Aus dem Fachbereich Medizin
der Johann Wolfgang Goethe-Universität
Frankfurt am Main

betreut im
Zentrum der Gesundheitswissenschaften
Institut für Arbeitsmedizin, Sozialmedizin und Umweltmedizin
Direktor : Prof. Dr. Dr. h.c. mult. David A. Groneberg

Determinants of Malaria in Indonesia

Dissertation
zur Erlangung des Doktorgrades der theoretischen Medizin
des Fachbereichs Medizin
der Johann Wolfgang Goethe-Universität
Frankfurt am Main

vorgelegt von
Hamzah Hasyim
B.Sc. (PH) Occupational Health and Safety
(MPH) Environmental Health

aus Ujung Pandang, South Sulawesi, Indonesia
Frankfurt am Main, 2019

Dekan/in	:	Prof. Dr. med. Josef Pfeilschifter
Referent/in	:	Prof. Dr. rer. nat. Ruth Müller
Korreferent/in	:	Prof. Dr. Maria Vehreschild
Tag der mündlichen Prüfung	:	09.12.2019

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Zusammenfassung

Malaria ist eine Umweltkrankheit, die nicht nur von den physischen und biologischen Umweltfaktoren, sondern auch von soziokulturellen Faktoren beeinflusst wird. Einige Faktoren, die eine mit der Krankheit verbundene hohe Morbiditätsrate verursachen, umfassen den Klimawandel, die geografische Umgebung, sozioökonomische Umstände, und das menschliche Verhalten. Weitere Risikofaktoren sind das Vorhandensein von Tieren, Wohnbedingungen mit schlechten sanitären Einrichtungen, fehlende Hygienepraktiken und unzureichende Gesundheitsdienste in Endemiegebieten. Die Bemühungen zur Beseitigung von Malaria und zur Beseitigung von Vektoren sind seit Jahrzehnten Gegenstand zahlreicher Tagungen und Initiativen im Bereich der öffentlichen Gesundheit. In Indonesien ist Malaria nach wie vor eine der Hauptursachen für Morbidität und Mortalität. Das Ziel dieser Studie ist es, die multiplen Determinanten von Malaria in den endemischen Gebieten Indonesiens zu analysieren, die mit soziodemografischen als auch physischen Umgebungen korrelieren. Wir teilen diese Forschung in drei Teilstudien auf, um ein Vorstellungsmodell zu entwickeln, das die Determinanten für Malaria in Indonesien umfassend beschreibt.

Diese Dissertation folgt einer Querschnittsdesignstudie. Die Forschungsdaten dieser Dissertation stammen aus vier Quellen: routinemäßige Berichterstattung über Malaria aus der Gesundheits-Provinz in Süd-Sumatra; die nationalen Grundlagenforschungsdaten (IDN-Akronym: Riskesdas); Klimadaten aus der Klimatologie-Agentur Meteorologie, Klimatologie und Geophysik (IDN-Akronym: BMKG); Geodaten von Geospatial Information Agency (IDN-Akronym: BIG). In dieser Studie wurde ein ganzheitlicher Ansatz verfolgt, der die folgenden univariaten, binär-logistische Regressionsanalyse, und multivariate-logistische Regressionsanalyse, um eine Modellierungsdeterminante von Malaria zu etablieren. Darüber hinaus haben wir beide Modelle, die geographisch gewichtete Regression (GWR) und die Methode der kleinsten Quadrate (OLS) verglichen. Wir verwendeten folgende statistische Programme für die Datenverarbeitung, Analyse, Visualisierung und die Entwicklung der Modelle: Statistisches Paket für die Sozialwissenschaften (SPSS), Stata, Aeronautical Reconnaissance Coverage Geographisches Informationssystem (ArcGIS) und Geographisch gewichtete Regression 4 (GWR4).

Die Prävalenz von Malaria variiert in Abhängigkeit von der lokalen Umgebung und diese Varianz wird durch die örtlich unterschiedliche physische Umgebung verursacht. Es zeigte sich in dieser Studie zudem, dass die Determinanten für Malaria in lokalen Regionen unterschiedlich waren. Wir folgern, dass ländliche Gebiete mit einem hohen Prozentsatz von Haushalten mit Nutz- und Haustieren einhöhere Malaria-Prävalenz aufwiesen als der nationale Durchschnitt in Indonesien. Darüber hinaus weist die Studie darauf hin, dass soziodemografische Variablen der Teilnehmer (z.B. Geschlecht, Alter, Bildungsgrad, Kenntnis der Zugänglichkeit und Nutzung von Gesundheitsdiensten, Maßnahmen zum Schutz vor Mückenstichen, und Wohnzustand der Studienteilnehmer) mit der Malariaprävalenz in endemischen Provinzen in Indonesien zusammenhängen.

