation, community-based health facilities and living areas in Myanmar and Cambodia border and malaria risk areas) were detected as having less probability of getting the delays with a significant association. Effective interventions such as community-based malaria services to increase accessibility, health education to change behaviours, and quality assurance of malaria services to maintain the standard, were already implemented.

Discussions: Significant factors influencing delayed malaria treatment should be integrated into the package of existing interventions. Key recommendations to national malaria program are sustaining malaria post intervention with standard quality, capacity building of health staff in potential areas and providing early diagnosis and treatment awareness focus on delayed groups. There is a unique issue, like in Thai-Malaysia border, which needs research and specific intervention.

Keywords: Malaria, Factors, Delayed malaria treatment, Thailand

Word count: 11,413

Introduction

I have been a professional public health technical officer at the Division of Vector-Borne Diseases (DVBD), Department of Disease Control, Ministry of Public Health, Thailand, for ten years. My responsibility is the malaria surveillance system, program planning and monitoring and evaluation at the national level. Thailand's national goal is to eliminate malaria in 2024, as we are committed to ourselves and the international community. Delay in malaria diagnosis and treatment can lead to more severity in cases and ongoing transmission. However, many factors are associated with delayed seeking treatment. For example, identifying and analysing the related factors can provide recommendations to the national malaria elimination program, to manage more effective interventions, to reduce severe malaria cases and local transmission.

Background

General information and demographic context of Thailand

Thailand, officially named the Kingdom of Thailand, is located in South-East Asia and borders four countries (Cambodia, Lao PDR, Malaysia, and Myanmar) (figure 1) (1)(2). Thailand has 77 provinces (Bangkok as the capital city) and 928 districts (3). Thirty-two percent of land area is forest, mainly in the Northern part and 46.5% is agricultural land use (paddy, crops, fruit trees, vegetable, and others)(4). Seasonal monsoon winds cause a tropical climate in 3 seasons: dry season (mid-February to mid of May), rainy season (mid of May to mid of October) and Winter season (mid of October to mid of February), and the average temperature is 27^{O}C (5)(6). In 2020, the country had 69,799,978 inhabitants within a 510,890 km^2 surface area (7). Three-quarters of the total residents are ethnic Thai, Thai-Chinese (14%), Malay (3%), and minority groups (8).

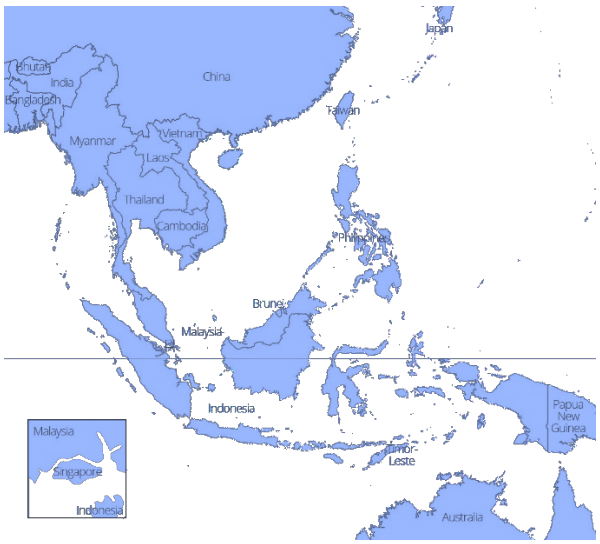


Figure 1: South-East Asia map

Thailand, as an upper middle-income country, has a USD 7,040 of Gross National Income (GNI) per capita (Atlas method) and 7,186.9 USD of Gross Domestic Product (GDP) per capita. The GDP growth rate also reduces to -6.1% from 2.3% during the COVID outbreak (7). The percentage of the population living below the national poverty line or poverty headcount ratio indicator is 6.8% of the population. 52% of the total population lives in urban areas, whereas 48% are still rural (9). Thailand also has 100,510 refugees by country or territory of asylum, mostly moved in from Myanmar (10).

In 2020, 49% of the total population was male. Thailand has been facing an aging society, 17.58% are the old age group (60 years and above), while the children age group (0-14 years) are 16.2%, and 64.44% are working age group (15-59 years) (figure 2)(11)(12). The population growth rate of Thailand is decreasing from 1% in 2000 to 0.3% in 2020, and a low fertility rate (1.5 birth/women) was reported. The mortality rate in adult males (182/1,000 male) is higher than in females (76/1,000 female). In terms of education, data from 2018 showed that the literacy rate was 94% in adults, ages 15 and above, whereas in youth (15-24 years old) it was 98%. Life expectancy at birth is increasing annually; the indicator showed females live longer (80.6 years) than males (73.6 years) (7).

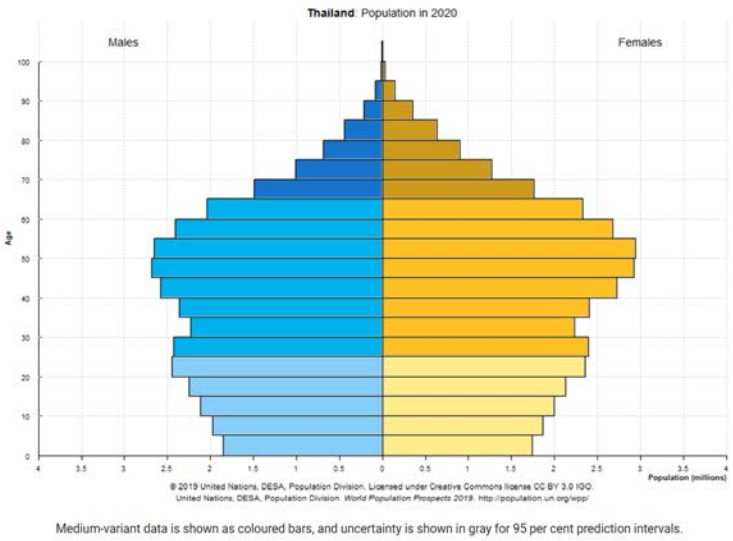


Figure 2: Population pyramid, Thailand 2020

Health status and health system

In the same situation as more developing countries, Thailand is in an epidemiological transition, that changes from infectious diseases to non-communicable diseases, because the quality of life and medical technology are improving to make people live longer and die in old age (13). Low maternal and neonatal mortality are reported. For example, 78% of causes of death in Thailand (2019) were non-communicable diseases such as cancers, cerebrovascular diseases, ischemic heart diseases, road traffic injury and diabetes (13). In contrast, respiratory infection, pneumonia, tuberculosis, and HIV/AIDS are still a problem(13). Ninety-nine percent of the Thai population are covered by health insurance (3 major schemes: 75.9% with universal coverage scheme (UCS), 17.72% by social health insurance (SHI) and 6.6% use civil servant medical benefits scheme (CSMBS)(13).

MOPH set up 9,765 health-promoting hospitals (HPHs) or health centres in all sub-districts as primary health care, to cover essential health services(14). In addition, village health volunteers are responsible for health prevention and control activities. Seven hundred seventy-five district hospitals, 92 provincial hospitals, and 34 regional hospitals are providing services countrywide. Also, other health facilities exist under other ministries, private hospitals and clinics (14).

Malaria epidemiology and burden

According to the services disruption during the covid-19 pandemic, globally 241 million malaria cases (a 6% increase compared to 2019) were reported by World Health Organization (WHO)(15). The WHO African region was found to have the highest number of patients (95% of the total). Malaria deaths were 627,000 in 2020, a 12% increase from last year and the WHO African region had the highest number of deaths (96% of all) according to falciparum malaria infection (15). While global cases were rising, the malaria situation in Greater Mekong Subregion (GMS) dropped (77,314 cases in 2020 and a 27% reduction from 2019). Seven million eight hundred thousand nine hundred fifty-six malaria suspected cases were tested, slightly decreasing (1% reduction from 2019). *Plasmodium vivax* was the dominant species in this region (75% of total species) (16)(17).

Thailand has a similar malaria situation trend as GMS. In 2021, 3,267 cases were reported (17% decline from 2020) and 95% were vivax species. 69% were male, and 77% were aged 5-44. Among malaria patients 40% were non-Thai. The high peak of the malaria burden occurs from April to August. Malaria transmission areas are along international borders, mostly at the Thai-Myanmar border. The population at risk are people who live in transmission areas (bordering areas, forest-fringe, mountainous areas), forest-related and agricultural occupations and cross-border mobile migrant population) (18). In 2020, 4 malaria deaths were reported in the whole country (19). The main malaria vectors are *Anopheles dirus, An. minimus* and *An. maculatus*. Breeding places are slow-running streams in the forest, forest fringe, hilly forested areas and rubber plantation areas (20).

Malaria program and elimination in Thailand

The Department of Disease Control (DDC), MOPH is the leading responsible organization for the malaria program. Division of Vector-Borne Diseases (DVBD) collaborates with 13 Offices of Disease Prevention and Control (regional level), 38 Vector Borne Disease Centres (provincial level), and 127 Vector Borne Disease Units (district level) and also coordinates with 76 provincial health offices (Figure 3). In addition, one hundred eighty-nine malaria clinics and 400 malaria posts provide malaria diagnosis and treatment, located in rural transmission areas. Only 495 out of 9,767 HPHs (5% of total) along the borders can test and treat uncomplicated malaria, whereas all levels of hospitals have potential (21,22). Previously, HPHs have had to refer the suspected malaria case to district hospitals due to no malaria services. The national program, with special projects, supports malaria commodities only for HPHs at the transmission areas, to improve early diagnosis and treatment. In addition, the government and international agencies (WHO, the Global Fund, USAID/PMI) support technical assistance and provide a financial malaria grant (23,24).

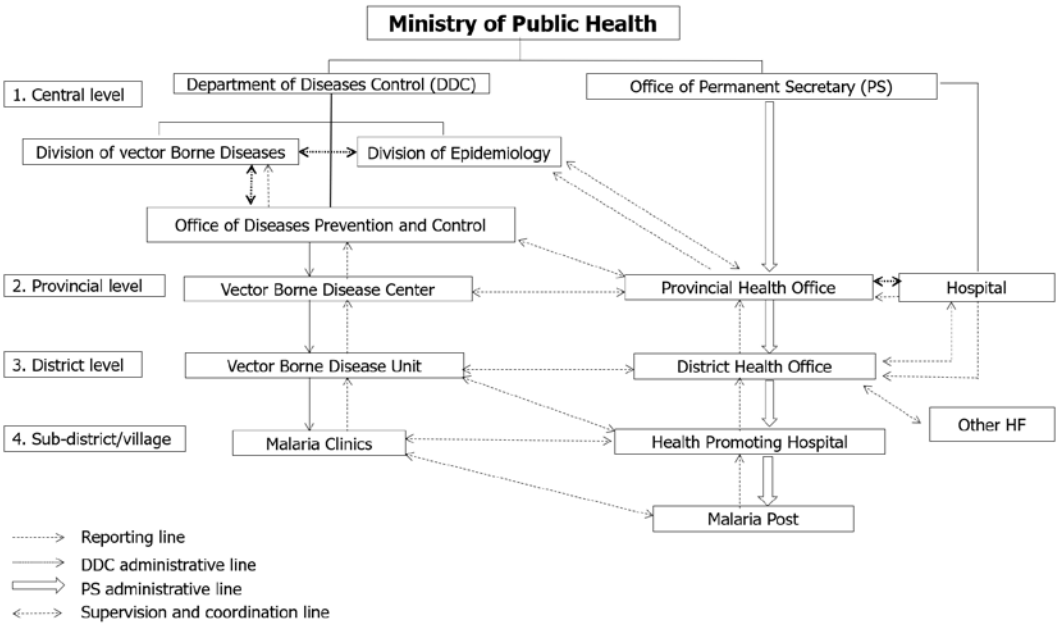


Figure 3*:* Malaria program in Thailand

WHO defines malaria elimination as “the interruption of local transmission of a specified malaria parasite species in a defined geographical area as a result of deliberate activities” (25) and recommends that countries step up from control to elimination programs, in cases of annual parasite incidence (API) < 1/1,000 population (26). The Global Technical Strategy (GTS) 2016-2030 is the main concept from WHO to succeed in malaria elimination. The target goal in 2030 is that at least 35 countries have eliminated malaria (27). Three main pillars (accessibility to malaria services, straightening on malaria elimination intention and changing surveillance system to primary interventions) and two supporting elements (innovations and enable environment) are the GTS strategic framework (27). The WHO set up a specific malaria elimination strategy for Greater Mekong Subregion (Cambodia, China (Yunnan province), the Lao People's Democratic Republic, Myanmar, Thailand, and Vietnam). The strategy emphasizes drug resistance elimination (28). Thailand is also launching a malaria elimination strategy from 2017-2026, aiming to be malaria-free in 2024 (29). The main concepts are followed by a global and regional strategy applied to Thailand's context.

Problem statement and justification

Problem statement

Thailand has been moving toward malaria elimination since 2017, according to the country's annual parasite incidence (API), which is lower than 1 per 1,000 population (WHO criteria) (26). Ten years of Thailand's malaria elimination strategy (2017-2026) was approved by the cabinet on April 26, 2016, and the national malaria elimination steering committee agreed upon 5-years of the operational plan (2021-2025) in 2021 (30). The strategy's ultimate goal is to be a malaria-free country in 2024. Four strategies are addressed to eliminate malaria; Strategy 1- accelerate malaria elimination, including strengthening case-based and drug resistance surveillance systems, improving coverage of malaria services and vector control prevention and increasing active case detection, as the primary approach. Strategy 2-create new technology and develop appropriate interventions; Strategy 3-collaborate with malaria stakeholders and national and international partnerships; and strategy 4-encourage and contribute to the community participation for sustainability are supporting strategies (29). The primary interventions are focused on people who live in transmission areas, mobile migrant populations (MMPs), and malaria patients.

According to the latest edition of the WHO malaria treatment guideline, malaria diagnosis and treatment should be made within 24-48 hours after fever (31). A systematic review and individual patient meta-analysis research in 2020, mentioned the relationship between early treatment and reduced opportunity to be severe malaria (32). A mathematic model, using individual data from endemic areas, presented that receiving treatment after 24 hours of fever raised onward transmission to 1.5 times compared hours <24 hour(33). An assessment of the effectiveness of malaria control activities, under the global fund, round 7 projects implemented in 28 endemic provinces, concluded that 49.9% of Thai and long-stay foreigner malaria patients received treatment >24h in 2010 and increased to 71.8% in the next year (34). In 2015, a study from Thailand in a high transmission area (Tak province), showed that 79.6% of malaria patients (n= 456) received malaria treatment > one day after fever presented (1-26 days) (35). For several years, malaria death investigation reports showed that some malaria deaths received malaria treatment after fever symptoms ≥ 3 days (36). Some areas in Thailand are classified as malaria-free and delayed malaria patients returning from endemic areas have the opportunity to introduce local transmission (reintroduction). In 2018, DDC verified 35 provinces, including Phuket, as malaria-free provinces. In the following year, one sub-village in Phuket was reclassified as a new transmission, according to malaria-infected migrants, who moved to a rubber plantation where local transmission occurred. Investigated result of the index case showed a delayed malaria treatment (11 days)(37). Achieving malaria elimination has to stop local transmission for three consecutive years and prevent reintroduction in the country, to maintain an elimination-free status.

