INCIDENCE AND SPATIAL DISTRIBUTION OF LYMPHATIC FILARIASIS IN SARAWAK, 2018-2022

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INCIDENCE AND SPATIAL DISTRIBUTION OF LYMPHATIC FILARIASIS IN SARAWAK, 2018-2022

by

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LIST OF ABBREVIATIONS

GIS	Geographical Information System
GPELF	Global Program to Eliminate Lymphatic Filariasis
IU	Implementation unit
KDE	Kernel Density Estimation
LF	Lymphatic Filariasis
LFEP	Lymphatic Filariasis Elimination Program
MDA	Mass Drug Administration
MF	Microfilaremia
MOH	Ministry of Health
NNI	Nearest Neighboring Index
TAS	Transmission assessment survey
WHO	World Health Organization

LIST OF SYMBOLS

n	numbers of sample
Zα	level significance 95% CI.
P	expected proportion of incidence
Δ	detectable different (precision)

INSIDEN DAN TABURAN RUANG LIMFATIK FILARIASIS DI SARAWAK 2018-2022

ABSTRAK

***Latar belakang**:* Filariasis limfatik adalah penyakit tropika terabai disebabkan cacing *Wuchereria bancrofti, Brugia malayi*, atau *Brugia timori*. Ia menyebabkan komplikasi teruk yang memberi kesan besar pada kesihatan. Analisis gugusan spatial membantu mengenalpasti kawasan titik panas di Sarawak, membolehkan aktiviti kawalan dan pencegahan dijalankan dengan lebih baik.

Objektif: Kajian ini bertujuan untuk menyiasat insiden dan taburan pemetaan kes filariasis limfatik dalam kawasan negeri Sarawak dari tahun 2018 sehingga 2022, mengenalpasti taburan gugusan ruang dan titik panas serta hubung kait kawasan yang mempunyai kes antara satu sama lain.

Metodologi: Kajian menggunakan data sekunder diperolehi daripada system e-vekpro Jabatan Kesihatan Negeri Sarawak untuk kes filariasis yang didaftarkan dari tempoh 2018 sehingga 2022. Data populasi di Sarawak diperoleh dari Jabatan Perangkaan Malaysia. Koordinat setiap kes ditukarkan kepada format sistem Kertau RSO Malaya (EPSG:3168). Kadar insiden kes filariasis dikira pada peringkat daerah dan analisis *point pattern* dijalankan menggunakan kaedah *kernel density estimator* (KDE) dan *nearest neighbouring index's* (NNI). Kajian juga untuk mengenalpasti lokasi titik panas menggunakan **gtsummary**, **tmap**, **spded**, **spatialeco** dan **spastat** dalam perisian R Versi 4.2.3.

Keputusan: Hasil kajian menunjukkan kadar insiden menaik dan menurun dengan kadar tertinggi adalah pada tahun 2018 sebanyak 4.7 kes bagi 100 000 penduduk, sementara 0.4 kes bagi 100 000 penduduk, 2.3 bagi 100 000 penduduk, 0.9 bagi 100 000 penduduk dan 2.7 kes untuk 100 000 penduduk masing-masing bagi tahun 2019, 2020, 2021 dan 2022. *Kernel density estimator (KDE)* menunjukkan kawasan berpotensi sebagai kawasan titik panas terutama di bahagian utara Sarawak di daerah Limbang. Analisis *Nearest neighbouring index (NNI)* menunjukkan terdapat *clustering* kes filariasis, walau bagaimanapun analisis menggunakan Global Moran's I tidak menunjukkan kes filariasis yang didaftarkan dalam system Vekpro ada kaitan spatial di antara daerah berdekatan.

Kesimpulan: Pelaksanaan pemberian ubat besar-besaran telah mengurangkan jangkitan filariasis di Sarawak. Walau bagaimanapun, risiko untuk jangkitan penyakit filariasis masih tinggi terutama melibatkan kawasan di bahagian utara. Penggunaan kajian menentukan gugusan ruang dan penemuan kluster dapat membantu membuat perancangan lebih tepat dalam menilai dan mengesan risiko gugusan ruang yang berbeza dalam komuniti. Ini dapat membantu mengenalpasti kawasan tinggi jangkitan, pencegahan penularan dan seterusnya mengelakkan penyakit kembali dalam skala yang lebih besar.

Kata Kunci: filariasis; Sarawak; spatial analysis; mass drug administration; incidence; hotspot

INCIDENCE AND SPATIAL DISTRIBUTION OF LYMPHATIC FILARIASIS IN SARAWAK 2018-2022

ABSTRACT

Introduction*:* Lymphatic filariasis is a neglected tropical disease caused by *Wuchereria bancrofti*, *Brugia malayi*, or *Brugia timori.* It leads to severe morbidity and have a significant impact on health. Spatial analysis helps identify hotspot areas in Sarawak, enabling better targeting and focusing of prevention and control activities.

Objective*:* To investigate the incidence and geographic dispersion of lymphatic filariasis in the region of Sarawak during the period ranging from 2018 to 2022, identify spatial distribution and hotspot area with present of any autocorrelation between cases.

Methodology*:* This study utilized secondary data from Vekpro online system, Sarawak State Health Department for all cases registered from period of 2018 till 2022. The data pertaining to the population of Sarawak were acquired from the Department of Statistics Malaysia. The coordinates were transformed into the format of Kertau Rectified Skewed Orthomorphic (RSO) Malaya (EPSG:3168). The incidence of filariasis was calculated at the district level, and point pattern analysis was conducted using Kernel Density Estimates and Nearest Neighboring Index (NNI). The study additionally examines the existence of hot spots in order to differentiate spatial risk at the district level.