In Süd-Sumatra, Indonesien sind die unabhängigen Variablen Höhe, Entfernung vom Wald und Niederschlag im globalen OLS Modell signifikant mit Malariafällen assoziiert. Das ergänzende GWR Modell zeigte schlüssig, daß die Ursache der Malariafälle auf der dörflichen Ebene erheblich variiert. Daher ist es für den Entscheidungsträger, d.h. die Regierung, sehr wichtig, ein tiefergehendes Verständnis der regionalen und ökologischen Faktoren zu entwickeln, welche die bestätigten Malariafälle beeinflussen. Auf Grundlage der vorliegenden Ergebnisse empfehlen wir die Entwicklung nachhaltiger regionaler Malariakontrollprogramme, welche Anreize für die Beseitigung von Malaria schaffen, und insbesondere auf Dorfebene. Das Vorhandensein von bestimmten Tieren stellt einen Hauptrisikofaktor für Malaria im ländlichen Indonesien dar und muß in Bekämpfungsstrategien berücksichtigt werden. Hier empfehlen wir insbesondere für das Untersuchungsgebiet einen One Health Approach mit Integriertem Vector Management (IVM), beispielsweise die simultane Umsetzung von insektizidbehandelten Bettnetzen (ITN) und insektizidbehandelten Nutztieren (ITL). Darüber hinaus sind auch soziodemografische Faktoren, zum Beispiel die gesundheitliche Versorgung für die lokale und regionale Malaria-Prävalenz wichtig.
Wir empfehlen den Ausbau von Bildung und öffentlichen Informationsmöglichkeiten und eine verbesserte Zugänglichkeit bzw. Nutzung der Gesundheitsfürsorge, um das Wissen und das Bewusstsein der Dorfbewohner bezüglich der Reduktion von *Anopheles* Stechmücken zu fördern. Wir empfehlen den Ausbau von Bildung und öffentlichen Informationsmöglichkeiten und eine verbesserte Zugänglichkeit bzw. Nutzung der

Gesundheitsfürsorge, um das Wissen und das Bewusstsein der Dorfbewohner bezüglich der Reduktion von Anopheles Stechmücken zu fördern.

Diese Forschungsarbeit zeigt, dass es einen Zusammenhang zwischen soziodemografischen Faktoren gibt, welche die Malaria-Prävalenz beeinflussen. Die unterschiedlichen Beziehungen zwischen Malaria und den soziodemografischen Faktoren, die die Krankheit beeinflussen können schliessen Merkmale der Teilnehmer ein. Diese Forschung stellt Faktoren dar, die verwaltet werden können und die Beseitigung der Malaria begünstigen würden. Dazu gehören eine Reihe von Präventionsverhalten auf individueller Ebene und die Nutzung der Netzwerke von primären Gesundheitszentren auf Gemeindeebene. Diese Studie legt nahe, dass die Verbesserung der Verfügbarkeit einer Vielzahl von Gesundheitseinrichtungen in endemischen Gebieten, insbesondere Informationen zu ihren Diensten und des Zugangs zu diesen wesentlich ist.

Schlüsselwörter: Geographisch gewichtete Regression (GWR), Methode der kleinsten Quadrate (OLS), Akaike Information Criterion (AIC), physikalische Umwelt, lokalKlima, Sumatra, Regenfälle, Elevation, Entfernung zum Wasser, Ländliches Gebiet, Vieh, Zooprophylaxe, Zoopotenzierung, Multivariate-logistische Regressionsanalyse, Malaria-prävalenz, Soziale Gesundheitsdeterminanten, Sozialepidemiologie und Gesundheitsdienste der Gemeinschaft.

Summary

Malaria is an environmental disease, influenced not only by physical and biological environmental factors but also by socio-cultural ones. These factors affect each other, and, in turn, cause the disease in endemic areas. Some factors that cause the high morbidity rate associated with the disease include climate change, physical environment that varies geographically, socio-economic circumstances, and human behaviour in the affected areas. Other risk factors include housing conditions and poor sanitation, lack of hygiene practices, and inadequate health services in endemic areas. Efforts to eliminate malaria have been a topic at various public health meetings for decades. However, in Indonesia, malaria continues to be one of the leading causes of morbidity and mortality. The research aimed to analyse and model the critical variables associated with malaria in endemic areas of Indonesia. So, this included relationships between malaria and both socio-demographic variables and physical environments. The research is in **three parts**, adding value to a model that determines malaria in Indonesia.

This dissertation follows a cross-sectional design survey. The research data in this PhD dissertation is drawn from four sources: routine reporting of malaria from provincial health departments in South Sumatra; the national basic health research data (IDN acronym: Riskesdas); climate data from the Meteorology, Climatology, and Geophysics Climatological Agency (IDN acronym: BMKG); spatial data from Geospatial Information Agency (IDN acronym: BIG). This study takes a holistic approach, integrating the following univariate, bivariate, and multivariable logistic regressions, to establish a modelling determinant of malaria. Additionally, the researchers compared the performance of both Geographically Weighted Regression (GWR) and Ordinary Least Square (OLS). It also used some statistical analysis software tools for data processing, analysis, visualisation, and the development of the model as follows: Statistical Package for the Social Sciences (SPSS), Stata, Aeronautical Reconnaissance Coverage Geographic Information System (ArcGIS) 10.3, and GWR 4.0 version 4.0.90 for Windows.