Justification of Study

Many studies worldwide, on factors associated with malaria delay treatment are published. In the high malaria transmission Africa region, delay of diagnosis and treatment were studied. Only 22% of children under 5 with malaria, received appropriate treatment in South-eastern Nigeria (38). The study concluded that there was an association between age, education level of the mother, maternal experience, marital status and socioeconomic status of the family and delayed treatment of their children. Low personal income (<25 USD), absence of community health insurance, and >30 min travel to health facilities were associated with delayed malaria treatment in North-west of Ethiopia (OR_{adj} = 15.7, 9.6, and 4.4 respectively) (39). For malaria patients under 15 years old in Equatorial Guinea, low socioeconomic status and receiving primary

treatment at home (paracetamol) were significant factors associated with delaying malaria treatment (OR_{adj} = 0.37 and 0.36), whereas living nearby health facilities <3 km was associated but not significant(40).

Delays in malaria diagnosis and treatment of patients who return from high malaria burden to non-transmission countries were also reviewed. The results showed that the variation of delayed treatment was between 1.5-4 days after fever, and the diagnostic delay was between 3-9 days(41). The average period of delay diagnosis and treatment was five days in Poland (1-27 days depending on malaria species) after malaria symptoms occur(42). According to the population movement to Europe, early diagnosis and treatment with an effective surveillance system, have been applied to prevent malaria outbreaks.

Few publications have been conducted on the delayed malaria treatment in Asia (China, Laos, Myanmar, Indonesia, and Thailand), where the malaria context differs from Africa. In China, malaria patients who seek healthcare, more than three days after fever, are defined as a delay in malaria treatment, which is studied in imported malaria infection (43). The study also indicated that the first visit at high levels of health facilities, *Plasmodium vivax* infection and no malaria history, were associated with delayed health seeking for treatment. Distance to health centres more than 3.6 km (OR_{adj} = 6.5) and previous experience with health services (OR_{adj} =4.7) were the significant factors that affected health-seeking behaviour for febrile symptoms in the rural district of Laos (44). A study in Indonesia, on factors related to poor understanding of the appropriate malaria treatment period (within 24 hours after onset date) in the rural setting province, showed that significant factors were; no education (OR_{adj} = 3.42), low socioeconomic status, distance to nearest health care providers > 3 km and housewife occupation (OR_{adj} = 1.87, 1.73 and 1.63 respectively)(45). In addition, the publication from Myanmar, on treatment-seeking behaviour in adult patients, who were living in transmission areas, showed that the significant factors related to delayed treatment >24 h were health personnel availability (OR=2.26), the distance of health facility more than 14 miles (OR=2.33) and high cost of malaria treatment (OR=2.13)(46). Other studies in Myanmar presented significant associations between the patients' characteristics (age, gender, level of education, married status, and occupation) and delayed diagnosis and treatment ($P<0.05$). Also, other determinants (poor treatment-seeking behaviours and low social support) were significantly associated (47).

The latest study, of factors influencing delayed treatment in Thailand, occurred in 2015 and the study site was in Tak province (high malaria transmission area). Significant factors associated with delaying in malaria-seeking treatment, were low social support (OR_{adj} = 2.58), hill tribe, malaria vivax infection and self-treatment (OR_{adj} = 2.32, 2.02, and 1.73, respectively)(35). The publication can be representative of the Thai-Myanmar border and transmission area. None of the publications, have been done at the country level. This study will analyse the data set of all malaria patients countrywide for seven years, collected from a routine surveillance system; the results can imply a national picture. Identifying and analysing factors related can provide recommendations to malaria elimination programs for effective case management.

Objectives

General objective

To identify and analyse factors associated with delayed treatment among malaria cases in Thailand, using surveillance data.

Specific objectives

1. To describe the delayed malaria treatment situation
2. To identify and analyse individual and treatment-seeking behaviour factors associated with delayed treatment, among malaria cases
3. To identify and analyse environmental and quality of healthcare factors associated with delayed treatment among malaria cases
4. To review the current strategy, interventions and activities related to delayed malaria treatment management
5. To provide recommendations to the national malaria elimination program.

Methods and Analytical Framework

A mixed-method study (secondary data analysis and literature review) was used. It first analyses secondary data from a national surveillance system, covering objectives 1-3, then literature reviewing for other factors, not mentioned in the analysis, to complete all dimensions of delays (objectives 2-3). Also, current strategies and interventions for delayed treatment management in Thailand and other countries (objective 4) were reviewed.

Secondary data analysis

Study type and data collection

The data set for secondary data analysis was collected by local health staff as routine surveillance data. Responsible health staff filled personal information of suspected malaria patients (name, age, gender, occupation, address) into a blood record form (EP.1) annex 1 and tested for malaria (typically 20-30 minutes). When malaria results came out, positive patients received treatment medicine and were interviewed. Investigation & radical treatment of malaria cases form (EP.3) annex 2. The one-page questionnaire includes the exact personal information for identity confirmation, positive results with malaria species and treatment regimen and onset date. Previous history of travel, previous malaria infection place characteristics, personal protection behaviours and the program activities were investigated, and identified for case classification (indigenous/imported malaria cases) and source of infection to plan for other malaria esponse activities. Completed documents (EP.1 and EP.3) were entered into an offline surveillance program at the health facilities, uploaded to the central database, and visualized on the website "malaria online". Summarize malaria situation and program response activities were analysed and visualized on the website https://malaria.ddc.moph.go.th/. Public access was opened only for general information. In addition, a hierarchy access control system was applied for detailed information and individual login and passwords of registered public health officers were provided by the DVBD.

DVBD approved the official letter for data use as data owner annex 3. Because the study uses secondary data from a routine surveillance system, a waiver from KIT-REC was required. The request letter was submitted, and KIT-REC approved for clearance, as shown in annexes 4 and 5. A data set with anonymous records is stored in the notebook, accessed by login and password.

Study area, population, and period

The study area covered country level and the study population includes all confirmed malaria patients (Thai and non-Thai) who receive diagnosis and treatment in any health facilities in Thailand, also from active case finding. Malaria is a notifiable disease under Communicable Diseases ACT B.E. 2558. All confirmed cases must be reported to a routine surveillance system within one day, investigated within three days, and responded to within seven days as a national guideline(48). Seven fiscal years of surveillance data from October 2014 to September 2021 as 77,501 malaria patient records were provided for the study.

Variables and statistical analysis

The data management and analysis were conducted using STATA software package version 17 for descriptive and analytical statistics. Nine Independent variables, 1) individual and treatment-seeking behaviour factors: age, gender, occupation, resident status, malaria infection species, and treatment place, and 2) environmental factors: living area in terms of bordering province and status of malaria risk area in

sub-village level), are regrouped to categorical variables. The year was a continuous variable. Occupation is regrouped into four categories (forest-related work, agriculture, rubber plantation, and other works). Malaria parasite species were classified as *P. falciparum, P. vivax,* other species *(P. malariae, P. ovale, and P. knowlesi)*, and mixed infection. Resident status, in the definition of the national malaria elimination program, was classified into three groups (Thai, long stay foreigner, and short stay foreigner). For treatment place, any health facility managed by a government officer, was defined as a public health facility, and trained local village health volunteers operated community-based health services. In this study, living in a place with a border, was defined at the provincial level: 10 provinces border with Myanmar, 7 provinces with Cambodia, 7 provinces with Laos and 4 provinces with Malaysia. The remaining provinces are defined as having no bordering. For malaria risk areas, the study categorized areas as high (active foci), low risk (residual nonactive foci), potential (cleared foci with receptive), and malaria-free area (cleared foci without receptive) in terms of the sub-village level.

In this study, delayed malaria treatment was defined as patients getting treatment more than 1 day from the onset. Delayed malaria treatment is only one dependent variable, calculated from the period of onset date to the treatment date (data collected by date). If the period is between 0-1 day, defined as no delayed treatment; if ≥ 2 days to 30 days, defined as delayed treatment. For example, Aug 1 was the onset date, and the patients who received malaria treatment within Aug 2, were counted as having no delay (within 1 day). They were identified as delayed if they got the malaria medicine on Aug 3. The list of variables and regrouping were showed in table 1.

Table 1: List of independent and dependent variables

Factors	Variables	Values	Type of data
Independent variables			
Individual and treatment-seeking factors	Age group	- <5 years old - 5-14 years old - 15-24 years old - 25-59 years old - +60 years old	Categorical
	Gender	- Male - Female	Categorical
	Occupation group	- **Forest-related work** (wood cutter, forest hunter, and forest cleaner) - **Agriculture** (Fruit orchard plantation, cassava plantation, sugar cane plantation, corn plantation, other crops plantation, farmer, agriculture, animal former and fishery) - **Rubber plantation** - **Other works** (military/police, government officer, sale, labour, priest, mining labour, tourist, general employee, specialist, public health officer, teacher, and other occupation)	Categorical
	Malaria parasite species	- *Plasmodium falciparum* - *Plasmodium vivax*	Categorical

Factors	Variables	Values	Type of data
Independent variables			
		- Other species (*Plasmodium ovale, Plasmodium malariae, and Plasmodium knowlesi*) - Mixed infection	
	Resident status	- **Thai** - **Long stay foreigners** (foreigners who live in Thailand > 6 months) - **Short stay foreigners** (foreigners who live in Thailand for < 6 months)	Categorical
	Type of treatment place	- **Public health facility** (malaria clinic, health-promoting hospital, public hospital, military hospital, and university malaria centre) - **Private health facility** (private hospital) - **Community-based health facility** (malaria post, border malaria post, and refugee camp)	Categorical
Environmental factors	Living area in terms of bordering province	- **Thai-Myanmar** (10 provinces) - **Thai-Cambodia** (7 provinces) - **Thai-Laos** (7 provinces) - **Thai-Malaysia** (4 provinces) - **No bordering** (49 provinces)	Categorical
	Malaria risk area status in terms of sub-village	- **High-risk area** (active foci) - **Low-risk area** (residual nonactive foci) - **Potential area** (cleared foci with receptive) - **Malaria-free area** (cleared foci without receptive)	Categorical
	Years	- FY2015-2021	Continuous
Dependent variable			
	Delayed treatment	- **Yes,** more than 1 day after fever - **No**, within 1 day after fever	Dichotomous

Checking for multicollinearity and correlation was done. The dependent variable (delay/not delay treatment) is dichotomous and logistic regression was used to identify the associations with other variables. Variables from bivariate analysis with a p-value <0.2 were included in a multiple logistic regression model. P-value <0.05 was defined as statistically significant. The logistic model identified the goodness of fit, using the Pearson chi-square and Hosmer–Lemeshow chi-square test. Map visualization of delayed malaria treatment situation at the district level, was done using the ArcMap 10.6.1 software program.

Inclusion and exclusion criteria of analysis

In this study, delayed malaria treatment is defined as the period between onset and treatment date is more than 1 to 30 days. Only records from passive case detection (malaria patients who are present and get treatment at health facilities) and have a period of onset date to treatment date between 0-30 days are included in the study. Outliers (delayed > 30 days), errors and missing data records are excluded.

The study's maps showed the distribution of delayed malaria treatment in proportion (percentage of delayed cases per total malaria cases) at the district level; the districts had ≤ 5 total cases excluded to avoid misleading of delayed situation.

Literature review

The Literature review used search engines: google scholar, VU Amsterdam, Pubmed, and ResearchGate. Global and country information was provided using the official website of WHO and Thai MOPH. Creating strings with "AND," "OR" of keywords relating to the thesis topic are used for review (annex 6). All publications, official reports, guidelines, strategies, and policies were accepted. This literature excluded other languages except for English and Thai publications. The routine surveillance system did not collect on education, socioeconomic status of the patients, distance, transportation cost, quality of health care providers, or national policy, which were the determinants, that may relate to delay in malaria treatment. A literature review explored these factors and reviewed strategies and interventions related to delayed malaria treatment management in Thailand and other countries, to suggest recommendations as in objective 5.

Analytical framework

The thesis was a study on factors associated with delayed malaria treatment. The well-known model for delays was the "Three delay model," which is regularly used in maternal and neonatal mortality (49). The model could be applied to other health problems, such as unsafe abortion, malnutrition and emergencies to identify barriers to health care utilization. In addition, there were 3 phases of delay include 1) seeking care decision delay, 2) accessibility to reach services delay, and 3) availability of health services delay (figure 4).

The model may also apply to malaria disease. For example, individual factors of malaria patients were age, gender, residence status, nationality, occupation, malaria species infection and previous malaria infection; these factors may affect the patients' decisions to seek care. The malaria species infection also had different patterns and severity. Patient-seeking behaviours such as treatment place, may link to decision-making. Accessibility to health care facilities refers to the distance from the patient's address to health services, transportation, opportunity cost and time consumption, where factors may link to patient decisions and delays in reaching care. The last factors expected to contribute to delays in treatment were the healthcare providers' quality. Reliable diagnostic tools, antimalarial drugs available, well-training health staff, working hours, practical strategy and policy support from the program, may affect patient decisions and receiving care. This study used the framework for objectives 2 and 3 (factors associated with delayed malaria treatment) and objectives 4 in terms of interventions.

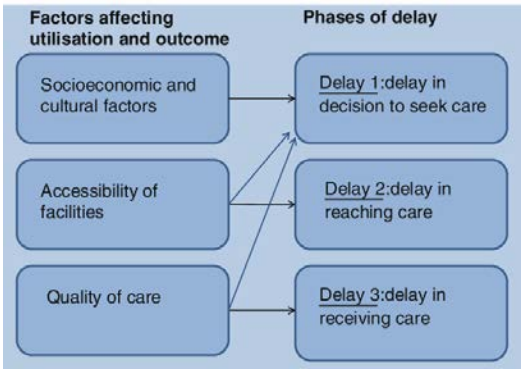


Figure 4: Three delay model

Results

Delayed malaria treatment situation

This study section described the situation of delayed malaria treatment in Thailand. Total confirmed malaria cases were 77,501 records, during seven fiscal years (FY) (October 2014 to September 2021). According to the study's inclusion criteria (passive case detection and period of onset date and treatment date between 0 to 30 days) and exclusion criteria (outlier, error, and missing data), 32,601 or 42% of malaria patients records are excluded. Thus, 44,900 records were eligible for descriptive and statistical analysis.

The average treatment time delay was 3.26 days after fever day and 3 days as the median. The majority age group was working aged, between 25-59 years old (21,893 cases, 48.7%), followed by youth (15-24) and children aged 5-14 (9,332 and 9,222 cases, respectively). The median age was 27 years old; the mean was 28.7 years old, and the 0 to 100 years range. Sixty-nine percent of eligible cases (30,930 cases) were male, and only 20.99% or 9,423 were foreign residents (mainly Myanmar). The primary occupation of the adult cases was rubber plantation (12,133 cases, 27% of total), followed by other works and agriculture (25.21% and 18.5%, respectively). Ninety-five percent of malaria cases lived in a province with an international border, especially Thai-Myanmar and Thai-Malaysia. During 7 years, 78.54% or 35,266 cases were infected with *P. vivax*, 20.11% with *P. falciparum*, and less than 2% were other parasite species (*P. ovale*, *P. malariae*, and *P. knowlesi*) and mixed infection. Three-fourths of malaria cases lived in malaria-risk areas (42.9% in high-risk and 32.8% in low-risk sub-villages).

For accessibility to malaria services, 60% of cases preferred to get malaria treatment at a community-based health facility in the village. Only 0.3% went to a private hospital. The demographic characteristics of eligible confirmed malaria cases are presented in table 2.