Analyses were done using the **gtsummary**, **tmap**, **spdep**, **spatialeco**, and **spastat** packages in R Software Version 4.2.3.

***Result*:** There were varying incidence rates, with the highest in 2018 at 4.7 cases per 100,000 population followed by fluctuation trend, which 0.4 cases per 100,000, 2.3 cases per 100,000, 0.9 cases per 100,000 and 2.7 cases per 100,000 population in 2019, 2020, 2021 and 2022 respectively. The kernel density estimator (KDE) showed the potential hotspot area in the northern region of Sarawak, mainly Limbang district. The nearest neighbouring index (NNI) showed there was statistically significant clustering of filariasis cases, but using Global Moran's I analysis, it showed there was no spatial autocorrelation between adjacent districts where confirmed filariasis was registered in Vekpro online system.

***Conclusion**:* The implementation of mass drug administration (MDA) has resulted in a reduction in filariasis infections in Sarawak. However, it is important to note that the risk of filariasis remains significantly high, particularly in the northern region. The application of spatial statistics and cluster detection techniques assists health planners in accurately evaluating and detecting spatial inequalities in risk among populations. Cluster analysis aids in the identification and prioritisation of regions with persistent transmission, preventing the spread of infection and subsequent resurgence on a larger scale.

KEYWORD: filariasis; Sarawak; spatial analysis; mass drug administration; incidence; hotspot

CHAPTER 1

INTRODUCTION

1.1 Background

According to the World Health Organization (WHO), lymphatic filariasis is classified as one of the neglected tropical diseases. It is a widespread condition, affecting an estimated 120 million people globally. The disease is endemic in 73 countries, putting approximately 1.1 billion people at risk of infection. Lymphatic filariasis is recognized as the leading cause of irreversible disfigurement worldwide and ranks as the second most prevalent cause of long-term disability (Lourens and Ferrell, 2019).

Lymphoedema, elephantiasis, and scrotal enlargement are debilitating conditions that manifest in visible physical deformities and chronic pain. These conditions typically develop in later stages of life and can result in permanent disability. The observable symptoms of the ailment are a direct result of the pathological condition. Apart from the physical disabilities, these individuals also experience psychological, societal, and financial challenges that collectively lead to their marginalisation and financial difficulties (WHO, 2022). Lymphatic filariasis is caused by an infection with parasitic filarial worms, namely *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori*. The transmission of these worms to humans is facilitated by mosquitoes, particularly those of the genera Aedes, Anopheles, Culex, and Mansonia (WHO, 2013).

The World Health Organisation (WHO) classifies its constituent states into six discrete geographic regions. The Western Pacific Region is the largest geographical

area, and the prevalence of lymphatic filariasis infection within this region is considered to be epidemiologically intricate and diverse. The etiological agent, *Wuchereria bancrofti*, is accountable for a significant proportion of lymphatic filariasis cases in the Western Pacific Region. *Brugia malayi* has been reported as the prevailing species in Malaysia, Brunei, Cambodia, the Philippines, and Vietnam (Yajima and Ichimori, 2020).

In 1997, Resolution WHA50.29 was passed by the 50th World Health Assembly, which aimed to terminate lymphatic filariasis as a public health concern. The World Health Organisation (WHO) formulated a comprehensive strategy to achieve the goal of eradicating lymphatic filariasis. This plan involved interrupting transmission in regions where the disease is prevalent and implementing measures to manage and prevent disabilities associated with the condition. The World Health Organisation (WHO) established the Global Programme to Eliminate Lymphatic Filariasis (GPELF) in 2000 with the objective of eradicating lymphatic filariasis as a public health concern by 2020. The Global Programme to Eliminate Lymphatic Filariasis (GPELF) comprises of two distinct approaches: (i) the implementation of mass drug administration (MDA) in all areas where lymphatic filariasis is endemic, with the aim of interrupting its transmission, and (ii) the provision of morbidity management and disability prevention services to individuals who have been affected by the disease (WHO, 2011).

The Global Programme to Eliminate Lymphatic Filariasis (GPELF) has provided a total of over 8.2 billion treatments to a population exceeding 923 million individuals. The medications are designed to specifically target the parasites present in the bloodstream of infected individuals, thereby mitigating the risk of transmission

within the community. In certain areas, the prevalence of infections has decreased to an extent where a total of 649.1 million individuals no longer necessitate Mass Drug Administration (MDA) for the treatment of this incapacitating parasitic ailment. The global public health hazard of lymphatic filariasis, which was targeted for elimination by GPELF in 2000 with a deadline of 2020, will not be achieved. Notwithstanding the setbacks caused by the COVID-19 pandemic, the World Health Organisation (WHO) is poised to expedite its endeavours towards achieving the said objective by the year 2030. Recent global projections suggest that there has been a reduction of 74% in the number of individuals who have been infected since the establishment of the Global Programme to Eliminate Lymphatic Filariasis (GPELF). The proposed objectives for 2030 entail that 80% of countries with endemic cases would have fulfilled the criteria for validation of eradication as a public health concern, while the remaining 20% would be subject to post-treatment monitoring, thereby obviating the necessity for Mass Drug Administration (MDA) (WHO, 2022).