The prevalence of malaria varied according to the local area, which, in turn, was related to the local physical environment that varied geographically. The determinants for malaria cases varied locally and regionally as well. Rural areas with a high percentage of households keeping livestock/pets showed a higher proportion of malaria prevalence than the national average. Other socio-demographic risk factors included gender, age, occupation, knowledge about healthcare, protection against mosquito bites, and condition of dwellings. This study reveals that the independent variables - "rainfall", "altitude", and "distance from mosquito resting sites in the forest," in global OLS analysis- are significantly associated with malaria cases in South Sumatra, Indonesia.

On the other hand, in the GWR analysis, the determinants of malaria cases at the village level vary geographically. Therefore, it is essential for the decision maker, the government, to acquire a more in-depth understanding of region-specific, ecological factors that influence confirmed malaria cases. The findings lead to the recommendation for developing sustainable regional malaria control programs and incentivising malaria elimination efforts, particularly at the village level. In another setting, the research led to the conclusion that the presence of mid-sized livestock comprised a significant risk factor for contracting malaria in rural Indonesia. The recommendation, especially for the study area, is to employ integrated vector management (IVM), for example, the simultaneous implementation of insecticide-treated bed nets (ITNs) and insecticide-treated livestock (ITL). Other factors such as socio-demographic and use of health care facilities were also crucial as they related to malaria prevalence. Further, the research leads to the recommendation for increased education and increased promotion and utilisation of the health care framework to promote knowledge and awareness of villagers on how to protect themselves from Anopheles bites. Finally, improving information concerning the availability of health care services and access to various health facilities in endemic areas is essential.

Keywords: Geographically weighted regression (GWR), ordinary least squares (OLS), Akaike information criterion (AIC), physical environment, local climate, Sumatra, rainfall, elevation, distance to water, rural area, livestock, zooprophylaxis, zoopotentation, multivariable analysis, malaria prevalence, social health determinants, social epidemiology, and community health services.

List of abbreviations

An.	:	Anopheles
ANC	:	Antenatal care
ANOVA	:	Analysis of variance
AOR	:	Adjusted odds ratio
API	:	Annual parasite incidence (number of slides positive for parasite × 1000/total population)
ArcGIS	:	Aeronautical Reconnaissance Coverage Geographic Information System
Balitbangkes	:	Badan Penelitian dan Pengembangan Kesehatan (National Institute for Health Research and Development)
BIG	:	The Geospatial Information Agency (IDN acronym: BIG)
BMKG	:	Meteorology, Climatology, and Geophysics Climatological Agency
BPS	:	Central Agency on Statistics (IDN acronym: BPS)
CI	:	Confidence interval
CV	:	Cross validation
DEM	:	Digital elevation model
DOF	:	Degrees of Freedom
GRDP	:	Gross regional domestic product
GWR	:	Geographically weighted regression
HDI	:	Health Development Index
IDN	:	Indonesia
IRS	:	Indoor residual spraying reduction
ITL	:	Insecticide-treated livestock
ITNs	:	Insecticide-treated bed nets
IVM	:	Integrated Vector management
LLINs	:	Long-lasting insecticidal net
MDGs	:	Millennium development goals
MoH	:	Ministry of Health
MP	:	Malaria prevalence
NAD	:	Nanggroe Aceh Darussalam
NIHRD	:	The national institute for health research and development

NMCP	:	National malaria control programme
NMTDP	:	National Medium-Term Development Plan (IDN acronym:RPJMN)
NTB	:	West Nusa Tenggara
NTT	:	East Nusa Tenggara
OLS	:	Least squares regression
OR	:	Odds ratio / unadjusted odds ratio
P	:	*Plasmodium*
PHCs	:	Primary health centres
Polindes	:	Pos bersalin desa (village maternity clinic)
Poskesdes	:	Pos kesehatan desa (village health post)
Posyandu	:	Pos pelayanan terpadu (integrated health post)
Puskesmas	:	Pusat kesehatan masyarakat (primary health care centre)
Pv	:	P-values
RDTs	:	Rapid diagnostic tests
Riskesdas	:	Riset kesehatan dasar (Basic Health Research)
Ristekdikti	:	Ministry of Research, Technology and Higher Education (IDN acronym:Ristekdikti)
SPSS	:	Statistical Package for the Social Sciences
Susenas	:	the National Socioeconomic Survey (Indonesia acronym: Susenas)
Svy	:	Survey
UNICEF	:	United nations children's fund
VBDs	:	Vector-borne diseases
VIF	:	Variance inflation factor
WGS84	:	the World Geodetic System 1984
WHO	:	World Health Organization