Table 2: Demographic characteristics of confirmed malaria patients during FY2015-2021

Factors	**Delay in malaria treatment**		**Total**
	No, within 1 day n (%)	**Yes, More than 1 day n (%)**	
1. Gender (n=44,900)			
Male	6,431 (20.79)	24,499 (79.21)	30,930
Female	2,195 (15.71)	11,775 (84.29)	13,970
2. Age group (n=44,900)			
Under five	378 (17.70)	1,758 (82.30)	2,136
5-14 years old	1,746 (18.71)	7,586 (81.29)	9,332
15-24 years old	1,801 (19.53)	7,421 (80.47)	9,222
25-59 years old	4,367 (19.95)	17,526 (80.05)	21,893
60+ years old	334 (14.42)	1,983 (85.58)	2,317
3. Malaria parasite species (n=44,900)			
P. falciparum	2,029 (22.47)	7,000 (77.53)	9,029
P. vivax	6,534(18.53)	28,732 (81.47)	35,266
Other species	28 (8.86)	288 (91.14)	316
Mix infection	35 (12.11)	254 (87.79)	289
4. Occupation group (n=44,900)			
Forest related works	39 (16.25)	201 (83.75)	240

Factors	Delay in malaria treatment		Total
	No, within 1 day n (%)	Yes, More than 1 day n (%)	
Agriculture works	2,930 (35.17)	5,400 (64.83)	8,330
Rubber plantation	824 (6.79)	11,309 (93.21)	12,133
Children/student	1,957 (15.20)	10,920 (84.80)	12,877
Other works	2,876 (25.41)	8,444 (74.59)	11,320
5. Resident status (n=44,900)			
Thai	5,785 (16.31)	29,692 (83.69)	35,477
Long stay foreigner	1,258 (23.36)	4,127 (76.64)	5,385
Short stay foreigner	1,583 (39.20)	2,455 (60.80)	4,038
6. Living area (border type: province level) (n=44,900)			
No bordering	212 (10.33)	1,840 (89.67)	2,052
Thai-Myanmar	4,575 (24.40)	14,178 (75.60)	18,753
Thai-Malaysia	915 (5.56)	15,553 (94.44)	16,468
Thai-Cambodia	2,908 (38.95)	4,558 (61.05)	7,466
Thai-Laos	16 (9.94)	145 (90.06)	161
7. Malaria risk area in terms of sub-village level (n=43,739)			
High-risk area	3,578 (19.05)	15,209 (80.95)	18,787
Low-risk area	2,591 (18.01)	11,799 (81.99)	14,390
Potential area	898 (13.38)	5,812 (86.62)	6,710
Malaria free area	1,027 (26.66)	2,825 (73.34)	3,852
8. Treatment place (n=37,621)			
Public health facility	2,135 (14.31)	12,788 (85.69)	14,923
Private health facility	18 (14.40)	107 (85.60)	125
Community-based health facility	4,691 (20.78)	17,882 (79.22)	22,573

Among 44,900 malaria cases, 80.79% received delayed treatment for more than 1 day of fever, and only 19.21% (8,626 cases) were provided the treatment in time (figure 5).

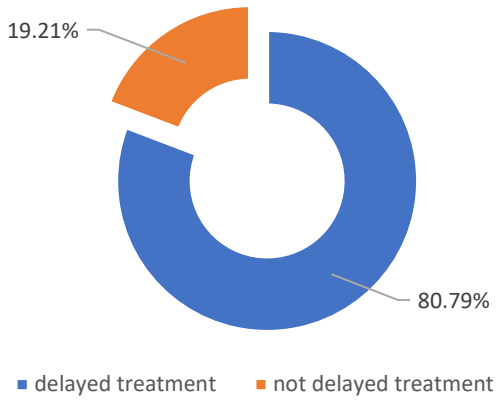


Figure 5: Proportion of delayed malaria treatment, FY2015-2021

Demographic characteristics of delayed malaria cases

This section study described demographic characteristics of malaria patients who delayed receiving treatment. Among 36,274 delayed malaria cases, the median time of delays was 3 days and 3.88 days after the onset date on average. The delayed proportion is also shown in table 2. Females had a delay treatment proportion higher than male patients (84.29%, compared to 79.21%) (*P=0.000*). Eighty to eighty-five percent of malaria patients in each age group received treatment ≥ 2 to ≤ 30 days. The highest delayed proportion were older adults (>60 years old) with 85.58%, followed by under-five children. The working-age group (25-59) was the lowest delay proportion (80.05%). Patients infected with *P. falciparum* seemed to get treatment within one day after the onset date, higher than other infections (only 77% of total *P. falciparum* cases were delayed, compared to other groups (81-91% range)). Among the occupation groups, the rubber plantation was the highest delayed proportion with 93.21%, followed by children/students (84.80%) and forest-related work (83.75%). Agriculture was the lowest proportion of delay in malaria treatment (64.83%). In the case of resident status, short stay foreigners who lived in the country for less than six months had a lower delayed proportion than the other two groups (long stay foreigners and Thai) by 60% delayed compared to 76% and 83%. Among provinces bordered by neighbouring countries, different delayed treatment proportions were found (between 61-94%), and the lowest delayed proportion was the Thai-Cambodia border. In addition, malaria patients, who lived in a malaria-free sub-village, received early malaria treatment more than in other areas (26% compared to 13-19%). The community-based health facility was the place that found a lower proportion of late treatment than a public and private health facilities. Seventy-nine percent of them were detected as delayed treatment, whereas others HF were 85%.

The trend of delayed malaria treatment during a 7 years period from FY2015-2021 is shown in figure 6. While malaria cases continuously decreased, the percentage of delayed treatment increased from 65.15% in FY2015 to 82.04% in 2016 and slightly rose from 2017 - 2019 (87.04% to 89.71%). During the Covid-19 pandemic period (FY2020-2021), the delayed proportion seemed slightly down (85.79% and 84.93%, respectively).

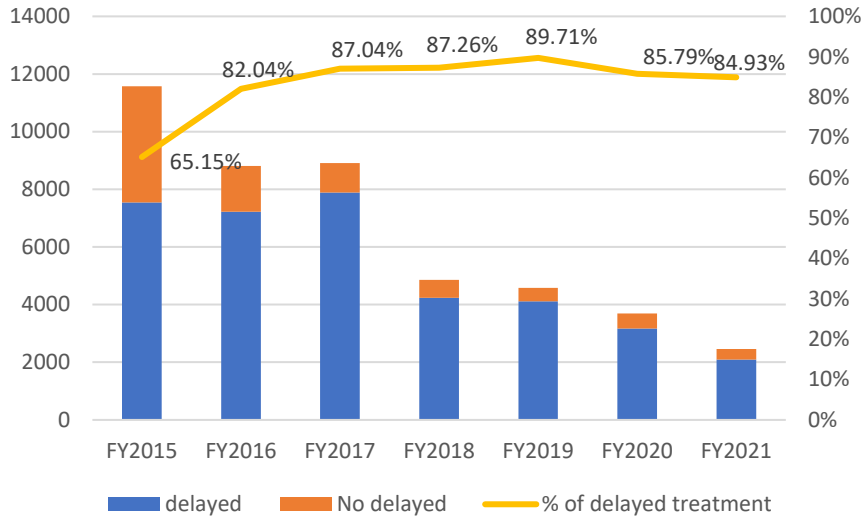
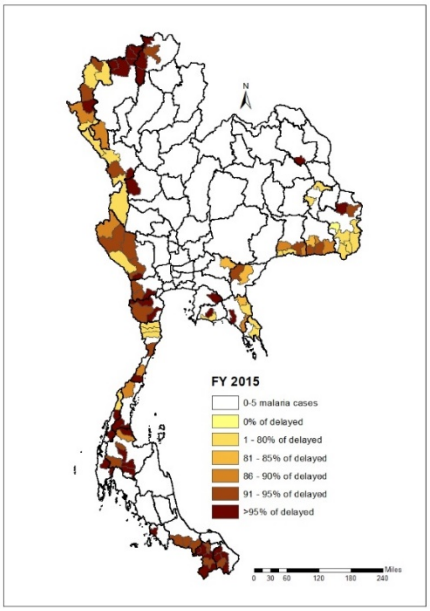
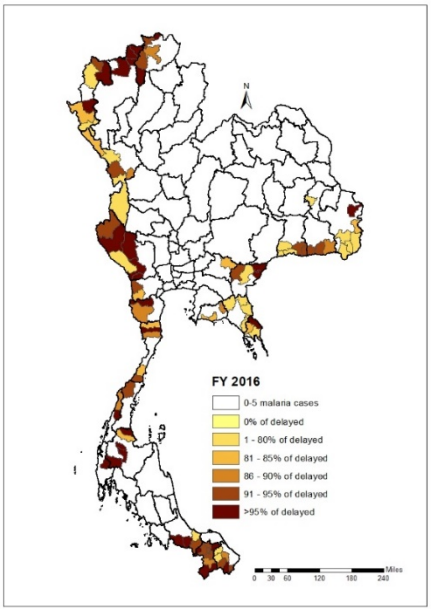


Figure 6: Trend of delayed malaria treatment, FY2015-2021

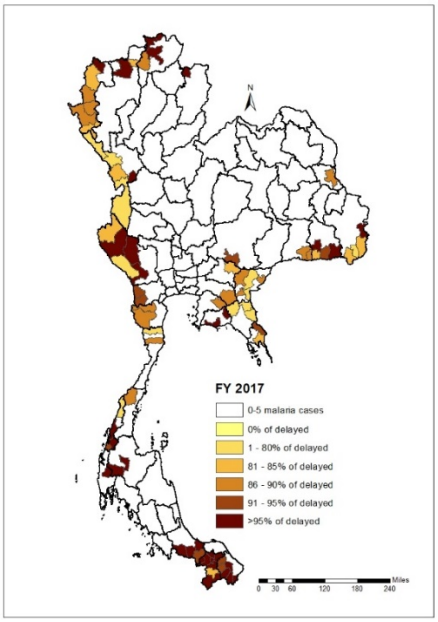
According to maps of delayed malaria treatment at the district level during FY2015-2021, the distribution of delayed malaria treatment was found along the international border, especially in the Western, Eastern, and Southern parts of the country (Thai-Myanmar, Thai-Cambodia, and Thai-Malaysia border). In FY2015, the highest proportion of delayed treatment was detected in the north and the south of the country. During west and east parts it found a lower proportion of delay. In FY2016 and 2017, the situation in the south slightly improved, whereas in the middle-west site it was the opposite, especially in Kanchanaburi province. In FY2018, the Eastern part of the country showed a higher delayed proportion than FY2017, similar to the south. In FY2019, the highest proportion of delays occurred in the same part of the country. While during the covid-19 pandemic, the situation of delay in malaria treatment looked better than in previous years. The district-level map of delayed malaria treatment distribution is present in figure 7.



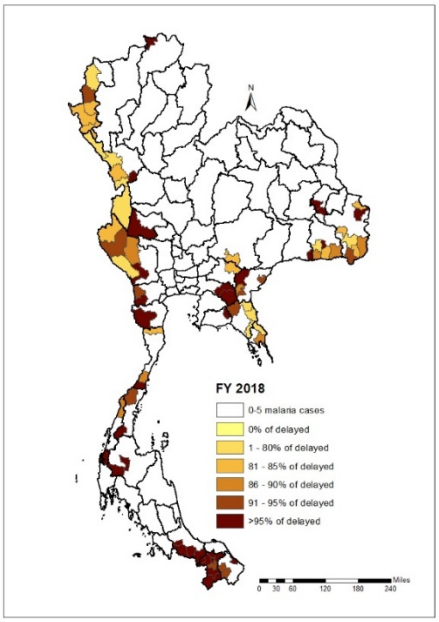
a) FY2015



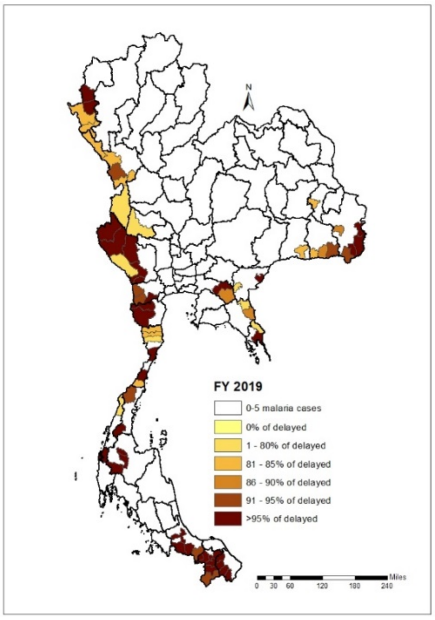
b) FY2016



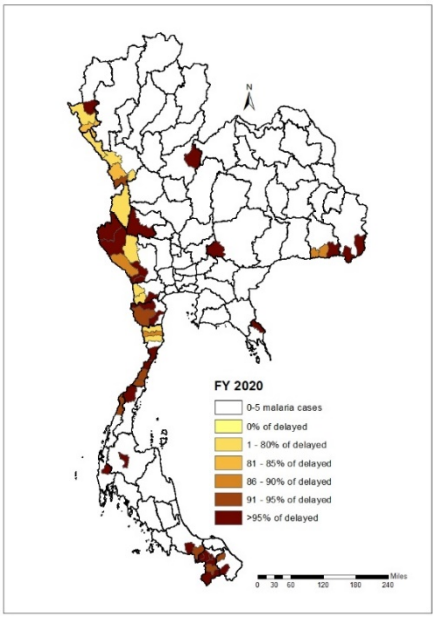
c) FY2017



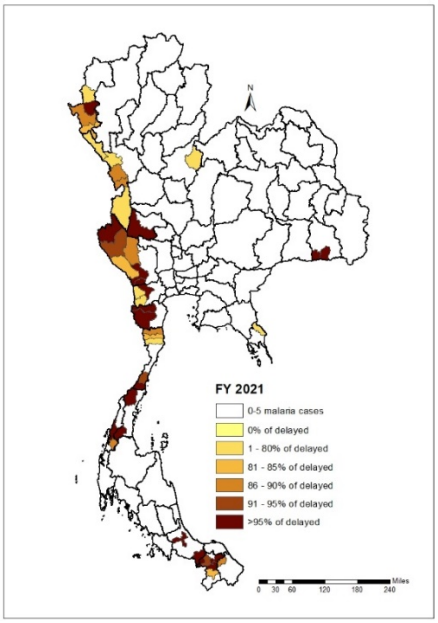
d) FY2018



e) FY2019



f) FY2020



g) FY2021

Figure 7: Map of delayed malaria proportion at the district level, FY2015-2021

Factors associated with delayed malaria treatment

In this study section, the association between each independent factor and delayed treatment from secondary data analysis and literature review, were identified in three main factors. First, there were individual and treatment-seeking behaviour factors, related to delay in seeking care; second, environmental factors, linked to decision making and accessibility to health facilities and health care factors in terms of quality of health facilities. The children/students dropped out from the occupation group to avoid interaction between independent variables.