In 2001, Malaysia launched the Lymphatic Filariasis Elimination Programme (LFEP) in emulation of the GPELF. The study revealed that there was a total of 127 implementation units (IUs) that were endemic in nature, and distributed across eight distinct states, namely Kedah, Perak, Johor, Pahang, Terengganu, Kelantan, Sabah, and Sarawak. Between 2004 and 2008, all indigenous units (IUs) achieved successful completion of five cycles of mass drug administration (MDA), leading to a coverage of over 85% of the eligible population. As of 2018, the total number of endemic implementation units (IUs) was 105. Approximately 82.7% of these IUs had successfully completed TAS-3, while the remaining 21 endemic IUs are anticipated to complete TAS-3 by the year 2022 (MOH, 2019).

The prevalence rates of *B. malayi* microfilaria in Peninsular Malaysia, Sabah, and Sarawak were determined through pre-MDA surveys of the local populations. The rates were found to be 0.26–23.85%, 20.69%, and 0.9%, respectively. There is a lack of available data regarding morbidity associated with lymphatic filariasis in the Malaysian population.

A map depicting the distribution of lymphatic filariasis at baseline and the most recent period was generated by amalgamating government prevalence maps that were published in grey literature. At the implementation unit level, all nations were categorised as having endemicity. All countries, with the exception of Malaysia, had access to up-to-date cartographic representations (Dickson *et al.*, 2017).

However, the extent of disease prevalence in Malaysia subsequent to the Mass Drug Administration (MDA) remains unclear owing to the paucity of published literature pertaining to lymphatic filariasis within the nation. Sporadic instances of lymphatic filariasis have been detected in the Sarawak region of East Malaysia through post-mass drug administration surveillance. This phenomenon holds particularly true in the northern region of the state, potentially resulting in a postponement of the elimination initiative.

The objective of this research is to determine the incidence of lymphatic filariasis occurrence in Sarawak, analyse the geographical dispersion of the cases, detect areas with high concentration of cases, and assess the existence of autocorrelation in the spatial arrangement of lymphatic filariasis cases in Sarawak. The findings of the research may aid public health authorities in devising an improved strategy for the elimination initiative and identifying means to enhance its efficacy.

1.2 Problem statements

Research on the incidence of lymphatic filariasis in Sarawak and its inter-divisional variations is limited. Despite the fact that the majority of implementation units (IU) have completed MDA campaigns in accordance with WHO guidelines, there have been cases of lymphatic filariasis transmission that have been reported.

To the best of the available data, no investigation has been conducted regarding the spatial analysis of lymphatic filariasis in Sarawak. The research has the potential to facilitate post-Mass Drug Administration (MDA) surveillance efforts by identifying geographical locations with elevated transmission rates, which may serve as potential hotspots for lymphatic filariasis resurgence.

1.3 Rational of the study

To understand lymphatic filariasis in Sarawak, including incidence, disease distribution, and geographic pattern, more research is necessary. Location identification enables public health authorities to make control activity decisions more objectively and to create a foundation for more specialized and successful prevention campaigns. Moreover, this data will facilitate stakeholders in more effectively distributing resources and improving existing preventative and control measures.

1.4 Research Question

1. What is the incidence of lymphatic filariasis in Sarawak for 2018 to 2022?
2. What is the spatial distribution of lymphatic filariasis in Sarawak for 2018 to 2022?
3. Is there any hotspot area of lymphatic filariasis cases in Sarawak from 2018 to 2022?

1.5 Objectives

1.5.1 General objectives

To investigate the incidence and geographic distribution of lymphatic filariasis in the region of Sarawak from 2018 to 2022.

1.5.2 Specific objectives

1. To estimate the incidence of lymphatic filariasis in Sarawak from 2018 to 2022.
2. To describe the spatial distribution of lymphatic filariasis in Sarawak annually from 2018 to 2022
3. To determine the hotspot area of lymphatic filariasis in Sarawak annually from 2018 to 2022.

1.6 Research Hypothesis

1. There are significant nearest neighbors index (NNI) for lymphatic filariasis in Sarawak in 2018 to 2022.
2. There is spatial autocorrelation of lymphatic filariasis between geographical area in Sarawak for 2018 to 2022.

CHAPTER 2

LITERATURE REVIEW

The literature review process involved utilising various databases, including Scopus, PubMed, Science Direct, Springer Link, and Google Scholar. Various search techniques were employed, such as the utilisation of Boolean operators, specifically "AND", "OR", and "NOT". The search was conducted using keywords such as filariasis, incidence, prevalence, elimination, mass drug administration, transmission, and spatial.

2.1 Incidence and prevalence of lymphatic filariasis

Incidence of lymphatic filariasis was calculated using data from the Department of Statistics Malaysia. The numerator was the number of confirmed cases of filariasis that were found through a thick blood smear or a positive serological examination using a rapid test kit. The denominator was the number of people tested for filariasis, such as in the survey activity at the field or the total population living in that district in that year (Upadhyayula *et al.*, 2012). According to Ramaiah and Ottesen (2014) findings, there has been a 59% reduction in the global prevalence of lymphatic filariasis, with the percentage of affected individuals decreasing from 3.55% to 1.47%. Togo is classified as one of the 39 countries located in the African Region of the World Health Organisation (WHO) that exhibit endemicity for LF. In the year 2000, it was observed that seven out of 35 districts were endemic to lymphatic filariasis. The districts under consideration exhibited a range of baseline prevalence rates, spanning from 1% to 22% (Centers for Disease and Prevention, 2011).