Comprehensive Summary

1.1 An introduction with reference to the overall research question

Malaria, as a vector-borne disease is still a public health problem in the world, including in Indonesia.[1]. More than 80% of the deaths related to the *Plasmodium vivax* pathogen are in Ethiopia, India, Indonesia, and Pakistan. Although *Plasmodium vivax* infection is generally related to severe disease and death, the specific risks are uncertain[2]. Malaria is endemic in nine of the 11 countries of South-East Asia Region, accounting for approximately 70% of the burden outside the WHO African Region[3]. Almost 63% of the cases are due to *P. falciparum*. Indonesia accounted for 16% of the reported cases, and 30% of malaria deaths in 2016. Instead, 85% of estimated vivax malaria cases occurred in just five countries, including in Indonesia [3]. There are more than 3.3 million people at potential risk of malaria, who live in regions of high malaria transmission when the world changes the paradigm of the Millennium Development Goals (MDGs) to the Sustainable Development Goals (SDGs), it is crucial that the fight against malaria keep on [4]. Malaria elimination policy included in the MDGs target in 2015, and also contained in the Decree of the Minister of Health of the Republic of Indonesia, as well as in the national medium-term development plan (NMTDP) 2010-2014 with the target of reaching the annual parasite incidence (API) of 2015 is 1 ‰. National Strategic of Ministry of Health 2015 – 2019: number of districts with API < 1 per 1,000 (under MoH monitoring). The emphasis on health development is done through preventive and curative approaches by improving public health to reduce malaria morbidity[5]. Currently, as in medium-term development plan of 2015-2019 has a target enhanced control of communicable and non-communicable diseases. Numbers of districts/cities that are succeeded in eliminating malaria from initial status is 212 of districts/cities in 2013 to achieve target 300 of districts/cities in 2019 [6]. The Indonesian government has set a national goal for Indonesia to be malaria-free by 2030 [1,7,8]. However, malaria is still one of the leading causes of morbidity and mortality in Indonesia [9]. The National Malaria Eradication Program of 1959-1968; which we called of KOPEM (Komando Operasi Pembasmian Malaria, the Malaria Eradication Operation Command) was set up in 1962 by the first Presiden Indonesia, who initiated malaria control efforts, and Indonesia has set the year 2030 as a deadline for the elimination of malaria in the archipelago [10,11]. However, malaria remains a public health problem in Indonesia despite various attempts being made for its elimination, including its discovery and management, infection prevention, surveillance performance, availability of logistics and follow-up plans. There, 15 provinces with malaria prevalence higher than the national average. Each region has different geographical conditions, causing differences between the areas of malaria cases. The national prevalence of malaria (based on the diagnosis of health professional and respondent complaints) was 2.85% in 2007 and malaria prevalence in 2013 was 6.0 % [12,13]. Besides, malaria is a serious disease and a threat to life in South Sumatra Province, Indonesia. Some studies show the complexity of causes for malaria prevalence [14, 15, 16, 17]. Its target coincides with the level of malaria endemicity and the strength of the health infrastructure [18]. The country shows nationwide a continuously decreasing incidence of malaria, but at the district level, the situation is more complex[16]. For example, the regional deadline for malaria elimination for the island of Java was the end of 2015[7]. Some areas have shown efforts to eliminate malaria [7],[19]. Furthermore, the Purworejo Region, a malaria-endemic zone in Java with an API of 0.05 per 1,000 resident in 2009, wants to introduce this elimination phase[7]. To achieving malaria elimination, good evidence is needed concerning the relationship between malaria and environmental risk factors.

1.2 A presentation of the manuscripts respectively the publications

This present study explores some risk factors that influence malaria in Indonesia. Furthermore, this dissertation **divided into three studies** to get comprehensive information regarding determinants malaria in an endemic area in Indonesia, which evidence-based. An increased understanding of the dynamics of transmission of *falciparum* and *vivax* malaria could suggest improvements for malaria control efforts [20]. As an example, China has experienced noticeable changes in climate over the past 100 years, and modelling shows that the potential impact of climate change on the transmission of mosquito-borne infectious diseases poses a risk to Chinese populations[21]. Henceforth, malaria transmission is also affected by changes in meteorological conditions which influence the biology of the parasite and its vector [22]. There are a large number of factors that affect potential susceptibility to malaria that involves social, demographic and geographic dimensions[23]. The principal factors associated with malaria prevalence include environmental, socio-demographic and behavioural ones[24]. Infection with malaria parasites is directly dependent on mosquitoes and human characteristics. Environmental variables such as "altitude", and "land cover" are predicted to affect malaria[25]. Besides, the "rainfall", and "temperature" can predict the risk of malaria transmission and modify the breeding site of Anopheles. The regions with having a significant "precipitation" and higher "temperatures" are expected to possess a higher prevalence of malaria because this condition supports the breeding of many Anopheline species and reproduction of parasites in mosquitoes[26]. The analysis of the spatial malaria epidemiology can describe a geographical distribution of the prevalence of the disease. To analyse the elements of geographical influence (a risk factor for spatial epidemiology of malaria), so, a modelling approach can be used to uncover the relationship with malaria prevalence [27,28]. At its simplest, maps can identify the location of cases of malaria. There are issues to be overcome with the production of charts and analysis of data [29]. First, modelling can be used to map disease distribution and attempt to uncover underlying patterns. Second, is to analyse the spatial relationships between the variables: disease and critical factors). It is usually done at a regional level by aggregating local level data. Finally, general clustering is done to identify areas of unusual incidence [29]. Also, the presence of livestock in a rural area, and socio-demographic factors (gender, age, education, and job), the behaviour of participants (using insecticide-treated mosquito nets) influence malaria prevalence [30]. In Indonesia, the presence of livestock in households is common with 39.4% of households raise poultry, 11.6% raise medium-sized, 9.0% raise large-sized animals and 12.5% raise animals such as dogs, cats, or rabbits. Of the families who raise livestock, around 10-20% raise them in house[12]. Since malaria had been early acknowledged as being transmitted by zoophilic vectors, zooprophylaxis is used to prevent disease, but also zoopotentation has been observed. While the existence of livestock as a variable of interest for malaria risk has been widely accepted, the other outcomes of small-to-medium-sized studies are still highly debated. For example, Franco *et al.* (2014) stated that there was controversy over research on the presence of livestock, although based this was based on studies investigating. The presence of animals as a protection against malaria in countries such as New Guinea, Papua and Sri Lanka.