Secondary data analysis

For the secondary data analysis, this study used simple logistic regression to identify the association between each independent variable and the outcome variable, delayed malaria treatment. Multiple logistic regression is done to control the effect of confounding variables.

a) Individual and treatment-seeking behaviour factors

This study defined gender, age group, malaria infection species, occupation, and resident status as individual factors and treatment place as treatment-seeking behaviour factors. The associations were presented.

i. Gender

The simple logistic analysis between gender and delayed treatment showed that gender was significantly associated with delayed malaria treatment. The odds of females were 1.41 times higher for delayed treatment than the male gender (95% CI: 1.33-1.49). After adjusting for other variables, by multiple logistic regression, there is no significant association between females and late malaria treatment (P value = 0.359) shown in table 3

ii. Age group

The bivariate analysis result showed that under five, young children and old age patients were significantly associated with delay in receiving the treatment, compared to the working group as a reference level (OR = 1.16, 1.08, and 1.48, respectively). The three-age groups were more likely to get delayed malaria treatment and the elderly were the highest more than the under-five and young. In contrast, only two age groups were significantly associated in multiple logistic regression analysis (under five and children 5-14 years old) with OR_{adj} = 0.43 (95%CI: 0.28-0.65) and 0.43 (95%CI: 0.35-0.53). The adjusted odd ratio showed that children under 15 years old are less likely to get a delay in malaria treatment than the working-age group. The detail is presented in table 3.

iii. Malaria parasite species

After a simple analysis, using falciparum species as a reference, there was a significant association between all groups of malaria parasite species (*P. vivax,* other species, and mixed infection) and delayed treatment (*P=0.000*). The odds of other infection species (*P. ovale, P. malariae,* and *P. knowlesi*) was 2.98, followed by mixed infection (OR = 2.10) and *P. vivax* (OR = 1.27). After controlling confounding factors, other species of malaria infection had no significant association with delayed treatment (P = 0.146). The odds of delay in mixed malaria infection were 1.92 times the odds of falciparum malaria (95%CI: 1.26-2.93), and the patients who were

infected with vivax malaria were less likely to get delayed treatment compared to falciparum malaria (OR_{adj} = 0.82, 95%CI: 0.76-0.90) as shown in table 3.

iv. Occupation

The occupation was significantly associated with delayed malaria treatment using a bivariate analysis of forest-related works, agriculture, and rubber plantation (*P*=0.000). Like farmers, the patients who work in the forest and rubber plantations, were more likely to receive late malaria treatment than other workers (OR = 1.76, 95%CI: 1.24-2.48 and OR = 4.67, 95%CI: 4.30-5.08, respectively). Otherwise, agriculture workers seem to receive early malaria treatment compared to other workers (OR = 0.63, 95%CI:1.43-1.62). In comparison, the result from multiple logistic regression showed that agriculture and rubber plantations were significantly associated with delays in malaria treatment (P-value = 0.000). The patients who worked in agriculture sessions were less likely to receive a delay in malaria treatment than other occupations (OR_{adj} = 0.71, 95%CI: 0.65-0.77). For the rubber plantation group, the patients were more likely to experience late malaria treatment (OR_{adj} = 2.41, 95%CI: 2.11-2.76). No significant association between forest-related work and delayed treatment was found, as in table 3.

v. Resident status

Resident status was statistically significant at the significance level of 0.05 associated with delayed malaria treatment in simple logistic regression. Compared to Thai residents, migrant status was less to get delayed treatment (OR = 0.64, 95%CI: 0.60-0.68 and OR = 0.30, 95%CI: 0.28-0.32). Only malaria patients, who were short-stay foreigners, showed significant association with delayed treatment in multiple analyses (OR_{adj} = 0.49, 95%CI: 0.44-0.55). As a result, these patients were less likely to receive delayed malaria treatment than Thai patients. For the long-term migrant, no significant association was found, as shown in table 3.

vi. Treatment place

The simple logistic regression showed a significant association between community-based health facilities and delayed malaria treatment (OR = 0.66, 95%CI: 0.60-0.67). In multiple analyses, a similar negative association, with a statistically significant, was detected from community malaria services (OR_{adj} = 0.62, 95%CI:0.57-0.66). In addition, malaria patients who visit community health facilities were less likely to receive delayed treatment, compared to the public sector. No association was found between the private sector and late malaria treatment in both analyses (P = 0.976 and P = 0.187), as shown in table 3.

b) Environmental factors

In this study, environmental factors were; living areas concerning malaria risk in sub-village levels and provinces with the international border related to accessibility to health facilities. The associations between these factors and delayed treatment were presented.

i. Malaria risk area

A malaria risk area was statistically significantly associated with late treatment in a simple and multiple logistic regression analysis (*P*=0.000). Compared to the patients who lived in a malaria-free area, the odd of patients who got delayed treatment was 2.39 times higher in a potential area (no indigenous case and primary *Anopheles* vector was detected in the village or

no endemic areas but had the potential to be new transmission). High and low risk of malaria also has a positive association with the delay (OR = 1.55, 95%CI: 1.43-1.67 and OR = 1.65, 95%CI:1.52-1.80) in a simple analysis. After adjusting the effect, the potential area showed the same positive association with delayed treatment (OR_{adj} = 1.22, 95%CI:1.08-1.39). In contrast, malaria cases who lived in high and low risk of malaria areas, were more likely to get delayed treatment than those who lived in malaria-free areas (OR_{adj} = 0.60, 95%CI:0.54-0.67, and OR_{adj} = 0.70, 95%CI:0.62-0.78) as shown in table 3.

ii. Living area in terms of the province with border to neighbouring countries

Different associations were found in a simple logistic regression analysis. Only malaria cases who lived in a province with the Thai-Laos border were not significantly associated with delayed treatment (*P*=0.874) compared to no bordering provinces. Patients who lived in Thai-Myanmar and Thai-Cambodia provinces were less likely to get delayed in malaria treatment with statistically significant (OR = 0.36, 95%CI:0.31-0.41 and 0.18, 95%CI:0.16-0.21, respectively) compared to who lived in the central part of the country. While people who stayed at the border with Malaysia were more likely to receive treatment for more than 1 day after onset (OR = 1.96, 95%CI:1.67-2.29).

In multiple analyses, three bordering provinces, Thai-Malaysia, Thai-Myanmar, and Thai-Cambodia, showed significantly associated delayed malaria treatment. People who lived in the southern part of the country bordering Malaysia, were more likely to receive a delay in treatment (OR_{adj} = 1.64, 95%CI:1.34-2.01). In contrast, those who lived in Eastern and Western provinces (border with Cambodia and Myanmar) were less likely to experience the delays (OR_{adj} = 0.32, 95%CI:0.27-0.38, and OR_{adj} = 0.80, 95%CI:0.67-0.96) as shown in table 3.

Period

The result of logistic regression indicated that when time increased, the delay in malaria treatment was more likely to happen (OR_{adj} = 1.31, 95%CI: 1.28-1.34), as shown in table 3.

Table 3: Factors associated with delayed malaria treatment using logistic regression

Factors	OR (95% CI)	P-value	OR_{adj} (95% CI)	P-value
1. Gender				
Male	1		1	
Female	1.41 (1.33-1.49)	0.000*	0.96 (0.88-1.05)	0.359
2. Age group				
Under five	1.16 (1.03-1.30)	0.013*	0.43 (0.28-0.65)	0.000*
5-14 years old	1.08 (1.01-1.15)	0.012*	0.43 (0.35-0.53)	0.000*
15-24 years old	1.01 (0.93-1.10)	0.399	1.00 (0.91-1.08)	0.921
25-59 years old	1		1	
60+ years old	1.48 (1.31-1.67)	0.000*	1.00 (0.86-1.15)	0.978
3. Malaria parasite species				
Plasmodium falciparum	1		1	1
Plasmodium vivax	1.27 (1.20-1.35)	0.000*	0.82 (0.75-0.90)	0.000*
Other species	2.98 (2.02-4.41)	0.000*	1.38 (0.89-2.16)	0.146
Mixed infection	2.10 (1.47-3.01)	0.000*	1.92 (1.26-2.93)	0.002*

Factors	OR (95% CI)	P-value	OR_{adj} (95% CI)	P-value
4. Occupation group				
Forest related works	1.76 (1.24-2.48)	0.001*	1.23 (0.83-1.82)	0.305
Agriculture works	0.63 (1.43-1.60)	0.000*	0.71 (0.65-0.77)	0.000*
Rubber plantation	4.67 (4.30-5.08)	0.000*	2.41 (2.11-2.76)	0.000*
Other works	1		1	
5. Resident status				
Thai	1		1	
Long stay migrant	0.64 (0.60-0.68)	0.000*	0.92 (0.81-1.04)	0.177
Short stay migrant	0.30 (0.28-0.32)	0.000*	0.49 (0.43-0.55)	0.000*
6. Living area (border type: province level)				
No bordering	1		1	
Thai-Myanmar	0.36 (0.31-0.41)	0.000*	0.80 (0.67-0.96)	0.015*
Thai-Malaysia	1.96 (1.67-2.29)	0.000*	1.64 (1.34-2.02)	0.000*
Thai-Cambodia	0.18 (0.16-0.21)	0.000*	0.32 (0.27-0.38)	0.000*
Thai-Laos	1.04 (0.61-1.78)	0.874	0.72 (0.40-1.30)	0.281
7. Malaria risk area				
High-risk area	1.55 (1.43-1.67)	0.000*	0.60 (0.54-0.67)	0.000*
Low-risk area	1.65 (1.52-1.80)	0.000*	0.70 (0.62-0.78)	0.000*
Potential area	2.35 (2.13-2.60)	0.000*	1.22 (1.08-1.39)	0.002*
Malaria free area	1		1	
8. Treatment place				
Public health facility	1		1	
Private health facility	0.99 (0.60-1.64)	0.976	1.72 (0.77-3.87)	0.187
Community-based health facility	0.66 (0.60-0.67)	0.000*	0.62 (0.57-0.66)	0.000*
9. Year period				
Fiscal year period	1.31 (1.29-1.33)	0.000*	1.30 (1.28-1.34)	0.000*

*p-value < 0.05, statistically significant

The mean variance inflation factor (VIF) among variables was 1.18, which showed that no collinearity was detected (VIF > 5 indicated collinearity). The model was tested for goodness of fit, using Pearson and Hosmer–Lemeshow chi-square. Both analyses found *P=0.000*.

Literature review

Few publications on delayed malaria treatment in Thailand were found. This study was more explored in the publication in the neighbouring countries and the Asia Pacific, representing the same malaria context.

a) Individual and treatment-seeking behaviours factors

i. Education and socioeconomic status

Literacy influences delayed malaria treatment in terms of seeking health care. Studies in many countries such as Eritrea, India, and Myanmar showed that literacy was significantly associated with early malaria treatment (P<0.05), not only among patients themselves but also the caregivers, such as the under-fives mothers (50–54). No literacy or low education related to delayed malaria treatment. In Boudh district, Orissa state, India, caste was associated with timely

and effective treatment (P<0.05). The person who was member of the scheduled tribe was more experienced with delayed services than other groups (52)

ii. Family income

Income issues are the factor that affects the malaria treatment decision. More household earnings related to less delay of treatment. For example, fever patients who had low family income (<200 USD/year) in rural Myanmar were more likely to get delayed treatment >24h after fever illness (53). Another study in Myanmar showed that the medium monthly income (73-108 USD) was higher to get prompt malaria treatment (OR_{adj} = 2.831, P-value = 0.016) compared to the low (54).

iii. Local belief

In Myanmar's rural malaria endemic area, traditional methods (local herb or belief activities) for initial treatment were one factor, that affected receiving malaria treatment in time. The patients who followed local beliefs were an opportunity to receive delayed treatment (55). This factor is also related to self-treatment.

iv. Family decision making

In Wa ethnic minority, Myanmar, family decision-making was significantly associated with delayed treatment. Wife or co-decision among partners was more likely to receive treatment < 24h when compared to husband decision alone (OR = 2.65, 95%CI: 1.58-7.18) (53).

v. Malaria knowledge

Knowledge of malaria was the factor that related to receiving prompt and effective treatment. The study in Myanmar showed that poor basic knowledge of malaria and behaviour were significantly associated with delayed treatment and more likely to get delayed (OR_{adj} = 65.5 and 3.889)(54).

vi. Self-medication

Self-treatment with antipyretic was related to receiving delayed malaria treatment. In many countries in Asia, self-medication is the typical behaviour. In Thailand, 70% of malaria patients receive malaria treatment after treating themselves with an antipyretic drug (56). In Vietnam, the family always stocked up on the common drug to treat themselves (57). In northern Sri Lanka, a malaria-endemic and conflict area, self-treatment with paracetamol was associated with delayed malaria treatment of patients. The relative risk was 3.55 (95% Cl 1.23-10.24) (58). Self-medication with western medicine was also related to delayed treatment in local villagers of Shan state and Myanmar migrant workers (55). In the remote part of Vanuatu, fever patients preferred to use local medicine or treat themselves at home (59).

b) Environmental factors

i. Transportation

Because of poor road conditions, Myanmar migrant workers in northern Shan state claim delayed malaria treatment (55). Poor transportation and unpredictable weather were barriers to seeking care for Vanuatu villagers (59). Paying for transportation to visit health facilities also

service costs were the barriers to receiving appropriate malaria treatment for caregivers (OR_{adj} = 0.52, 95% Cl 0.33-0.83)(51). The factor related to delays to seeking care.

ii. Distance

Some patients with a high malaria burden in Vietnam prefer to visit private clinics or pharmacies, than commune health stations to seek treatment according to the outlets near their house (1-5 km.). Even though the treatment at the health station was free, the patients had to pay for transportation and consultation costs instead (57). In addition, people who travelled less than 5 km from their location to health facilities, received treatment faster than those far away (52). For example, a Thai study in Suratthani province showed that malaria patients who lived near health facilities get early treatment (60).

iii. Place of resident

The study of seeking treatment of fever people, in malaria endemic area in Assam, India, showed that geographical areas are associated with delayed treatment. People who lived in rural areas were more likely to get delayed treatment than those who lived in urban areas with OR_{adj} = 1.52 (95%CI: 1.11-2.09) (61). The same study concluded that long distances (>5 km.) and no appropriate health facilities for malaria services nearby their house, were the accessibility barrier to seeking treatment.

iv. Living area in terms of security

An unstable situation, such as armed or ethnic conflict, affected seeking malaria treatment in Myanmar and Sri Lanka (55,58). Some patients wait a day to refer to a health facility, even in serious emergencies. The factor also linked to accessibility to health facilities similar to other environmental factors.

c) Quality of health care factors

The quality of health care providers is also associated with delayed malaria treatment according to the three-delay model. Community volunteers in rural areas of Myanmar, provide only malaria diagnosis with a rapid test but not antimalarial drugs. The example showed inappropriate malaria services in place (55). Long waiting times at health facilities, open hours and availability of healthcare providers were the factors related to delayed treatment in Vanuatu. Some interviewees mentioned that because of the low quality of aid post workers in their village, they decided to go to a health facility instead (59). In addition, forest goers and malaria patients in Vietnam were more likely to visit private clinics, to treat malaria because of operation time and the friendliness of providers (57).

In addition, some health providers in India mentioned that providers' low quality of care (low qualified staff, stock out and side effects of drugs, etc.) caused people not to trust community volunteers (52). Health system factors are also barriers to receiving prompt malaria treatment in Palaw township, Myanmar (54). Misunderstanding communication, due to different speaking languages between patients and public health providers, often causes delayed malaria treatment of local villagers in northern Shan State, Myanmar (55). In this case, it was found in local villagers who speak local languages while health staff speaks Burmese. The language was not a barrier to Myanmar migrant workers, who mostly speak Burmese.

Current strategy, interventions, and activities related to delayed malaria treatment management in Thailand and other countries

This section presents malaria strategy, interventions and activities related to delayed treatment management in Thailand, other GMS countries and eliminated countries (China and Sri Lanka). The summary of interventions related to preventing delayed malaria treatment is shown in table 4.

a) Thailand

Increasing coverage and access to malaria case management services, in all populations, were the main interventions to accelerate the malaria elimination in strategy 1 (29). Malaria clinics located mainly in the transmission area along the borders played a significant role for malaria service providers for several decades (62). Community-based services or malaria posts that provide malaria diagnosis and treatment were set up under the global fund grant, to increase the accessibility of risk groups, in remote endemic areas. The national program trained local villagers to operate the intervention as malaria post workers. They set their home up as the office to provide malaria diagnosis with the rapid test kit and effective radical treatment for uncomplicated malaria patients (63). The program also trained health officers at HPHs (only in endemic areas with no malaria services) to provide malaria diagnosis and treatment. Free-of-charge malaria services were also applied in public sectors and community-based HFs. The malaria referral was integrated into a routine effective referral system. Active case finding in high-risk areas was implemented annually before malaria peak season. Providing health education to the population at risk, was mentioned in strategy 4 (promote community participation for sustainability). A key message, related to early diagnosis and treatment, is developed to raise their awareness. An online supply management system was developed under networking collaboration (29).

b) GMS countries

Almost all GMS countries applied community-based health services as a critical intervention to increase service coverage in the high malaria burden. Trained village health volunteers operated malaria diagnosis and treatment activities. The country's malaria program identified the targeted groups or populations at risk. Bordering people and mobile migrant populations (MMPs) were the key vulnerable groups in GMS, due to the difficulty of identifying, tracking and reaching health services. Community-based services are financially supported by the Global Fund project in almost all GMS countries (24).