The World Health Organisation (WHO) conducted a study on lymphatic filariasis blood surveys in Thailand from 1951 to 1952. The average rate of microfilarial

positivity was 21.0%, attributed to *Brugia malayi* infections. The study also examined the implementation of Mass Drug Administration (MDA) in Thailand from 2002 to 2011. MDA coverage fluctuated from 68.0% to 95.4% between 2002 and 2012. The discontinuation of MDA assessments in 11 endemic provinces in 2006 led to nine MDA-positive instances in seven provinces. The research found that TAS-1, TAS-2, and TAS-3 determined transmission threshold rates for *B. malayi* microfilariae among seropositive children. A health assessment of 23,477 migrants from 2002 to 2017 showed a positivity rate of 0.7% (Rojanapanus *et al.*, 2019).

A recent investigation conducted in Indonesia involved a comprehensive analysis of the national database on lymphatic filariasis. The findings reveal a notable rise in the occurrence of lymphatic filariasis over the past 17 years, coinciding with the implementation of the MDA programme. The lymphatic filariasis cases reported in Indonesia in 2017 were 12,667, representing an increase of nearly two-fold compared to the 6,535 cases recorded in 2001 in absolute terms. Thus, the incidence rate recorded in 2017 was 39 occurrences per 100,000 individuals (Aisyah *et al.*, 2022a).

Pre-era of mass drug administration was the only period for which reliable data on incidence and prevalence were available in Malaysia. The study categorised the data into three distinct regions, namely Peninsular Malaysia, Sabah, and Sarawak. The prevalence rates of the filariasis were found to be 0.26-23.85%, 20.69%, and 0.90%, respectively, during the period under studies (Dickson *et al.*, 2017). There were only two studies published in the last decade that mention the prevalence of lymphatic filariasis in Malaysia; one of the studies done in Pangkor Island found no cases, and the other study found 31.1% of prevalence in Sabah (Ahmad *et al.*, 2014; Zakaria and Avoi, 2021)**.**

2.2 Transmission of lymphatic filariasis

Lymphatic filariasis (LF) in humans is the result of infection by three separate species of filarial nematodes that are transmitted through mosquito bites. These species are *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori*. The transfer of parasites to human beings takes place through infected mosquito vectors, which deposit infective larvae onto the surface of the human skin. The larvae penetrate the dermis and then proceed to migrate towards the lymphatic vessels, where they undergo a process of maturation into male and female adult nematodes that spans several months. Upon reaching maturity and fertilisation, female worms release a substantial number of diminutive mf into the bloodstream.

Upon the consumption of microfilariae by a vector during a hematophagous event, the emergence of infective larvae occurs after an incubation period of roughly 10-14 days. These organisms migrate towards the proboscis of the mosquito and subsequently transmit to a human host during a subsequent blood feeding event. The significance of mosquito vectors cannot be overstated in the perpetuation of infection life cycles and their propagation. Various species of mosquitoes that serve as vectors in different parts of the world feed on humans. The study of the ecological and environmental factors that influence the distribution and abundance of vector species is essential in determining the specific habitats that may promote the transmission of parasites. (Simonsen and Mwakitalu, 2013a).

The most prevalent human lymphatic filarial parasite, *W. bancrofti*, has infected over 100 million individuals in Asia, Africa, Central and South America, as well as the

Pacific region. Transmission is facilitated by various mosquito species that pertain to the genera Aedes, Anopheles, and Culex.

Aedes serve as the principal vectors in Polynesia, with small freshwater reservoirs such as leaf axils, tree cavities, crab holes, coconut shells, cans, bottles, and similar objects serving as the primary breeding grounds.Anopheles spp. serve as the principal vectors in Africa, Papua New Guinea, and specific areas of South Asia, where they also function as malaria vectors. Certain Anopheles species have developed the ability to breed in peri-urban and, on occasion, even central urban regions, thereby proliferating in adequate numbers to facilitate the transmission of urban malaria. Culex spp. have been identified as the primary vectors in substantial regions of Asia, Central and South America, and East Africa, and are believed to be accountable for over 50% of *W. bancrofti* transmission.

Culex quinquefasciatus is a commonly occurring vector, specifically. Due to its ability to proliferate in water with a substantial amount of organic material, such as latrines, this organism is frequently detected in significant quantities in metropolitan areas, particularly in locales with insufficient sewage and drainage infrastructure (Simonsen and Mwakitalu, 2013a).

Infections caused by *B. timori* are geographically restricted to the eastern islands of Indonesia and are believed to impact a population of less than one million individuals. *Anopheles barbirostris* has been identified as the sole vector responsible for transmitting the disease, and its predominant breeding grounds are located in rural regions characterised by high levels of rice cultivation. *B. malayi* infections exhibit a

higher incidence rate in the regions of South and Southeast Asia, with an estimated 12 million individuals being affected. The predominant vectors are Mansonia, which are characterised by their larval coexistence with specific species of flourishing aquatic plants that float on freshwater bodies. Anopheles species have been observed to transmit *B. malayi* in regions with limited space. The proliferation of vectors for both human Brugia species is highly contingent on the accessibility of unpolluted freshwater bodies in rural areas (Fischer *et al.*, 2004). Figure 2.1 and 2.2 below depict the life cycle of lymphatic filariasis.