On the contrary, cattle have been proven to be a risk factor for malaria in several countries, such as Pakistan, Philippines and Ethiopia [31]. Habtewold *et al.* (2001) analysed the habits of *An. arabiensis and An. quadriannulatus* are known as a low proportion of human blood meal occurrence [32]. In this study, based on the Riskesdas questionnaire, the animal domestic categorised are livestock, pets, and poultry. The term livestock includes here large-sized animals (cattle, horses, buffaloes), medium-sized animals (goats, sheep, pigs). Additionally, poultry, such as chicken and ducks, and pets, such as dogs, cats and rabbits, are included in the term of *pets* [12]. The proportion of households who raise livestock indoors is lower in urban areas than in the countryside [12]. The present study investigates if the prevalence of malaria is higher amongst participants who raise cattle in rural malaria endemic areas. Indeed, malaria is a global health challenge and is an increasing concern, especially in the endemic provinces in Indonesia. Further explanatory variables are the accessibility to and utilisation of health services, environmental sanitation as well as the quality of drinking water, primary water source, distance to drinking water, wastewater disposal associated with malaria prevalence. However, the extent to which the explanatory variables influence malaria prevalence remains poorly understood. A range of environmental risks, socio-demographic, behaviour, and structural factors have been implicated affect malaria prevalence. This study used data from the large-scale survey Riskesdas to explore the accessibility and utilised of healthcare facilities such as a public hospital or government hospitals; private hospitals; primary health care (PHC) and investigated their connection with malaria prevalence. In addition, healthcare facilities others are clinics or doctor practices, midwife practices or maternity hospital; and integrated health posts (Posyandu). The participants were also asked for utilised and access healthcare of rural health posts (Poskesdes) and rural clinics (Polindes). Next to these potential explanatory variables for malaria prevalence, environmental sanitation like and preventative behaviour against mosquito bites by using mosquito repellent, or insecticide sprays, anti-malaria drugs, and housing conditions were investigated.

The present study aimed to analyses multiple potential determinants of malaria in Indonesia. Data collection described the local physical environment, presence of livestock in a rural area and socioeconomic data not only from regular health reporting in the endemic area but also from large-scale surveys in Indonesia 2007 and 2013, respectively. The data were integrated and analysed utilising an epidemiological modelling approach.

The specific objective of this research was divided into three studies. Firstly, the particular goal of this dissertation is to examine the relationship between confirmed malaria cases and local environmental risk factors in high malaria endemic areas with spatial analysis. (**Study #1**). Secondly, the objective of this paper is to determine the effect of the presence of livestock on malaria prevalence in malaria-endemic rural areas in Indonesia, in a large endemic setting. (**Study #2**). Thirdly, the last part explored the relationship between the prevalence of malaria and social and demographic factors (**Study #3**). The research data in this dissertation was drawn from four primary sources: routine reporting malaria from health provinces in South Sumatra; the national basic health Research data (Indonesia

(IDN) acronym: Riskesdas); climate data from Meteorology, Climatology, and Geophysics Climatological Agency (IDN acronym: BMKG); and spatial data from Geospatial Information Agency (IDN acronym: BIG) [30,33,34]. In general, these sources provided data for the years 2007 and 2013 [12,13]. The research generated descriptive data for all variables, and the data were analysed using bivariate, and multivariable logistic regression analyses to predict malaria prevalence at a significance level of P value < 0.05. For s**tudy #1**, The malaria cases were distributed over 436 out of 1,613 villages. This study performs both Ordinary least square (OLS) and geographically weighted regression (GWR) analyses to demonstrate connection confirmed malaria cases and potential ecological predictors [33]. The research explored the global pattern and spatial variability relationships among of six potential environmental predictors: were the altitude, aspect, distance from the river, distance from lakes and pond, distance from the forest, and rainfall and confirmed malaria cases in the study area [33]. Local variations in environmental variables potentially predicted confirmed cases of malaria. Therefore, the local spatial epidemiology and the distribution of risks of malaria cases were investigated and associated environmental risks identified using spatial discrimination. This study analysed environmental risk factors for malaria that performs at the global OLS and local GWR modelling at the regional level in South Sumatra.