Cambodia: According to the strategic plan to eliminate malaria from 2011-2025, Cambodia will be a malaria-free country in 2025 (64). One of the strategic objectives was to provide early diagnosis and treatment by increasing the accessibility of malaria services. Malaria case management services at the community level, were set up in the endemic village >5 km, far from the public hospital. All sectors (public, private, and community) are provided free of charge on malaria services. The national program expanded early diagnosis and treatment to MMPs and cross-border people, by setting up malaria services at border checkpoints. In addition, appropriate health promotion channels were implemented to change behaviours. A new intervention for forest goers was studied. Test performance and preventive measures must be considered(65). Since 2018, no malaria deaths have been reported and 15,891 confirmed cases in 2021 (15).

Vietnam: National strategic plan on malaria control and elimination 2021-2025 launched and targeted to eliminate malaria in 2030. The main objective was to ensure access to malaria diagnosis and treatment for all populations. The main activities were; maintaining microscopy posts in malaria endemic communes and engaging private hospitals and clinics, to provide malaria services. Village health workers

provided malaria case management in high-burden and remote mountainous villages. Malaria posts were conducted at specific access points (construction sites and forest borders) to provide malaria tests and treatments for MMPs, farmers, and the border population. Behaviour change communication activities were implemented (66). No malaria deaths have been reported since 2019, and 1,422 confirmed cases in 2021 (15)

Myanmar: Among GMS countries, Myanmar is the highest malaria burden country. It was targeted to be a malaria-free country in 2030 (67). Equity in access to malaria services was the principle of elimination strategy. The Myanmar malaria program conducted community-based malaria services in hard-to-reach areas or >2km from health facilities, operated by village health volunteers (VHVs). Malaria services were integrated into the job description of VHVs (usually, they responded to diarrhoea in under-five and respiratory infections). Malaria clinics/posts provided malaria services to MMPs at selected informal cross-border checkpoints. In some situations, one person was trained to test with RDT and treat the migrant groups when they moved. A study in 2018 applied early diagnosis and treatment and mass drug administration to the high burden of *P. falciparum*. The result showed that malaria incidence decreased significantly (68). The world malaria report presented that among 58,836 malaria cases, only 10 deaths were found in 2021 (15).

Laos PDR: The Ministry of Health set up three phases of a strategic plan for malaria elimination to achieving the target in 2030 (69). Like Myanmar, Multi-task (malaria and other diseases services) were applied in the VHVs role. The public, private mixed health facility was the practical approach to increase service coverage in Laos. In addition, a procurement and supply management system was developed to ensure sufficiency of all malaria commodities. Comprehensive health promotion activities focused on treatment-seeking behaviour. Mobile malaria teams and posts were set up to improve access to MMPs at work sites and travel routes. Early diagnosis (with rapid test) and treatment (with artemisinin combination therapy) by VHVs at the village level showed effective performance. Training on knowledge, patient care, and treatment need to be considered (70). Only 3,503 malaria cases were detected in 2021 and no malaria deaths have been reported since 2019 (15).

c) Malaria-free countries

Sri Lanka: The WHO certified Sri Lanka as a malaria-free country in 2016. After eliminating malaria, Sri Lanka applied a national strategic plan to prevent reintroduction (2018-2022), which still mentioned an early diagnosis and treatment approach (71). The program maintained high geographical coverage of health care (both public and private sector) and mobile malaria clinics to support malaria services for remote areas and the at-risk population. The stock of diagnostics and antimalarial drugs must be sufficient at the point of care. In case of stock out, required commodities had to deliver within a few hours (72). No malaria deaths were reported in Sri Lanka for ten years (2010-2020), and only 30 imported cases were found in 2021 (15).

China: The WHO certified China as a malaria-free country in 2021. During the pre-elimination phase, China implemented an early test and treated strategy, through a robust service delivery system (73). The national malaria elimination strategy focused on timely case findings. Both public and private sectors at all levels could diagnose and treat with malaria medicine. No malaria deaths have been reported since 2012, and China found only 1,050 imported cases in 2021 (15).

Table 4: Strategy, interventions, and activities related to delayed malaria treatment management in several countries

Country	Deaths from malaria	Strategy/interventions/activities related to delayed treatment management					
		Increase accessibility of malaria services in an endemic area	Provide free of charge of services	Improve referral system	Provide health education/awareness	Provide malaria services to specific targeted group	Manage Procurement & Supply
Thailand	4 (2021)	• implement community-based HF • Improve the capacity of public HF at the sub-district level	Public sectors and community-based HF	Integrated with the existing system	Yes, pop at risk	MMPs and people lived in an endemic area	Yes
Cambodia	0 (2018-2020)	• implement community-based HF	All sectors	Yes	Yes, pop at risk	MMPs, cross border pop at border checkpoints	Yes
Vietnam	0 (2019-2020)	• implement microscopy posts and community-based HF	ND	Yes	Yes, pop at risk	MMPs at specific assessment points	Yes
Myanmar	10 (2020)	• implement community-based HF	ND	Yes	Yes, pop at risk	MMPs at specific assessment points	Yes
Laos PDR	0 (2019-2020)	• implement community-based HF	ND	Yes	Yes, pop at risk	MMPs at work sites and travel routes	Yes
Sri Lanka	0 (2010-2020)	• Maintain mobile malaria clinics	ND	Use existing system	Yes, people who return from endemic areas, travellers, and health personnel	Traveller and migrant at the port of entry	Yes
China	0 (2012-2020)	• Use existing health care system (public and private sectors)	ND	Use existing system	ND	ND	Yes

ND = No data

Discussion

Discussion

In this study, out of 44,900 malaria cases during FY2015-2021, 80.79% were delayed malaria treatment > 1 day of fever. From the secondary data analysis, factors significantly associated with late malaria treatment were being under five and 5-14 years old, vivax malaria and mixed infection for malaria species, and the short stay migrant. For seeking behaviour, community-based malaria service was a significant factor associated with delayed treatment. In the case of environmental variables, the factors significantly associated with delayed service were malaria risk areas (high-risk, low-risk, and potential area) and living provinces with borders except for Thai-Laos. The fiscal year is also a significant factor associated with receiving treatment. In the case of literature, several factors were associated with delayed malaria treatment, such as education, income, transportation, distance, and quality of care. General interventions related to early diagnosis and treatment were implemented among GMS countries to reduce malaria deaths and transmission.

1. Delayed treatment of malaria situation from FY2015-2021

Compared to the total confirmed malaria cases, similar demographic characteristics of delayed treatment patients were detected in terms of individual, accessibility to service delivery and environmental variables. In this study, the result of delayed proportion was slightly higher than the previous studies, which was conducted in 28 transmission provinces (49.9% and 71.8%) (34) and Tak province (79.6%)(35). Whereas the study's result aligned with the delayed treatment proportion in Asia (45.5%-87.5%)(43,53,55,58) and African countries (46.7%-87.8%)(38,40,50,74).

For the distribution of delayed malaria treatment, a high proportion was found in the high endemic area within the international border, especially in the south of the country. In addition, 3 provinces in the deep south of Thailand (Yala, Pattani, and Naratiwas province) were identified as a conflict zone for decades. Insecurity issues were a strong barrier to access to health facilities; even the government conducted community-based malaria services. Compared to the south, 46% of total malaria cases were non-Thai at the Thai-Myanmar border. Malaria posts are also set up in these border areas, to provide early diagnosis and treatment. The delayed proportion was slightly reduced during the covid outbreak (2020-2021). Fever was the common symptom in both malaria and covid (75). More awareness in covid infection may cause early visit to health facilities of the fever patients. The study's result was not aligned with other findings, which mentioned that covid 19 pandemic affects delayed treatment, because positive covid patients may not test on malaria and disruption of the health system (75,76).

2. Factors associated with delayed malaria treatment

2.1 Individual and treatment-seeking behaviour factors

Gender

After multiple logistic regressions, gender was not significantly associated with delayed malaria treatment. Some confounding factors may affect this variable. A similar result was found in a Thai study in Tak province, Thailand (35) and Shan State, Myanmar (46). Other publications from Myanmar showed that the patients' families were less likely to get early treatment if the fever member was female (53). Different gender roles still occur in many Asian countries; men earn more than women. Because of their illness, family income may

reduce. Gender is also influenced by culture (77). Another sample from India showed that the female was the risk group for inappropriate care due to their housework (52).

Age group

The analysis showed that malaria patients younger than 15 were less likely to get delayed treatment. This result disagreed with the studies from India (52). In comparison, one study showed that malaria families were more likely to receive the treatment in the case of patients younger than 15 (53). Not only malaria but also most communicable diseases, where children are the vulnerable group. They are always taken care of by caregivers such as parents, grandparents even neighbours to receive rapid treatment when they become sick. In addition, malaria knowledge and treatment behaviour of caregivers were affected by child treatment. The studies on the seeking behaviour of caregivers mentioned that poor malaria knowledge and treatment-seeking behaviour were associated with delayed treatment of their child (51). In addition, malaria-infected children have a chance of being more severe sick than adults (78), and people in Thailand are constantly aware of their children's illness. MOPH also implemented the royal project for malaria in primary schools in rural transmission areas to improve malaria awareness among students and their families (79).

Malaria parasite species

This study showed that malaria patients with *P. vivax* infection were less likely to get delayed treatment than those infected with *P. falciparum*. A result from the previous publication mentioned that vivax malaria cases gets more delayed (35,43). Generally, vivax malaria infection has a less disease severity than falciparum (16.9% and 36.3%, respectively) (80). A study from Indonesia showed that, after many episodes of malaria infection, individuals with vivax were more likely to die in the hospital than falciparum patients (81). In Thailand, the majority of malaria species are vivax malaria (>80%), and more than 1 episode per year of malaria infection with vivax is found with an increasing trend (18). Patients who have experienced vivax infection more than once, may be familiar with the symptoms that cause early treatment at health facilities. Mixed infection is also significantly associated with delayed treatment but opposite to vivax. For example, a study mentioned that the violence of falciparum malaria was interrupted by vivax species (82). According to characteristics of mixed infection in Thailand, almost all cases were infected with falciparum and vivax malaria (18). Delay of malaria severity may relate to delayed malaria treatment of mixed infected patients. Thailand's proportion of mixed infection is relatively low (<2% of total malaria cases).

Occupation

The result from simple logistic regression found that occupation was significantly associated with delayed malaria treatment. After controlling confounding factors, no significant association between forest-related occupation and delayed malaria treatment was found. The explanation could be a different number of forest-related groups (n=240) compared to the reference group (n=11,320). The results were contrasted with the study from Myanmar (Chin state, Rakhine state, and Tanintharyi Division), showing that forest-related work was significantly associated with the delays (47). Agriculture occupation got early malaria treatment, whereas rubber plantation occupation received more delay than other works. Compared to other work like officers, agriculture can be more flexible, regarding working time and independent work. For example, they may visit close by health facilities earlier. Opposite to the agriculture group, rubber plantation workers, especially latex collection in Thailand, mostly work at night to get more productivity and rest in the daytime. Most health facilities were open at working hours (8.30-16.30), which was the same time as their rest. Thai

study showed that the rubber plantation group received more delayed experience than the other workers (student, fruit orchard plantation, and labour) (60). Occupation related to decision to seek malaria treatment.

Resident status

The analysis in the study presented that short-stay migrants were more likely to receive malaria treatment within 24h compared to Thai residents. The result agreed with the Thailand malaria survey, that mobile household members sought malaria treatment within 24h after fever, whereas Thai members sought more time (83). In contrast to another study from Thailand, that showed hill tribe ethnicity were more likely to get deleted malaria treatment than Thai, because of their cultural belief (35). These patients gave as reason that they had malaria illness experience before, so self-medication with traditional healers was the first choice. This study found that resident status was significantly associated with the delay in treatment. Thai people were getting later treatment than a migrant. Resident status related to the border type. More than 99% of malaria cases on the Thai-Malaysia border were Thai residents.

Short-stay migrants were foreigners from neighbouring countries who crossed the border for work (receive more income) or seek better care due to the good quality of care in Thailand. At the border areas, malaria services at the community level (malaria posts) were free of charge; also, they are bilingual. The illegal migrant may feel comfortable using the services there and the distance is not a barrier because it is easy to cross the border by a river. Another reason could be explained by the specific malaria activities that focused on mobile migrants, implemented over several years by the government, civil society organizations and international organizations. The activities included providing early diagnosis and treatment at the border and distributing long-lasting insecticide-treated hammock nets free of charge, when migrants visit health facilities to test for malaria. The key activities were hiring malaria post workers in the remote villages and migrant health volunteers, who can speak their language and conduct bilingual information materials. In addition, the MMPs survey in Cambodia showed that all MMPs subgroups (construction, seasonal workers, forest goers, and security personnel) were willing to seek malaria treatment at health facilities (84).

Treatment place

Community-based health facilities showed a significant association with delayed malaria treatment. Compared to a public health facility, malaria patients, who visit community-based, were less likely to get delayed treatment. It may be related to accessibility to health facilities factor; distance of their location, near the patient's house. Mostly community-based healthcare is located in the village. The national malaria program conducts malaria posts in rural endemic villages, along international borders. The objective is to increase access to malaria services in at-risk populations. The criteria of malaria posts were located within the village where there was no other health facility. A village member was selected as the worker to give a more friendly service. Even malaria post workers operate part-time jobs, but they can provide malaria services after working hours or at night, which is convenient for villagers (63). Community-based can relate to easy access to health facilities, in terms of distance and good quality of care. In contrast, there were no associations between the private sector and delay in malaria treatment. In addition, the number of patients who visit the private sector in Thailand, was relatively low, compared to the public sector as a reference group (125 cases and 14,923 cases).

2.2 Environmental factors

Living province in terms of bordering with international border

The Thai border with Myanmar, Malaysia, and Cambodia was significantly associated with delayed malaria treatment. Malaria cases in Thai-Malaysia bordering provinces were more likely to experience delayed treatment than those in the central area. Whereas Thai-Myanmar and Cambodia sites were more changed to get early treatment. The national malaria program implemented malaria activities focusing on transmission areas common at the border (21). People who lived in these areas were more familiar with malaria services than those who lived in the middle of the country. The southern part of Thailand also has malaria-endemic areas, especially Yala and Naratiwas province, a conflict zone. Insecurity issues were a barrier to reaching healthcare, as the studies in Sri Lanka and Myanmar showed a significant association between conflict and delayed malaria treatment (55,58). The resident status factor is also related to the border. In the south, 99% of malaria cases were Thai, whereas only 52% of Thai malaria patients lived along the Myanmar border. For Cambodia's bordering province, good transportation and fewer mountainous areas than Myanmar's site led to more early malaria treatment.

Malaria risk area

In the multiple logistic regression, the malaria risk area was significantly associated with delayed treatment. Patients with a high or low malaria risk were more likely to get rapid treatment, than those who lived in a malaria-free area. Same as the explanation in border areas, they were familiar with malaria disease and prevention and control activities. The potential area was also significantly associated with delayed treatment. People who lived in the potential area, were more likely to experience the delay, than those who lived malaria-free. Malaria immunity may be involved in this case. To acquired malaria immunity is present in people who live in transmission areas (85). The immunity reduces the severity of malaria disease to uncomplicated or asymptomatic malaria. People who live malaria-free do not have this natural immunity and it causes more serious malaria symptoms than those live endemic area. Severe symptom related to early visit to health facilites.