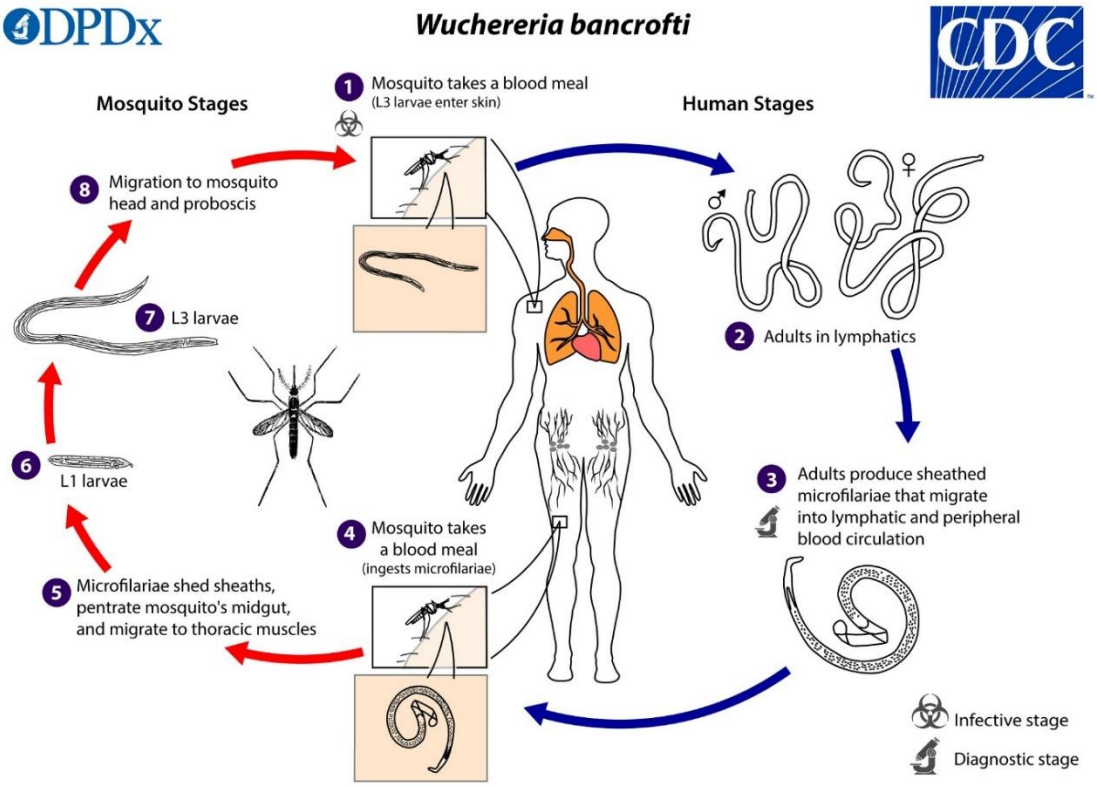

Figure 2.1 *Wuchereria Bancrofti* lifecycle. Adapted from CDC (2019)

Third-stage filarial larvae are dropped by an infected mosquito onto the human host's epidermis during a blood meal, where they enter the bite wound picture. Adults who normally reside in the lymphatic system are when they develop. The male worms

are roughly 40 mm by 1 mm in size, while the females are between 80 and 100 millimetres in length and 0.24 and 0.30 millimetres in diameter.

With the exception of microfilariae from the South Pacific, which lack a distinct periodicity, adults generate microfilariae that measure 244 to 296 µm by 7.5 to 10 µm, are sheathed, and exhibit nocturnal periodicity. As they migrate into lymph and blood channels, the microfilariae actively move through lymph and blood vessels. During a blood meal, a mosquito consumes microfilariae.

Microfilariae lose their sheaths after digestion, and some of them move to the thoracic musculature via the proventriculus and cardiac region of the mosquito's midgut. Microfilariae undergo a first-stage larval transformation there before developing into third-stage infective larvae. The third-stage infectious larvae move from the hemocoel to the *proboscis* picture after the mosquito has a blood meal and can infect another person (CDC, 2019).