Further, **study #2** using Riskesdas 2007, the subset included 259,885 study participants who resided in the rural area at 176 regencies of 15 provinces with malaria prevalence higher than the national average. The research used multivariable logistic regressions to investigate the role of several variables in the prevalence or status of malaria. These included "the existence of livestock" and other independent demographic, social and behavioural variables [30]. The participants had been diagnosed positive for malaria by a health professional (i.e., with malaria during the past month). Generally, rapid diagnostic tests (RDTs) and microscopy by health services confirmed the diagnosis. Independent questionnaire data at the individual and household level added further information. This included characteristics of participants (gender, age, education, principal occupation), mosquito bite avoidance behaviour (e.g., sleeping under a mosquito net, using net insecticide, defecating habits), and access to and use of health services (health services access by travelling), environmental sanitation (type of container/media, sewage canal, sewage canal conditions), and, for medium and large livestock, the location of cages. The binary categories of the independent variables were "yes" and "no" and led to an analysis of a potential relationship with the response variable malaria.

Furthermore, s**tudy #3** used Riskesdas 2013 data[13]. The current study **(# 3**) included 130,585 participants (the population of five provinces in 83 districts endemic to malaria). The third study investigated the relationship between socio-demographic determinants and malaria prevalence using multivariable logistic regression analysis [34].