Other factors

Environmental factors include distance, transportation cost, and road conditions, related to delays in reaching healthcare. The effective intervention, recommended by the WHO, was to conduct community-based health facilities, to improve the accessibility of malaria services (27). Good quality of care was the standard intervention to reduce delays in malaria treatment.

Period

The analysis showed a high probability of more delayed malaria treatment when time increased. Thailand is moving toward malaria elimination with no local transmission in the country. In eliminated countries, people may experience less awareness of the disease. Also, health personnel cause delays in diagnosis and treatment(71). For example, the median time of delayed malaria treatment in the endemic area was 3 days (35), whereas in non-endemic countries it was more than 3 days (41,42).

3. Strategy, interventions, and activities related to delayed treatment management

Early diagnosis and treatment strategy to reduce malaria morbidity and mortality and onward transmission, was the global and regional key strategy (27,28). All GMS countries and Sri Lanka set this

strategy as the main concept. The most common intervention in GMS countries was, conducting malaria case management at the community level, to increase the accessibility of malaria services, especially in remote and high malaria burdened villages. The services are operated by community health volunteers trained to provide rapid tests and effective antimalarial drugs, when a positive is detected. The effective intervention also faces the challenge of the quality of services. Lack of appropriate refresher training, supervision, and regular supply of malaria commodities (rapid test kit and malaria medicine) must be considered (86). Lack of malaria equipment and an effective referral system, low remuneration, lack of trust by community members, and security risks of female community health workers were obstacles in sub-Sahara Africa (87). These challenges were linked to delayed malaria treatment of the patients, as delay in seeking care decisions and delay in receiving care. Almost all of community malaria services were free of charge according to support from external funding. Integrated into community ownership and using local funds are the solutions to the sustainability of the intervention.

Relevance of the analytical framework

In general, the three-delay model is commonly used for maternal mortality. It showed 3 main factors, which are socioeconomic and cultural, accessibility of facility and quality of care, that affect health facility utilization in 3 delays. In the case of malaria, this study applied the model as a framework and found that it can help identify factors, related to delayed treatment for each delayed phase and also current interventions.

Strengths and limitations of the study

Seventy-seven thousand five hundred and one confirmed malaria records (Thai and non-Thai residents) during 7 years (FY2015-2021) were collected from a routine surveillance system. The study is the first analysis of factors associated with delayed malaria treatment, representing the country level and covering all populations. One study published, in the international journal, related to factors of delayed malaria treatment in Thailand, was found in 2015 and focused on malaria patients who had the Thai nationality (n=456) and who lived on the Thai-Myanmar border (35).

Even though all malaria cases were provided, some records showed incomplete information for several reasons. For example, different data collection forms were used in some health facilities; different variables were collected. For example, some data was categorized in the same group, such as children and students were in the same occupation group. Some were not specific to identify, like treatment place. Anonymous, missing data and entry errors were detected and excluded during the analysis. The dependent variable in this study is a delayed treatment, calculated from onset to treatment date. Recall bias of malaria patients on the start of fever symptoms, may occur during data collection by interview. Covid-19 pandemic also affected to the results due to treatment-seeking behaviours changed.

The poor quality of the goodness of fit result of the model was detected in this study. Goodness of fit test indicated how well of the model explain the dataset. Result showed that the current model did not sufficiently explain the variance of the study's dataset. The study analysed the secondary data, collected from a routine surveillance system. The dataset was not designed and collected in the way of this study’s purpose; many factors confound each other. Secondary data analysis often has this limitation.

Conclusion and Recommendation

Malaria in Thailand is still a challenge in terms of elimination. Delay in malaria treatment causes more disease severity and onward transmission. The study analysed the factors influencing delay in malaria treatment using surveillance data for the first paper at the country level.

The study mentioned a high proportion of delayed malaria treatment during FY2015-2021 (average 80.79% of total malaria cases). Most of the high proportion of delayed malaria treatment was found in the high malaria burden areas along the international borders, especially in Malaysia and Myanmar. The delay trend slightly decreased during the covid-19 outbreak. Covid awareness can be reason for early visit to health facilities.

Significant factors, associated with the delays, were under 15 years old, *P. vivax* infection, mixed *plasmodium* infection, short-stay migrants, agriculture work, rubber plantation, community-based health facilities, type of border and malaria risk areas. The study presents, that malaria patients infected with mixed parasite species, who worked in rubber plantations, lived at the Thai-Malaysia border and in potential areas, were more likely to receive delayed treatment than their reference. Malaria species infection is the uncontrol factors, while national program can focus more on rubber plantation occupations as priority group. For Malaysia border could be related to conflict situation. Specific interventions need to be studied. In addition, interventions for some targeted groups such as schools project for children, and malaria campaigns in short-stay migrants related to their better treatment-seeking behaviours. The neglected groups like Thai residents should be more interested.

Early diagnosis and prompt treatment, effectively reduce malaria morbidity, mortality and transmission. Critical interventions were implemented, related to the three delays model: 1) delay in seeking care which focuses on behaviour change, was provided with health education to improve malaria awareness, 2) delay in reaching care was set up community-based health facilities in the rural and high burden of malaria to increase access and coverage of malaria services and 3) delay in receiving the care ensured the standard of malaria services at health facilities to improve the quality of treatment.

In order to reduce the delayed malaria treatment, a package of effective interventions should be implemented considering influencing factors. In addition, the study will recommend the national malaria program to reduce delays in malaria treatment.

1. Maintain existing community-based facilities in remote endemic areas. The program can focus on the quality of malaria posts, by providing refresher training of malaria post workers, rapid test kits and antimalarial drugs and frequent supervision.
2. Improve capacity building of the HPH staff in potential areas to provide malaria diagnosis and treatment. Potential areas showed a high risk of delayed treatment but low malaria cases. Improving existing health facilities' capacity can make them more effective than conducting the new ones.
3. Provide key early diagnosis and treatment messages, focusing on Thai residents and working aged groups. Public awareness of malaria disease in potential and malaria-free areas should also be mentioned.
4. Strengthen outreach of case-finding activities in high-risk areas. For example, high-risk groups of delayed treatment, such as Thai residents, working aged groups and rubber plantation occupations should be prioritized.

5. Conduct research related to delayed treatment in the future. According to limited resources, collaboration with local universities or related institutes is the best option to initiate the research project. The research topics are proposed:
    a. Quantitative research focuses on treatment-seeking behaviour and quality of care factors associated with delayed malaria treatment.
    b. Qualitative research for factors influencing delayed malaria treatment. The qualitative study can answer the “why” questions of the delayed malaria treatment. The outcome can improve more effective interventions that appropriate to specific context.
    c. Operational research on specific interventions for the Thai-Malaysia border. Because of conflict issues, the appropriate approach has to be studied. The project can initiate as sentinel sites (1-2 sub-districts) and expand later.
    d. Cost benefit analysis of the community-based health facility on malaria case management. Convincing local authorities to participate in financial can make sustain of community-based health facilities (malaria posts were supported by external funding). To be ownership is the key factor of sustainability. The research can indicate on value of the intervention.

References

1. Association of South East Asian Nations. *About ASEAN*. Available from: https://asean.org/about-us/ [Accessed 12 May 2022].
2. Asean up. *Southeast Asia Map*. Available from: https://aseanup.com/wp-content/uploads/2016/11/Southeast-Asia-map-white.jpg [Accessed 18 Jul 2021].
3. Office of the Royal Society. *Geographic classification*. Available from: https://www.orst.go.th/ [Accessed 12 May 2022] (Thai version).
4. National Statistical Office Thailand. *Land utilization*. Available from: http://www.nso.go.th/sites/2014en/ [Accessed 18 Jul 2022] (Thai version).
5. Climate Change Knowledge Portal. *Thailand - Climatology*. Available from: https://climateknowledgeportal.worldbank.org/country/thailand/climate-data-historical [Accessed 12 May 2022].
6. Thailand Meteorological Department. *Season of Thailand*. Available from: https://www.tmd.go.th/info/info.php?FileID=22 [Accessed 12 May 2022].
7. The World Bank. *Thailand | Data World bank*. Available from: https://data.worldbank.org/country/thailand?view=chart [Accessed 12 May 2022].
8. World Population Review. *Thailand Population 2022*. Available from: https://worldpopulationreview.com/countries/thailand-population [Accessed 12 May 2022].
9. The World Bank. *Urban population (% of total population) - Thailand | Data world Bank*. Available from: https://data.worldbank.org/indicator/SP.URB.TOTL.IN.ZS?locations=TH [Accessed 25 Jul 2022].
10. The World Bank. *Refugee population by country or territory of asylum - Thailand | Data world Bank*. Available from: https://data.worldbank.org/indicator/SM.POP.REFG?locations=TH [Accessed 25 Jul 2022].
11. National Statistical Office Thailand. *Age group distribution*. Available from: http://www.nso.go.th/sites/2014en/ [Accessed 13 May 2022] (Thai version).
12. Department of Economic and Social Affairs- population Division, United Nations. *World Population Prospects*. Available from: https://population.un.org/wpp/Graphs/DemographicProfiles/Pyramid/764 [Accessed 18 Jul 2022].
13. Ministry of Public Health. *Public Health Statistic A.D.2019*. Nonthaburi: Strategy and Planning Division, Ministry of Public Health; 2020. (Thai version).
14. Ministry of Public health. *Health facilities code*. Available from: http://203.157.10.8/hcode_2020/query_02.php?provcode=22 [Accessed 25 Jul 2022] (Thai version).
15. World Health Organization. *World Malaria Report 2021*. Geneva: World Health Organization; 2021.
16. Mekong Malaria Elimination Program. *Mekong Malaria Elimination Program, epidemiology summary*. Mekong Malaria Program. 2020. vol 9: Jan-Mar. Available from: https://www.who.int/publications/i/item/WHO-UCN-GMP-MME-2020.02 [Accessed 10 Jun 2022].

17. Mekong Malaria Elimination Program. *Mekong Malaria Elimination Program, epidemiology summary*. Mekong Malaria Program. 2021. vol 15: Jul-Sept. Available from: https://www.who.int/publications/i/item/WHO-UCN-GMP-MME-2021.03 [Accessed 10 Jun 2022].

18. Division of Vector-Borne Diseases. *Thailand malaria surveillance system*. DDC, MOPH. Available from: http://malaria.ddc.moph.go.th. [Accessed 10 Jun 2022] (Thai version).

19. Ministry of Public Health. *Health vital statistic*. Available from: https://vitalstat.dcs.moph.go.th/ [Accessed 25 Jul 2022] (Thai version).

20. Division of Vector-Borne Diseases. *Guideline on Malaria Elimination for public health in Thailand*. Nonthaburi. Division of Vector-Borne Diseases. 2019. Available from: http://malaria.ddc.moph.go.th. [Accessed 10 Jun 2022] (Thai version).

21. Division of Vector-Borne Diseases. *Guideline for implementation of The Regional Artemisinin Initiative to Elimination (RAI3E)*. Nonthaburi. Division of Vector-Borne Diseases. 2021. (Thai version).

22. Division of Vector-Borne Diseases. *National Treatment Guideline for Malaria*. Nonthaburi. Division of Vector-Borne Diseases. 2021. Available from: http://malaria.ddc.moph.go.th [Accessed 10 Jun 2022] (Thai version).

23. U.S. Agency for International Development (USAID). *Inform Asia | Fact Sheet | Regional Development Mission for Asia*. Available from: https://www.usaid.gov/asia-regional/fact-sheets/inform-asia [Accessed 18 Jul 2022].

24. UNOPS. *Regional Artemisinin-resistance Initiative (RAI).* Available from: https://raifund.org/en [Accessed 18 Jul 2022].

25. World Health Organization. *WHO malaria terminology 2021 update*. Geneva: Global Malaria Programme; 2021.

26. World Health Organization. *Malaria elimination, A field manual for low and moderate endemic countries.* Geneva: World Health Organization; 2007.

27. World Health Organization. *Global Technical Strategy for malaria, 2016-2030*. United Kingdom: World Health Organization; 2015.

28. World Health Organization. *Strategy for malaria elimination in the Greater Mekong Subregion: 2015-2030.* Geneva: World Health Organization; 2015.

29. Ministry of Public Health. *National Malaria Elimination Strategy Thailand 2017-2026*. Nonthaburi: Division of Vector-Borne Diseases; 2016.

30. Division of Vector-Borne Diseases. *Operational Plan for malaria elimination in Thailand, 2021-2025*. 2021.

31. World Health Organization. *Guidelines for the treatment of malaria Third edition*. Italy. World Health Organization. Available from: https://apps.who.int/iris/bitstream/handle/10665/162441/9789241549127_eng.pdf?sequence=1 [Accessed 10 Jun 2022].

32. Mousa A, Al-Talar A, Anstey NM, Badaut C, Barber B E, Bassat Q, et al. The impact of delayed treatment of uncomplicated *P. falciparum* malaria on progression to severe malaria A systematic review and a pooled multicentre individual-patient meta-analysis. 2020. *PLoS Med*. Vol 17(10). Oct 19. Available from: DOI: 10.1371/journal.pmed.1003359. [Accessed 10 Jun 2022].

33. Challenger J D, Goncalves B P, Bradley J, Bruxvoort K, Tiono A B, Drakeley C, et al. How delayed and non-adherent treatment contribute to onward transmission of malaria a modelling study. *BMJ Global Health*. 2019. Dec 10:4(6): e001856. Available from: doi: 10.1136/bmjgh-2019-001856 [Accessed 10 Jun 2022].

34. Pina Chamnan. Effectiveness of Malaria Control in Endemic Provinces under the Global Fund Project, Thailand. *Journal of Health Science*. 2013;22(6) (Thai version).

35. Sonkong K, Chaiklieng S, Neave P, Suggaravetsiri P. Factors affecting delay in seeking treatment among malaria patients along Thailand-Myanmar border in Tak Province, Thailand*. Malaria Journal*. 2015;14(1).

36. Chaichur P, Sommart A, Loijiw K, Jitmanee M. *Report on malaria deaths investigation*. SongKhla Public Health Office. 2022. (Thai version)

37. Division of Vector-Borne Diseases. *Report of investigation and radical treatment of malaria case*. Department of Disease Control, MOPH. 2019 (Thai version).

38. Chukwuocha UM, Okpanma AC, Nwakwuo GC, Dozie INS. Determinants of Delay in Seeking Malaria Treatment for Children Under-Five Years in Parts of South Eastern Nigeria. *Journal of Community Health*. 2014 Oct 31;39(6):1171–8.

39. Tiruneh M, Gebregergs G B, Birhanu D. Determinants of delay in seeking treatment among malaria patients in Dera district, NorthWest Ethiophia: a case control study. *African Health Sciences*. 2018;18(3):522–59.

40. Romay-Barja M, Cano J, Ncogo P, Nseng G, Santana-Morales MA, Valladares B, et al. Determinants of delay in malaria care-seeking behaviour for children 15 years and under in Bata district, Equatorial Guinea. *Malaria Journal*. 2016 Mar 31;15(1).

41. Bastaki H, Carter J, Marston L, Cassell J, Rait G. Time delays in the diagnosis and treatment of malaria in non-endemic countries: A systematic review. *Travel Medicine and Infectious Disease*. Elsevier USA; 2018. Vol. 21p. 21–7.

42. Czepiel J, Goldman S, Szlauer-Stefańska A, Mielimonka A, Biesiada G, Kalinowska-Nowak A, et al. Delay in diagnosis and treatment of patients with cases of imported malaria in Poland – One center's experience. *Family Medicine and Primary Care Review*. 2017;19(2):93–7.