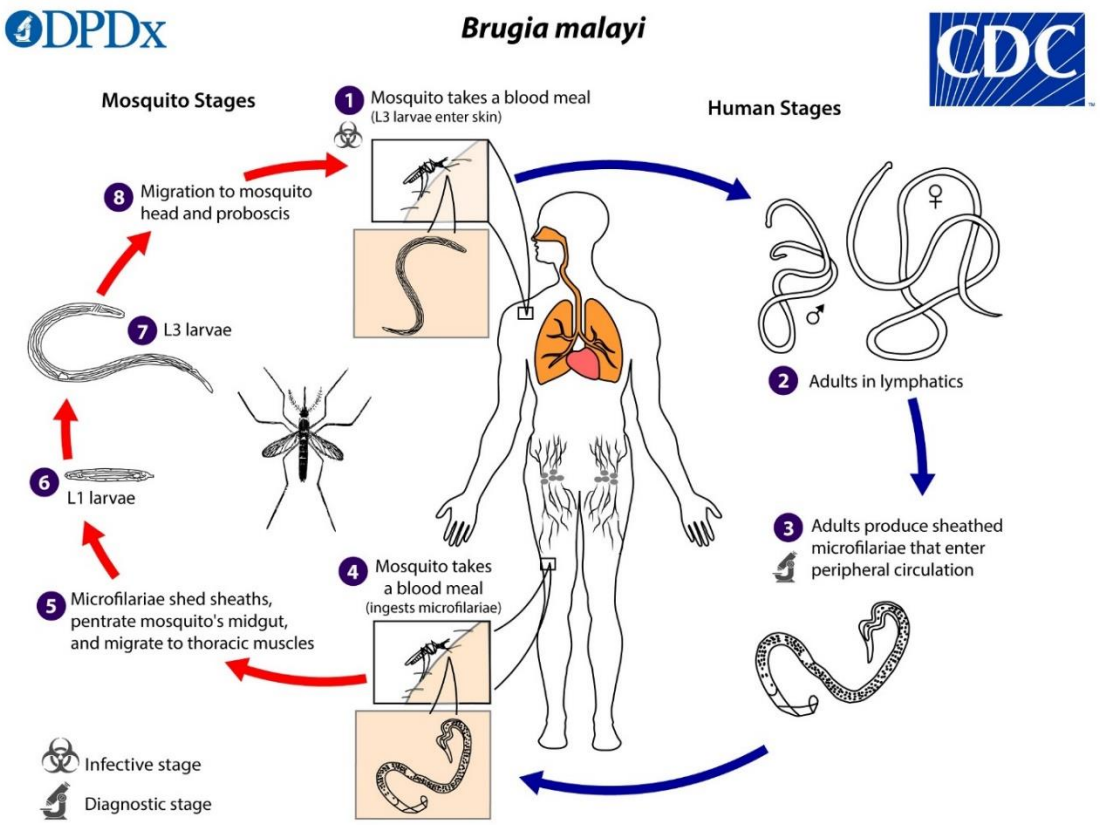

Figure 2.2 *Brugia malayi* lifecycle. Adapted from CDC (2019)

Mosquitoes that have been infected, usually belonging to the Mansonia and Aedes species, undergo maturation into adults that commonly reside within the lymphatic system. The mature nematodes bear a resemblance to *Wuchereria bancrofti*, albeit with a relatively reduced physical stature. The length and width of female worms range from 43 to 55 mm and 130 to 170 mm, respectively, whereas male worms exhibit a length and width range of 13 to 23 mm and 70 to 80 mm, respectively.

Microfilariae that are sheathed and exhibit nocturnal periodicity are generated by adult hosts, with a length ranging from 177 to 230 mm and a width of 5 to 7 mm. It is worth noting that *B. pahangi* infections typically do not result in the production of microfilariae. The microfilariae undergo migration via the lymphatic system and

subsequently infiltrate the bloodstream, ultimately arriving at the peripheral blood vessels.

The process of blood feeding by a mosquito leads to the ingestion of microfilariae. Upon ingestion, microfilariae undergo ensheathment and traverse the proventriculus and cardiac regions of the midgut en route to the thoracic musculature. At that location, microfilariae undergo a transformation process into images of first-stage larvae and subsequently into images of third-stage larvae. The larvae in the third developmental stage undergo migration through the hemocoel towards the proboscis of the mosquito, thereby facilitating transmission to a new human host upon the mosquito's consumption of blood. (CDC 2019).

2.3 Diagnosis and notification of lymphatic filariasis

The conventional method for diagnosing active infection involves the microscopic examination of a blood smear, with the primary aim being the identification of microfilariae. The microfilariae responsible for lymphatic filariasis exhibit nocturnal periodicity, circulating in the bloodstream during night-time hours. It is recommended that blood collection be conducted during night-time hours to align with the emergence of microfilariae The utilisation of contemporary card test technology, which is characterised by its simplicity and specificity, enables the detection of the parasite through a blood sample obtained via finger prick, at any given time (Ministry of Health, 2016).

In order to mitigate potential errors in diagnosis and parasite identification, each affirmative slide will be forwarded to a laboratory at the state level for further

verification. Various methods are available for identifying active filarial infection, including the detection of mf through microscopy on nocturnally drawn blood samples, the detection of circulating filarial antigen (CFA) in blood, and the detection of filarial DNA via molecular techniques such as polymerase chain reaction (PCR). Currently, the predominant method involves detecting CFA in blood due to its combination of sensitivity, specificity, and convenience. This approach can be performed using blood samples collected at any time of day (Pantelias *et al.*, 2022).

In the event of a positive case, prompt notification will be made to the nearest district health office for the purpose of conducting further investigation and implementing control measures. Cases that have been verified by detecting microfilaria through a blood smear or by utilising an antigen-antibody test kit will be classified as confirmed cases and will be recorded in the Vekpro system, which is accessible online. (Prevention and Control of Infectious Diseases Act 1988).

2.4 Spatial analysis of lymphatic filariasis

Spatial analysis is a branch of geography that examines patterns, relationships, and processes in geographic data. It entails the application of numerous approaches and tools to investigate, examine, and understand spatial patterns and events. To acquire insights into spatial distributions, spatial linkages, and spatial interactions, spatial analysis blends principles from geography, statistics, mathematics, and computer science (Goodchild and Longley, 1999).

Within the GIS literature, particularly in system manuals and brochures, it is commonly asserted that spatial analysis involves the manipulation of spatial data through a set of deterministic functions. These functions typically include fundamental

spatial queries, buffering, overlaying via basic map algebra, and the computation of surface derivatives such as slope and aspect. The process of manipulating spatial data can be referred to as "spatial data manipulation." This capability to manage spatial data in a spatial context is what sets a GIS apart from other database management systems, making it a crucial component of any information system that purports to be geographically oriented. This characteristic serves as a distinguishing factor between a genuine Geographic Information System (GIS) and software tools for computer-aided design or mapping purposes. Spatial statistical analysis employs process knowledge to anticipate potential spatial patterns, and subsequently, an examination of one or more of its realisations is conducted to determine the probability of any observed pattern being a consequence of this process. Exploratory spatial data analysis, in contrast, scrutinises an observed distribution and endeavours to deduce the process that generated it. Typically, the aim is to identify significant patterns within the data that align with the investigators' pre-existing domain expertise (Unwin, 1996).