1.3 Discussion of the results obtained and their relevance with regards to the research question.

Detecting the spatiotemporal distribution and mapping of high-risk areas are useful to strengthen malaria control efforts and ultimately achieve elimination[35].Therefore, understanding the spatial epidemiology of malaria is essential for developing strategies for disease control and elimination[36]. This study provides an exciting opportunity to advance our knowledge of the role of physical environment locally, the presence of livestock in the rural area, and sociodemographic influences on malaria prevalence. Based on the research questions, this study shows that in **study #1** reveals that the most significant correlations with malaria were with the independent variable altitude, distance from forest, and rainfall (global OLS) [33]. However, as noted by the GWR model and in line with recent reviews, the relation between malaria and environmental influences in South Sumatra was found to vary spatially greatly between different regions. The global OLS model reveals that rainfall had a significant positive coefficient, whereas altitude and distance to the forest had substantial negative coefficients. These indicated a meaningful relationship with confirmed malaria cases. Regions with high rainfall, lowland, and areas adjacent to the forest had high malaria cases globally. Whereas there was no meaningful relationship between malaria, and. Environmental factors such as aspect or direction towards the slope, distance from the river, and the distance from lakes and pond globally. On the other hand, in the GWR analysis indicate the determinants of malaria cases at the village level vary geographically. For example, the variable "altitude" and "distance from lakes and ponds" shows a positive correlation and "aspect" presents a negative association with confirmed malaria cases in the North study area (Musi Banyuasin) locally. Also, "Rainfall" and "distance from the river" parameter denotes a positive connection with malaria cases in the eastern part of Musi Rawas and Lahat. Besides, variable "aspects", "distance from lakes and ponds" and "distance from forests" were positively associated with confirmed malaria cases which reported in most study areas. In line with previous studies, climatic factors that influence the prevalence of malaria include precipitation (rainfall), temperature and humidity[37]. Variations and changes in local weather and meteorological conditions are well known to affect malaria transmission. The effect of climate on the *Anopheles* populations is well established [38]. Rainfall, temperature and humidity are associated with malaria transmission and are important determinants of the dynamics, and the spread of the malaria vector population [38, 39, 40,41, 42.] Altitude significantly influences the type of malaria vectors [25,43]. Moreover, the density of the vector and the frequency of bites on humans [25]. Also, both altitude and direction toward the slopes contribute to the transmission of malaria in the highlands [44]. However, some studies have shown that the drivers of malaria seasonality are not always clear [14]. The understanding concerning the complexity of malaria transmission from climate aspects is still found a significant gap. So, it needs there have been motivated efforts to develop more comprehensive models [15]. At best case, climate variability can provide information for an early warning system for epidemic malaria, and this has been investigated in previous studies [45]. It is crucial that we have a better knowledge of the spatial and temporal patterns of determinants of malaria risk for the prevention and control of the malaria program [46]. Furthermore, GIS presentation of environmental health data could provide an efficient means of translating this knowledge to lay audiences[9]. Further, in **study #2** was in rural malaria endemic areas of 15 highly malaria-endemic provinces in Indonesia and indicated that certain livestock facilitated malaria prevalence and was not suitable as a prophylactic tool. The research found that the participants who raised medium livestock (1.16%, OR = 1.80) had a significantly increased risk of malaria ($P < 0.001$). After adjusting for gender, age, education, job, use of insecticide-treated mosquito nets, and keeping of pets, participants who raised goats, sheep and pigs had an increased likelihood of having malaria (adjusted for other variables; AOR = 2.809; 95% CI 2.207–3.575; $P < 0.001$) [30]. These proceeds lead to the conclusion that the existence of medium-sized livestock (e.g., goats, sheep, and pigs), is a significant risk factor for malaria in the study area. Other principal factors affecting the prevalence of malaria are demographic factors: for gender, age, education, job, use of insecticide-treated mosquito nets, and keeping of pets. The existence of livestock as an essential variable for malaria risk has already been assessed in small to medium scale surveys in both developed and developing countries and has been controversially discussed. One notable finding is the planned control of using livestock to divert the vector bites, called "zooprophylaxis", or as a switch to draw vectors to insecticide sources, called "insecticide-treated livestock (ITL)." These strategies have been used since malaria was acknowledged to be transmitted by zoophilic vectors [31]. Zooprophylaxis is defined by WHO as “The value of wild or domestic animals, which are not the source hosts of a given condition, to alter the blood-seeking mosquito vectors from the human hosts of that disease"[47]. Active zooprophylaxis consists of strategically placing animals between mosquito breeding sites *and* people's houses. Meanwhile, passive zooprophylaxis is the protective effect of the constant presence of animals within a community [48]. Researcher, Escalar G (1933), Saul A (2003) Kawaguchi (2004), Killeen (2007), et al. in the study stated that since the early 1900s, zooprophylaxis has been recognised as an essential tool to decrease malaria transmission to people in some locations of the world and this approach has been evaluated for another vector-borne disease [48]. Livestock has been considered the most appropriate host for this strategy. The term used to refer to livestock includes cattle and small and large ruminants and other domestic animals, such as buffalo, sheep, goats, donkeys, horses, and pigs [31]. Studies have revealed that ownership of livestock investigated at the household level has a substantial impact on the behaviour of the malaria vector. However, there is no clear risk of malaria exposure to livestock presence [49]. The profusion of *An. gambiae* and *An. arabiensis* in housing is related to the spread of domestic animals and humans[50]. Additionally, livestock is thought to be mostly accountable for generating high mosquito densities. With further analyses, the researchers Bouma and Rowland revealed a strong, positive correlation between the cattle-to-man ratio and malaria incidence [51]. Furthermore, in **study #3** revealed, using multivariable analysis, that independent socio-demographic risk variables were related to malaria prevalence. These were: gender, age, occupation, knowledge about healthcare services, preventative measures against mosquito bites, and housing conditions. Participants who did not know about the available health facilities were 4.2 times more likely to have malaria than those who did know adjusted odds ratio (AOR) = 4.18; 95% CI 1.52 - 11.45; P = 0.005, adjusted by other covariates [34]. Healthcare facilities included in the data were government hospitals, private hospitals, primary healthcare (puskesmas), clinics, midwife practices, integrated health posts (posyandu), village health posts (poskesdes), and village maternity clinics (polindes). The study concluded that health services, as well as their networks, are essential for malaria elimination. To guide the development of effective strategies for malaria elimination needs an understanding of the connections between malaria and other factors. In Indonesia, little is known about the determinants of malaria prevalence among sociodemographic factors. The potency of the PHC system in achieving those most at risk and reducing the disease burden and that inadequate approach is a significant risk factor particularly for the poor households [52]. Currently, a major component of malaria control strategies to reduce malaria-related mortality and severe morbidity is early diagnosis and prompt treatment at peripheral health services such as village health posts and dispensaries[53]. The study demonstrates that the incidence of hospitalised malaria more than doubled as travel time to the nearest primary care resource built from ten minutes up to two hours. Good access to PHC facilities may reduce the burden of disease by 66%[54]. Recently illustrated from a Tanzanian demographic surveillance site (DSS) section suggests that the most impoverished infants and kids under five years old had higher risks of death than those in the least-poor socio-economic quintiles [23]. Primary education on the prevention of malaria should be built up by the National Malaria Control Programme (NMCP) in all the countries to reduce malaria prevalence, particularly among under-five children[55]. Also, ITN use and the age of the child were found to be significantly related to fever incidence[23]. To focus on the shortcomings in local education about malaria, health personnel worker serving in malaria-endemic regions should be skilled in providing more proper counselling for changing certain deeply ingrained traditional behaviours such as settling time outdoors in the evening, inappropriate use of bed nets and occasional use of insecticides during sleep [56]. This research concludes as follows: **firstly,** regarding the analysis using GWR that the importance of different environmental and geographic parameters for malaria disease was shown at global and village levels in South Sumatra, Indonesia. It has been conclusively shown that the independent variables altitude, distance from forest, and rainfall in global OLS were significantly associated with malaria cases. However, as shown by the GWR model and in line with recent reviews, the relationship between malaria and environmental factors in South Sumatra strongly varied spatially in different regions (**Study #1**). **Secondly,** it has been noted that the presence of only certain livestock is the major risk factor for contracting malaria in rural Indonesia. Raising medium-sized animals in the house was a significant predictor of malaria prevalence (OR = 2.980; 95% CI 2.348–3.782, $P < 0.001$) when compared to keeping such animals outside of the house (OR = 1.713; 95% CI 1.515–1.937, $P < 0.001$). After adjusting for gender, age, access to the community health facility, sewage canal condition, use of mosquito nets and insecticide-treated bed nets, the participants who raised medium-sized animals inside their homes were 2.8 times more likely to contract malaria than respondents who did not. (**Study #2**). **Thirdly,** this study indicates that there is a relationship between socio-demographic factors and their influence on malaria prevalence. This study reported that the different relationships between malaria and those variables, the socio-demographic factors can affect malaria included characteristics of participants. The analysis of baseline socio-demographic data revealed the following independent risk variables related to malaria prevalence: gender, age, occupation, knowledge of the availability of healthcare services, measures taken to protect from mosquito bites, and housing condition of study participants. Multivariable analysis showed that participants who were unaware of the availability of health facilities were 4.2 times more likely to have malaria than those who were aware of the health facilities. Factors that can be managed and would favour malaria elimination include a range of prevention behaviours at the individual level and using the networks at the community level of primary healthcare centres (**Study #3**). In addition, this research recommends a multi-disciplinary approach to be able to understand transmission. The four components, i.e. human, vector, parasite, and environment, all play an essential role in the system. Therefore, the vector component of the system, the parasite component of the system, those that address environmental and the last two each address the human element. The findings reported here suggest that attention needs to be given to vulnerable populations. Also, improving the accessibility and utilisation of health services to protect the community from malaria effectively. Improving proper environmental sanitation, promoting prevent techniques from mosquito bites, and improving housing conditions. Ensuring appropriate systems, services, and support for reducing malaria prevalence should be a priority for vulnerable groups. Besides, this study recommends having interventions for all components systems that are being scaled up in malaria-endemic areas. The strategies are not enough to focus on in the parasite side, that is treatment, and they address the vector component. So, one of the reasons is that those interventions have prominent implementation protocols that have been designed. The findings of this study have some significant implications for future practice. Taken together, these findings support strong recommendations to campaign for the reduction and elimination of malaria in an endemic area. Finally, providing resources to implement recommendations is essential.