43. Lu G, Cao Y, Chen Q, Zhu G, Müller O, Cao J. Care-seeking delay of imported malaria to China: implications for improving post-travel healthcare for migrant workers. *Journal of Travel Medicine*. 2022;29(4):1–9.

44. Adhikari B, Phommasone K, Pongvongsa T, Koummarasy P, Soundala X, Henriques G, et al. Treatment-seeking behaviour for febrile illnesses and its implications for malaria control and elimination in Savannakhet Province, Lao PDR (Laos): A mixed method study. *BMC Health Services Research*. 2019 Apr 24;19(1).

45. Dole Guntur R, Kingsley J, Islam FMA. Malaria treatment-seeking behaviour and its associated factors: A cross-sectional study in rural East Nusa Tenggara Province, Indonesia. *PLoS ONE*. 2022;17(2):1–20.

46. Lin Htut N, Wongsawass S, Mongkolchati A, Laosee O. Delay in Seeking Treatment among Adults with Malaria Experience in Shan State, Myanmar. *J Sci & Tech*. 2017;14(8):655–62.

47. Than MM, Min M, Aung PL. The Determinants of Delayed Diagnosis and Treatment Among Malaria Patients in Myanmar: A Cross-Sectional Study. *The Open Public Health Journal*. 2019 Mar 19;12(1):78–85.

48. Division of Vector-Borne Diseases*. Manual for Malaria elimination for public health officers at district and sub-district levels*. Nonthaburi: Division of Vector-Borne Diseases; 2019.

49. Thaddeus' S, Maine D. Too Far To Walk: Maternal Mortality In Context. *Sm Sci Med*. 1994;38(8):1091–110.

50. Andegiorgish AK. Knowledge, Attitude and Treatment Seeking Behavior for Malaria in May-Aynee Administration, Eritrea. *Biomedical Journal of Scientific & Technical Research*. 2019 Oct 17;22(1).

51. Mor Moe Thandar, Myat Phone Kyaw, Jimba M, Yasuoka J. Caregivers' treatment-seeking behavior for children under age five in malaria-endemic areas of rural Myanmar: a cross-sectional study. *Malaria Journal*. 2015;14(1):1–10.

52. Das A, Sundari Ravindran TK. Factor affecting treatment-seeking for febrile illness in a malaria endemic block in Boudh district, Orissa, India: policy implications for malaria control. *Malaria Journal*. 2010;9(377):1–10.

53. Xu JW, Xu QZ, Liu H, Zeng YR. Malaria treatment-seeking behaviour and related factors of Wa ethnic minority in Myanmar: A cross-sectional study. *Malaria Journal*. 2012;11(417):1–7.

54. Zar Naing Z, Kanchanakhan N. Barriers to prompt and effective malaria treatment among malaria infected patients in Palaw township, Tanintharyi region, Myanmar. *Journal of Health Research*. 2018; 32:104–11.

55. Aung YK, Zin SS, Tesfazghi K, Paudel M, Thet MM, Thein ST. A comparison of malaria prevention behaviours, care-seeking practices and barriers between malaria at-risk worksite migrant workers and villagers in Northern Shan State, Myanmar—a mixed method study. *Malaria Journal*. 2022 Dec;21(1).

56. Sonkong K, Suggaravetsiri P, Chaiklieng S. Treatment seeking behaviour and prevalence of treatment delay among malaria patients along Thailand-Myanmar border in Tak province. *Asian Pacific Journal of Tropical Disease*. 2015. Apr 1;5(4):279–83.

57. Chen I, Thi Thanh H N, Lover A, Thao P T, Luu TV, Thang H N, et al. Malaria risk factors and care-seeking behaviour within the private sector among high-risk populations in Vietnam a qualitative study. *Malaria Journal*. 2017; 16(414):1–14.

58. Reilley B, Abeyasinghe R, Pakianathar M V. Barriers to prompt and effective treatment of malaria in northern Sri Lanka. *Tropical Medicine and International Health*. 2002; 7(9):744–9.

59. Tynan A, Atkinson JA, Toaliu H, Taleo G, Fitzgerald L, Whittaker M, et al. Community participation for malaria elimination in tafea province, Vanuatu: Part ii. Social and cultural aspects of treatment-seeking behaviour. *Malaria Journal*. 2011; 10(204):1–12.

60. Muernrat Y, Suwannarat S, Suwan V. Factor related to delayed malaria treatment in Suratthani Province. *Journal of the Vector-borne Disease*. 2011;7(2):1-11 (Thai version).

61. Chaturvedi HK, Bajpai RC, Tiwari P. Determination of cut-off and correlates of delay in treatment-seeking of febrile illness: A retrospective analysis. *BMC Public Health*. 2020 Apr 28;20(1).

62. Sudathip P, Kitchakarn S, Thimasarn K, Gopinath D, Naing T, Sajjad O, et al. The evolution of the malaria clinic: The cornerstone of malaria elimination in Thailand. *Tropical Medicine and Infectious Disease.* 2019;4(4).

63. Bureau of Vector-Borne Diseases. *Malaria post: A novel intervention reaching the poorest and most vulnerable populations*. Department of Disease Control, MOPH. 2018.

64. Ministry of Health. *Strategic Plan for Elimination of Malaria in Cambodia, 2011-2025*. 2011.

65. Kunkel A, Nguon C, Iv S, Chhim S, Peov D, Kong P, et al. Choosing interventions to eliminate forest malaria: preliminary results of two operational research studies inside Cambodian forests. *Malaria Journal.* 2021 Dec 1;20(1).

66. Ministry of Health. *National Strategic Plan on Malaria Control and Elimination 2021-2025, Vietnam*. 2020.

67. Ministry of Health and Sports. *National Strategic Plan: Intensifying Malaria Control and Accelerating Progress towards Malaria Elimination 2016-2020, The Republic of the Union of Myanmar*. 2016.

68. Landier J, Parker DM, Thu AM, Lwin KM, Delmas G, Nosten FH, et al. Effect of generalised access to early diagnosis and treatment and targeted mass drug administration on *Plasmodium falciparum* malaria in Eastern Myanmar: an observational study of a regional elimination programme. *The Lancet*. 2018 May 12;391(10133):1916–26.

69. Ministry of Health. *National Strategic Plan for Malaria Control and Elimination 2016-2020, Lao People's Democratic Republic*. 2016.

70. Phommanivong V, Thongkham K, Deyer G, Rene JP, Barennes H. An assessment of early diagnosis and treatment of malaria by village health volunteers in the Lao PDR. *Malaria Journal*. 2010;9(1).

71. Ministry of Health. *National Strategic Plan for Prevention of Re-introduction of Malaria in Sri Lanka 2018-2022, Sri Lanka*. Anti Malaria Campaign. 2018.

72. Premaratne R, Wickremasinghe R, Ranaweera D, Gunasekera WMKTDAW, Hevawitharana M, Pieris L, et al. Technical and operational underpinnings of malaria elimination from Sri Lanka. *Malaria Journal.* 2019 Jul 29;18(256):1–12.

73. Feng X, Huang F, Yin J, Wang R, Xia Z. Key takeaways from China's success in eliminating malaria: leveraging existing evidence for a malaria-free world. *BMJ Global Health*. 2022 Apr;7(4): e008351.

74. N. Paraïso M, Kpozèhouen A, Glèlè Ahanhanzo Y, Facely C, Sossa-Jerome C, Massougbodji A. Determinants of Delays in Health Care Utilization for Malaria Treatment (HCUMT) in Children under Five in Benin Southern Setting. *Universal Journal of Public Health*. 2019 Jan;7(1):9–18.

75. Ajayi I O, Ajumobi O O, Falade C. Malaria and COVID-19: commonalities, intersections and implications for sustaining malaria control. *PanAfrican Medical Journal*. 2020;2.

76. The Global fund and Unite to Fight. *The Impact of Covid-19 on HIV, TB and malaria services and systems for health: A snapshot from 502 health facilities across Africa and Asia*. Switzerland; Global Health Campus. 2021. Available from: https://openknowledge.worldbank.org/bitstream/handle/10986/34496/9781464816024.pdf. [Accessed 28 Jul 2022].

77. Angelica-Nicoleta Neculaesei. Culture and Gender Role Different: Theoretical article. *Cross-Cultural Management Journal*. 2015; XVII (1(7)):31–5.

78. World Health Organization. *Management of severe malaria: a practical handbook. Third edition*. Italy: World Health Organization; 2012.

79. Division of Vector-Borne Diseases. *Malaria KAP survey in student under royal project*. Division of Vector-Borne Diseases. 2021.

80. Saravu K, Rishikesh K, Kamath A, Shastry AB. Severity in Plasmodium vivax malaria claiming global vigilance and exploration - A tertiary care centre-based cohort study. *Malaria Journal*. 2014 Aug 8;13(1).

81. Dini S, Douglas NM, Poespoprodjo JR, Kenangalem E, Sugiarto P, Plumb ID, et al. The risk of morbidity and mortality following recurrent malaria in Papua, Indonesia: A retrospective cohort study. *BMC Medicine*. 2020 Feb 20;18(1).

82. Mohapatra M K, Dash L K, Barih P K, Karua P C. Profile of mixed species (*Plasmodium vivax* and *falciparum*) malaria in adults. *J Assoc Physicians India*. 2012; Oct (60):20–4

83. Division of Vector-Borne Diseases. *Thailand Malaria Survey*. Division of Vector-Borne Diseases 2020.

84. Kheang S T, Collins E L, Preaton A, An Y, Ir P, Phalla H, et al. Health seeking behaviour and access to care for mobile and migrant populations in Cambodia. *Prev Med Commun Health*. 2019; 2:1–7.

85. Alyssa Barry and Diana Hansen. Naturally acquired immunity to malaria. *Parasitology*. 2016; 143: 125–8.

86. Nyunt MH, Aye KM, Kyaw KT, Han SS, Aye TT, Wai KT, et al. Challenges encountered by local health volunteers in early diagnosis and prompt treatment of malaria in Myanmar artemisinin resistance containment zones. *Malaria Journal*. 2016. Jun 6;15(1).

87. Boakye Michelle D S, Owek C J, Oluoch E, Wachira J, Afrane Y A. Challenges of achieving sustainable community health services for community case management of malaria. *BMC Public Health*. 2018;18(1150):1–8.

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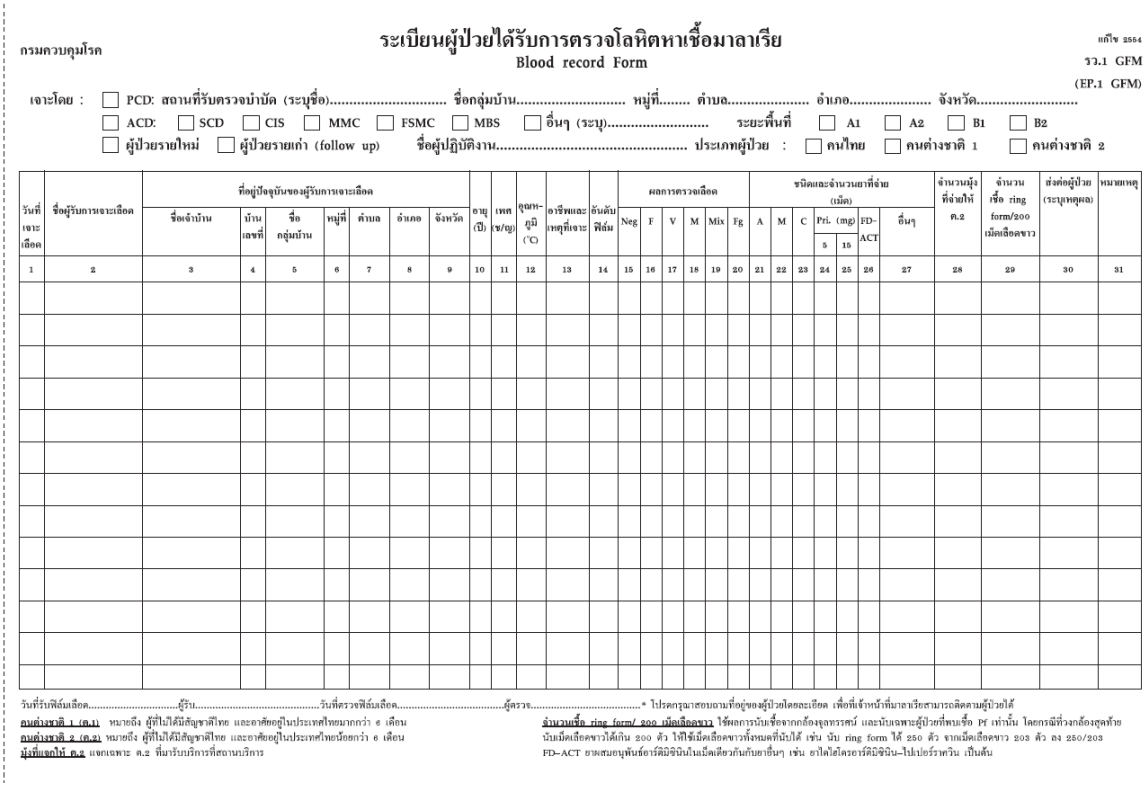
Finally, I would like to thank MPH and MIH friends for sharing valuable experiences in Amsterdam.

Annexes

Annex 1: EP.1 report form – Thai version



กรมควบคุมโรค

ระเบียนผู้ป่วยได้รับการตรวจโลหิตหาเชื้อมาลาเรีย

Blood record Form

แก้ไข 2564

รว.1 GFM

(EP.1 GFM)

เจาะโดย : ☐ PCD: สถานที่รับตรวจบำบัด (ระบุชื่อ)..... ชื่อกลุ่มบ้าน..... หมู่ที่..... ตำบล..... อำเภอ..... จังหวัด.....