The research conducted in American Samoa has illustrated the significance of spatial analysis in identifying the possible residual foci of antigen-positive adults, by accurately determining their location and size. In order to mitigate the likelihood of emergence, it is necessary to implement tactics aimed at monitoring both cluster inhabitants and individuals belonging to high-risk categories (Lau *et al.*, 2014a).

A study utilised a comprehensive worldwide collection of georeferenced surveyed locations to model the prevalence of lymphatic filariasis across 73 nations that have either been previously or are currently affected by the disease. The utilisation of mapping estimations can facilitate the identification of areas characterised by a reduced likelihood of encountering infection thresholds. In light of the considerable ambiguity

surrounding the prognostications, supplementary data acquisition or intervention may be requisite prior to the termination of MDA initiatives (Cromwell *et al.*, 2020).

The kernel intensity estimator was employed to detect areas exhibiting varying degrees of intensity in filarial infection cases. The heterogeneity of cases was observed across the entire municipality. The implementation of the kernel estimator enabled the detection of spatial agglomerations of instances, thus signifying areas with an elevated level of transmission intensity. The foremost advantage of employing this type of analysis lies in its ability to rapidly and easily pinpoint areas with a highest incidence of cases. Consequently, this facilitates the advancement, oversight, and monitoring of efforts aimed at eliminating filariasis. The application of geoprocessing and spatial analysis techniques constitutes a noteworthy tool for incorporation into the Global Programme to Eliminate Lymphatic Filariasis (GPELF) (Medeiros *et al.*, 2012).

In a study in Brazil, filariasis cases found in the investigation were georeferenced as points using the global positioning system navigation tracker. The location of residence of the affected individuals served as the point of reference. Subsequently, the point sample of instances was subjected to the application of the kernel estimator. The estimator was derived by the utilisation of a mathematical model. The input parameters of this model included the quantity of points and their corresponding geographical places, the level of smoothing applied to the resulting surface, and the search band width or radius. The resulting output parameter manifested as a smoothed density surface, which effectively identified spatial clusters. These clusters corresponded to locations exhibiting either a higher or lower density of points per unit area (Bonfim *et al.*, 2011).

In recent times, there has been a notable upsurge in scientific inquiry aimed at enhancing comprehension of the spatial patterns of parasitic diseases. The identification of disease prevalence and severity is essential in guiding the implementation of control measures. The utilisation of disease prevalence or intensity maps can facilitate the accurate categorization of disease risk confronted by communities, thereby enabling dependable spatial arrangement of intervention endeavours. Additionally, it can aid in the identification of the most severely impacted regions, which can be prioritised for intervention efforts (Pullan *et al.*, 2012).

Mapping studies can serve as a means to explore the fundamental causes of infection risk by integrating spatial data on parasite prevalence with geographic information on biotic and abiotic ecological variables. This approach can enhance our comprehension of the transmission ecology of parasitic diseases. The investigation of the correlation between the prevalence of illnesses and environmental or climatic factors is a valuable approach to explore the potential impact of climate change on the transmission and distribution of diseases over time. The research revealed that the prevalence of LF is significantly impacted by spatial autocorrelation among locations, while exhibiting a minimal correlation with environmental factors. The prevalence of infection, however, has been observed to be correlated with fluctuations in population density. The interrelationships among crucial environmental and demographic factors exhibit intricate and nonlinear patterns. It is anticipated that the occurrence of LF will exhibit significant variation throughout Africa, with regions along the West and East African coasts expected to experience a predominance of high prevalence rates (>20%), while the lowest prevalence rates are projected for the central regions of the continent. The error maps indicate a requirement for further surveys to tackle the inadequacy of

data in the latter and other areas. The examination of forthcoming fluctuations in prevalence indicates that the anticipated rise, fall, and dissemination of LF throughout the continent will be primarily influenced by population growth, as opposed to climate change. The study's results suggest that these findings may have significant implications for the development of strategies that are optimally tailored to achieve parasite elimination objectives at both local and global levels, while also accounting for the potential impact of climate change on parasitic infection (Slater and Michael, 2013).

As per the results of a previous investigation, the demographic of children exhibits a notable incidence of microfilaremia, which is indicative of ongoing transmission. The utilisation of the social deprivation index in tandem with spatial distribution facilitated the identification and characterization of regions exhibiting the greatest incidence of infection. This approach enabled the pinpointing of localities where children are most susceptible to filarial transmission, while also accurately gauging the correlation between social deprivation and infection prevalence among this demographic. The utilisation of this analytical approach holds significant value in strategizing interventions within the Global Programme to Eliminate Lymphatic Filariasis (GPELF). It serves as a means to devise measures for curtailing and eradicating LF, while also pinpointing key demographics that require targeted interventions aimed at fostering environmental and socioeconomic enhancements (Brandão *et al.*, 2015).

The available data indicate that the risk of filarial infection in Indonesia exhibits inter-provincial variation. The incidence of cases is most pronounced in the eastern and western regions of Indonesia. The incidence rate of lymphatic filariasis in Indonesia

exhibits a high degree of variability, which can be attributed to the country's significant geographical fragmentation and ecological factors. In order to achieve the objectives of controlled LF management and eventual elimination as outlined by the WHO and Indonesian authorities, it is imperative that future public health interventions and strategic decisions take into account the unique contextual factors of the local setting (Aisyah *et al.*, 2022a).