Overview of the manuscripts and publications accepted for release

Malaria is a public health hassle inside the international included in Indonesia. The causes of malaria prevalence are quite complex. Understanding the link among the environmental risk factors, the presence of livestock, and socio-demographic factors will help the decision maker to create a strategy for elimination and eradication of the disease in Indonesia and beyond. Factors which potentially influence malaria prevalence, and which were investigated in the present studies included not only the presence of livestock in a rural area that may affect vector abundance, density, or activity but also physical environmental factors, socio-demographic and behavioural factors. The research also described the direct cause of malaria: plasmodium parasites and vector specificity in Indonesia. The research described spatial epidemiology, climate and the physical environment, livestock issues, and socio-demographics as one determinant of malaria. The general purpose of this doctoral dissertation was to analyse the determinants of malaria in malaria-endemic areas of Indonesia. Relevant analytical methods included univariate, bivariate, and multivariable logistic regression analysis (including Geographically Weighted Regression (GWR)) to explore the relationships between malaria incidence and other epidemiological, local weather, geographic, and socio-demographic data. The overview of the publications accepted for release is below.

Publication #1 summarises the main findings of this PhD dissertation that malaria prevalence was related to different local environments, which varied geographically. This chapter analysed temporal and spatial variations of malaria prevalence and described territories and periods with a higher risk of malaria on a local geographic scale within the endemic malaria country, Indonesia. The research identified local environmental risk factors by comparing GWR and OLS analysis to understand the influence of the local environment on malaria cases. This study hypothesised that the global OLS and local GWR modelling could be performed to analyse the environmental risk factors for malaria case in South Sumatra province, Indonesia, that varied geographically at the regional level. This result of this research expected that would be useful for malaria elimination in a defined geographic area. **Publications #2 - #3**, showed that the presence of livestock and socio-demographic determinants affect malaria prevalence based on the analysis of secondary data from Indonesian regular reporting on malaria and large-scale survey Riskesdas. **Publication #2** used data from the large-scale survey Riskesdas 2007 and hypothesised that there was a relationship between malaria and livestock presence in rural endemic areas in Indonesia. This part of this paper showed that the presence of livestock was associated with malaria prevalence in eastern Indonesia. Similarly, another study revealed associations between malaria risk and environmental, socio-demographic, and behavioural variables in western Kenya of East Africa [24]. **Publication #2** assessed the significance of the presence of livestock for malaria prevalence in rural areas that had a higher proportion of malaria disease than the national average in Indonesia. **Publication # 3** hypothesised that malaria prevalence (dependent variable) in endemic areas in Indonesia was influenced by the socio-demographic characteristics of the population (independent variable). The research explored socio-demographic variables related to malaria prevalence, characteristics of participants, including gender, age, education, and employment and behaviour (e.g., use of bednets). The large-scale cross-sectional survey of the national basic health research (Riskesdas 2013) provided the socio-demographic data for this study. The design of the overall Riskesdas investigation was mainly to describe the health problems of all the people of Indonesia. It focused on many Indonesian health problems, including malaria and its potential drivers and data specific for this dissertation were derived from this. **Publication #3** analysed the socio-demographic factors noted above and behavioural factors, including accessibility and utilisation of health services and environmental health factors related to malaria prevalence. The socio-demography epidemiological models resulting from the present study are expected to produce comprehensive information both for spatial and non-spatial issues and to provide information for decision-makers to develop effective strategies to reduce and eradicate malaria in Indonesia. The doctoral dissertation may also strengthen national capacities for epidemic preparedness and response in support to the national implementation of the malaria prevention and elimination program in malaria-endemic areas. The success of roadmaps of national malaria elimination programs depends on using a sophisticated One Health approach and local interventions, namely interconnecting biological, social, physical, ecological, vector, local environment topography and weather, and technological processes. The government, academic institutions and some related agencies and the multidisciplinary professional team should support these efforts. At the same time, community awareness must be established to support the country's malaria elimination goals through knowledge sharing, capacity building, operational research, and advocacy.