☐ ACD: ☐ SCD ☐ CIS ☐ MMC ☐ FSMC ☐ MBS ☐ อื่นๆ (ระบุ)..... ระยะพื้นที่ ☐ A1 ☐ A2 ☐ B1 ☐ B2

☐ ผู้ป่วยรายใหม่ ☐ ผู้ป่วยรายเก่า (follow up) ชื่อผู้ปฏิบัติงาน..... ประเภทผู้ป่วย : ☐ คนไทย ☐ คนต่างชาติ 1 ☐ คนต่างชาติ 2

วันที่เจาะเลือด	ชื่อผู้รับการเจาะเลือด	ที่อยู่ปัจจุบันของผู้รับการเจาะเลือด							อายุ (ปี)	เพศ (ช/ญ)	อุณหภูมิ (°C)	อาชีพและเหตุที่เจาะ	อันดับฟิล์ม	ผลการตรวจเลือด						ชนิดและจำนวนยาที่จ่าย (เม็ด)							จำนวนผู้ป่วยที่จ่ายให้ ค.2	จำนวนเชื้อ ring form/200 เม็ดเลือดขาว	ส่งต่อผู้ป่วย (ระบุเหตุผล)	หมายเหตุ
		ชื่อเจ้าบ้าน	บ้านเลขที่	ชื่อกลุ่มบ้าน	หมู่ที่	ตำบล	อำเภอ	จังหวัด						Neg	F	V	M	Mix	Fg	A	M	C	Pri. (mg) 5	Pri. (mg) 15	FD-ACT	อื่นๆ				
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31

วันที่รับฟิล์มเลือด.....ผู้รับ.....วันที่ตรวจฟิล์มเลือด.....ผู้ตรวจ..... * โปรดกรุณาสอบถามที่อยู่ของผู้ป่วยโดยละเอียด เพื่อที่เจ้าหน้าที่มาลาเรียสามารถติดตามผู้ป่วยได้

คนต่างชาติ 1 (ค.1) หมายถึง ผู้ที่ไม่ได้มีสัญชาติไทย และอาศัยอยู่ในประเทศไทยมากกว่า 6 เดือน

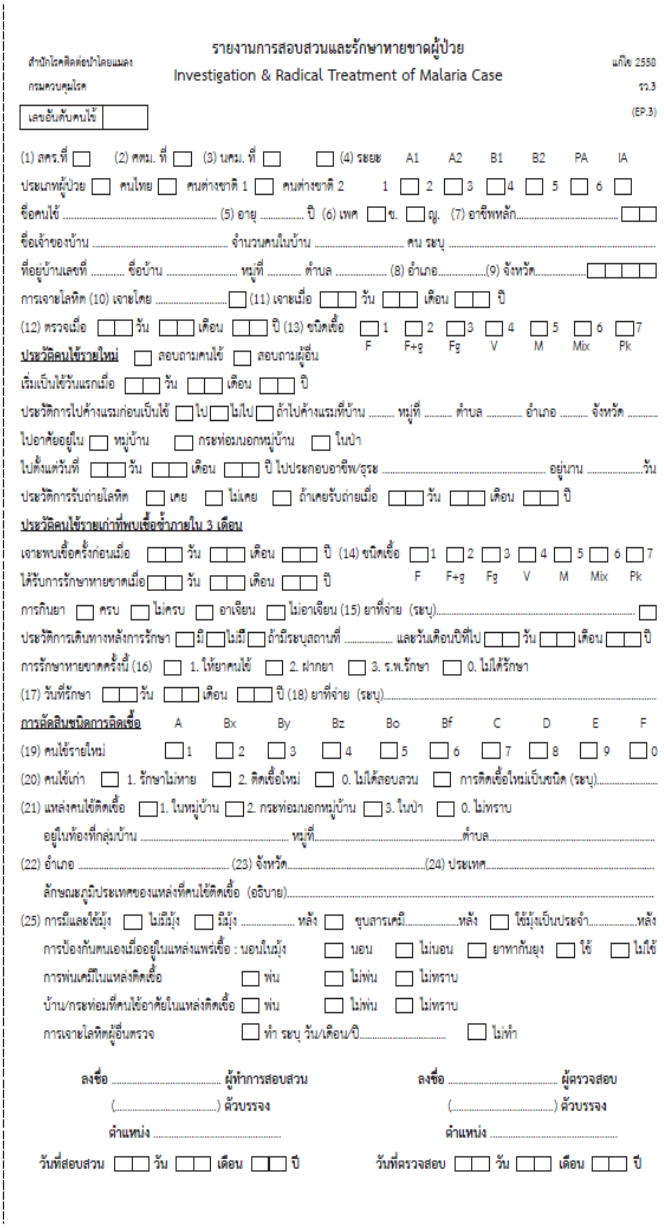
คนต่างชาติ 2 (ค.2) หมายถึง ผู้ที่ไม่ได้มีสัญชาติไทย และอาศัยอยู่ในประเทศไทยน้อยกว่า 6 เดือน

ผู้ป่วยที่แยกให้ ค.2 แจกเฉพาะ ค.2 ที่มารับบริการที่สถานบริการ

จำนวนเชื้อ ring form/ 200 เม็ดเลือดขาว ใช้ผลการนับเชื้อจากกล้องจุลทรรศน์ และนับเฉพาะผู้ป่วยที่พบเชื้อ Pf เท่านั้น โดยกรณีที่วงกล้องสุดท้ายนับเม็ดเลือดขาวได้เกิน 200 ตัว ให้ใช้เม็ดเลือดขาวทั้งหมดที่นับได้ เช่น นับ ring form ได้ 250 ตัว จากเม็ดเลือดขาว 203 ตัว ถง 250/203

FD–ACT ยาผสมอนุพันธ์อาร์ทีมิซินินในเม็ดเดียวกันกับยาอื่นๆ เช่น อาโทโวไควอร์ทีมิซินิน–ไปเปอร์ราควิน เป็นต้น

Annex 2: EP.3 report form – Thai version



สำนักโรคติดต่อนำโดยแมลง
กรมควบคุมโรค

รายงานการสอบสวนและรักษาหายขาดผู้ป่วย
Investigation & Radical Treatment of Malaria Case

แก้ไข 2558
ร.3
(EP.3)

เลขอันดับคนไข้ ☐☐☐

(1) สคร.ที่ ☐ (2) สคม. ที่ ☐ (3) นครม. ที่ ☐☐ (4) ระยะ A1 A2 B1 B2 PA IA

ประเภทผู้ป่วย ☐ คนไทย ☐ คนต่างชาติ 1 ☐ คนต่างชาติ 2 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐

ชื่อคนไข้ ..... (5) อายุ ..... ปี (6) เพศ ☐ช. ☐ญ. (7) อาชีพหลัก..... ☐☐

ชื่อเจ้าของบ้าน ..... จำนวนคนในบ้าน ..... คน ระบุ .....

ที่อยู่บ้านเลขที่ ..... ชื่อบ้าน ..... หมู่ที่ ..... ตำบล ..... (8) อำเภอ.....(9) จังหวัด..... ☐☐☐

การเจาะโลหิต (10) เจาะโดย ..... ☐ (11) เจาะเมื่อ ☐☐ วัน ☐☐ เดือน ☐☐ ปี

(12) ตรวจเมื่อ ☐☐ วัน ☐☐ เดือน ☐☐ ปี (13) ชนิดเชื้อ ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7
F F+g Fg V M Mix Pk

ประวัติคนไข้รายใหม่ ☐ สอบถามคนไข้ ☐ สอบถามผู้อื่น

เริ่มเป็นไข้วันแรกเมื่อ ☐☐ วัน ☐☐ เดือน ☐☐ ปี

ประวัติการไปค้างแรมก่อนเป็นไข้ ☐ไป ☐ไม่ไป ☐ถ้าไปค้างแรมที่บ้าน ..... หมู่ที่ ..... ตำบล ..... อำเภอ ..... จังหวัด .....

ไปอาศัยอยู่ใน ☐ หมู่บ้าน ☐ กระท่อมนอกหมู่บ้าน ☐ ในป่า

ไปตั้งแต่วันที่ ☐☐ วัน ☐☐ เดือน ☐☐ ปี ไปประกอบอาชีพ/ธุรกิจ ..... อยู่นาน .....วัน

ประวัติการรับถ่ายโลหิต ☐ เคย ☐ ไม่เคย ☐ ถ้าเคยรับถ่ายเมื่อ ☐☐ วัน ☐☐ เดือน ☐☐ ปี

ประวัติคนไข้รายเก่าที่พบเชื้อซ้ำภายใน 3 เดือน

เจาะพบเชื้อครั้งก่อนเมื่อ ☐☐ วัน ☐☐ เดือน ☐☐ ปี (14) ชนิดเชื้อ ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7
F F+g Fg V M Mix Pk

ได้รับการรักษาหายขาดเมื่อ ☐☐ วัน ☐☐ เดือน ☐☐ ปี

การกินยา ☐ ครบ ☐ ไม่ครบ ☐ อาเจียน ☐ ไม่อาเจียน (15) ยาที่จ่าย (ระบุ)..... ☐

ประวัติการเดินทางหลังการรักษา ☐มี ☐ไม่มี ☐ถ้ามีระบุสถานที่ ..... และวันเดือนปีที่ไป ☐☐ วัน ☐☐ เดือน ☐☐ ปี

การรักษาหายขาดครั้งนี้ (16) ☐ 1. ให้ยาคนไข้ ☐ 2. ฝากยา ☐ 3. ร.พ.รักษา ☐ 0. ไม่ได้รักษา

(17) วันที่รักษา ☐☐ วัน ☐☐ เดือน ☐☐ ปี (18) ยาที่จ่าย (ระบุ).....

การตัดสินชนิดการติดเชื้อ A Bx By Bz Bo Bf C D E F

(19) คนไข้รายใหม่ ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐0

(20) คนไข้เก่า ☐ 1. รักษาไม่หาย ☐ 2. ติดเชื้อใหม่ ☐ 0. ไม่ได้สอบสวน ☐ การติดเชื้อใหม่เป็นชนิด (ระบุ).....

(21) แหล่งคนไข้ติดเชื้อ ☐1. ในหมู่บ้าน ☐2. กระท่อมนอกหมู่บ้าน ☐3. ในป่า ☐ 0. ไม่ทราบ

อยู่ในห้องที่กลุ่มบ้าน ..... หมู่ที่..... ตำบล.....

(22) อำเภอ ..... (23) จังหวัด.....(24) ประเทศ.....

ลักษณะภูมิประเทศของแหล่งที่คนไข้ติดเชื้อ (อธิบาย).....

(25) การมีและใช้มุ้ง ☐ ไม่มีมุ้ง ☐ มีมุ้ง ..... หลัง ☐ ชุบสารเคมี..... หลัง ☐ ใช้มุ้งเป็นประจำ..... หลัง

การป้องกันคนเองเมื่ออยู่ในแหล่งแพร่เชื้อ : นอนในมุ้ง ☐ นอน ☐ ไม่นอน ☐ ยาทากันยุง ☐ ใช้ ☐ ไม่ใช้

การพ่นเคมีในแหล่งติดเชื้อ ☐ พ่น ☐ ไม่พ่น ☐ ไม่ทราบ

บ้าน/กระท่อมที่คนไข้อาศัยในแหล่งติดเชื้อ ☐ พ่น ☐ ไม่พ่น ☐ ไม่ทราบ

การเจาะโลหิตผู้อื่นตรวจ ☐ ทำ ระบุ วัน/เดือน/ปี..... ☐ ไม่ทำ

ลงชื่อ ..... ผู้ทำการสอบสวน
(.....) ตัวบรรจง
ตำแหน่ง .....
วันที่สอบสวน ☐☐ วัน ☐☐ เดือน ☐☐ ปี

ลงชื่อ ..... ผู้ตรวจสอบ
(.....) ตัวบรรจง
ตำแหน่ง .....
วันที่ตรวจสอบ ☐☐ วัน ☐☐ เดือน ☐☐ ปี

Annex 3: Data use permission letter

No. 0411.1.5 / 1360

Division of Vector Borne Diseases
Department of Disease Control
Ministry of Public Health
Tiwanon Road,
Nonthaburi 11000, Thailand
Tel : 66 2 590 3130 Fax : 66 2 591 8422

6 June B.E.2565 (2022)

Dear Miss Suravadee Kitchakarn,

Subject: Reply the permission letter to use data on malaria online surveillance system.

Thank you very much for your interest in the data on malaria online surveillance system. Your research topic "Factors associated with delayed treatment among malaria cases in Thailand" is very useful. I am glad to permit you to use the data for your study. I hope that it will benefit the malaria elimination in Thailand.

I sincere hope that your attempt will meet with great success. If you need any clarification or advice, please feel free to contact us.

Yours sincerely,

Chantana Padungtod

(Dr. Chantana Padungtod)
Director, Division of Vector Borne Diseases

Miss Suravadee Kitchakarn
Royal Tropical Institute,
Mauritskade 54, Amsterdam,
The Netherlands

Annex 4: Wavier letter for KIT-REC

From: Suravadee Kitchakarn

Royal Tropical Institute,
Mauritskade 54, Amsterdam,
The Netherlands

10 Jun 2022

To: Chair KIT Research Ethics Committee

Dear Sandra Alba,

This letter is to request a waiver of ethical clearance for a study on Factors associated with delayed treatment among malaria cases in Thailand. The data that use in thesis is one part of national malaria surveillance system which belong to Division of Vector Borne Diseases (DVBD), Department of Disease Control, Ministry of Public Health, Thailand.

The data set include malaria patient information, detail of malaria diagnosis, treatment and followed up and personal protection behaviors were collected by local health care staff as routine work and entered in online national malaria surveillance system. The summarize information (malaria situation and program response activities) are published on DVBD official website. The thesis will analyse these data from October 2014 to September 2021 (7 fiscal years). The mixed methods which are literature review and secondary data analysis will be done by Suravadee Kitchakarn in the context of KIT MPH thesis research. The purpose of the thesis study is to identify and analyse factors associated to delayed treatment among malaria cases. For secondary data part, the data set will be analysed using statistic tool (STATA program). The thesis will be used for provide recommendation and suggest more effective interventions to reduce delay in malaria treatment to national malaria elimination program for achieve elimination goal in 2024.

I would like to kindly request the Research Ethical Committee for a waiver of ethical clearance for this study for the following reasons:

1. The data have been anonymized and are stored in a safe place. With permission letter from data owner, responsible DVBD staff will send data set without name of patients by email. The data set will be stored only in my computer with login and password.

2. Data use has been approved by the data owner (Division of Vector Borne Disease, Department of Disease Control, Ministry of Public Health, Thailand).

3. Informed consent *has not been given* and it would not be feasible or practicable to ask informed consent to the participants to whom the data belong. The data collection is regular duty of the department to prevent and control diseases.

1

4. The research has important social, educational and/or scientific value, namely to success malaria elimination in few years, national malaria elimination program (NMEP) has to emphasize on early diagnosis and prompt treatment. Delayed in treatment causes severe malaria and onward transmission. Identify and analyse determinants associated with delayed treatment can suggest more effective interventions to the program.

5. The research poses no more than minimal risks to participants, including social and cultural risks such as discrimination, stigmatisation or psychological discomfort or harm and does not give rise to the disclosure of the participants' identities. The data set is anonymous according to patient's privacy also used for only this thesis purpose with permission letter from data owner.

I hope to have informed you sufficiently on the objective and content of this study to make a decision on our request.

Yours sincerely,

Suravadee Kitchakarn

Co-signer of academic advisor: Mahdi Abdelwahab

Co-signer Signature:

Date: 10 June 2022

Annex 5: KIT REC clearance letter

KIT Royal Tropical Institute

RESEARCH ETHICS COMMITTEE

Contact: Sandra Alba
s.alba@kit.nl

To: Suravadee Kitchakarn
By E-mail: s.kitchakarn@student.kit.nl

Amsterdam, 16-06-2022

Subject Decision Research Ethics Committee S-196

Dear Suravadee Kitchakarn,

The Research Ethics Committee (REC) of Royal Tropical Institute has reviewed your application for a waiver for a "Factors associated with delayed treatment among malaria cases in Thailand" (S-196) study that was originally submitted on 10-06-2022

Your proposal has been exempted from full ethical review based on the following considerations:

a. the data will be anonymized and stored in a safe place, only accessible for a selection of the research team;
b. the data has been approved by the data owner
c. informed consent has not been given but it would not be feasible or practicable to ask informed consent to the participants to whom the data belong (anymore);
d. the research has important social, educational or scientific value
e. the research poses no more than minimal risks to participants and does not give rise to the disclosure of the participant's identity

The Committee grants this waiver provided that you inform the GDPR project officer about your research project for GDPR monitoring purposes.

The Committee requests you to inform the Committee if substantive changes to the protocol are made, important changes to the research team take place or researchers are added to the research team. Moreover, the Committee requests you to send the final report of the research containing a summary of the study's findings and conclusions to the Committee, for research managing and training purposes of the REC. Failure to submit the report to the REC, or implement GDPR measurements may have consequences for your next research proposal.

Wishing you success with the research,

Sandra Alba
Co-chair of the KIT REC

The Netherlands
Fax +31 (0)20 568 8444

ABN AMRO 40 50 05 970
ABN AMRO USD 62 62 48 183

Annex 6: A searching strategy for literature review

		AND		
OR	Malaria Febrile illness Fever Mosquito Vector-borne diseases	Delayed treatment Early diagnosis and treatment Barrier Accessibility Strategy intervention	Determinants factors (socioeconomic status, quality of care, policy) Health seeking behaviour	Thailand Greater Mekong Subregion (GMS) South-east Asia countries Asia Malaria endemic areas Transmission area