2.5 Conceptual framework

The conceptual framework depicted in figure 2.3 outlines the variables that were integrated into the research study to determine the incidence of lymphatic filariasis cases and their spatial distribution. People, places, and times are the three categories into which all of the variables can be organised in accordance with the distribution of the diseases. The sociodemographic characteristics of an individual, such as age, gender, and country, will be included in the "person" domain. The address of the individual who has been diagnosed with lymphatic filariasis is converted into longitude and latitude inside the place domain. This allows us to postulate the distribution of the disease throughout the state of Sarawak. The cases of lymphatic filariasis that are diagnosed throughout the course of the study will be displayed in the temporal domain. The researchers were able to establish the annual occurrence of lymphatic filariasis over the length of the five-year study, which began in 2018 and ended in 2022. The analysis depicts the regional distribution of diseases and identifies disease hotspots. Furthermore, the presence of autocorrelation among the observed patterns of lymphatic filariasis within a single geographic region was assessed.

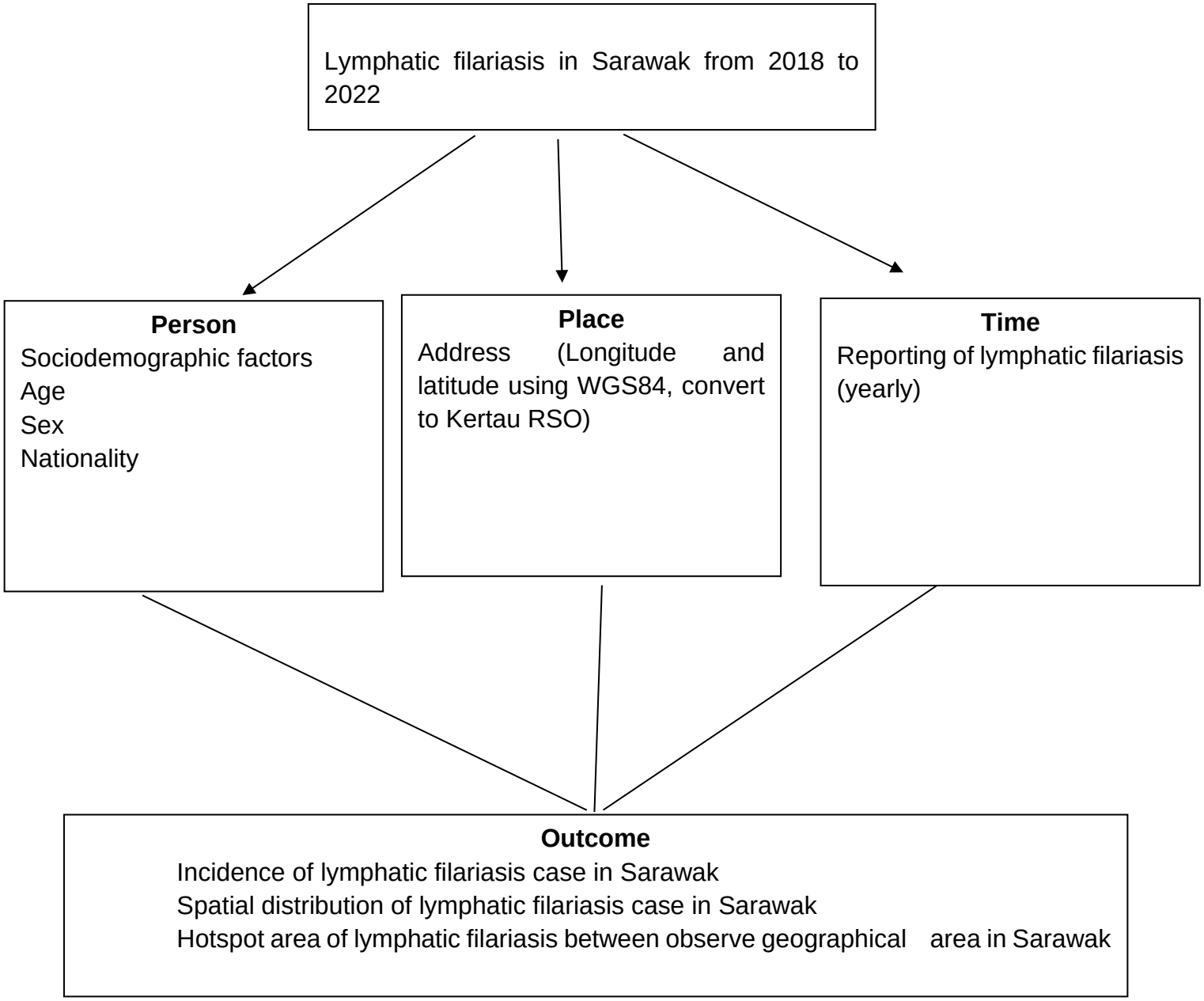

Figure 2.3: Conceptual framework of incidence and spatial distribution of lymphatic filariasis cases

CHAPTER 3

METHODOLOGY

3.1 Research design

A retrospective analysis of secondary data extracted from Vekpro online system spanning the years 2018 to 2022.

3.2 Study location

The research was carried out in the region of Sarawak, located in Malaysia. The collection of data was conducted by the Disease Control Division of the Ministry of Health. Sarawak is situated on the Borneo Islands, along with Sabah, Brunei Darussalam, and Kalimantan, Indonesia. The South China Sea acts as a barrier between the state and the rest of Peninsular Malaysia, and the state itself spans a total area of 124,444.51 square kilometres. According to the 2020 census carried out by the Department of Statistics in Malaysia, the country's total population is 2,907,500 people of various ethnicities. In Sarawak, there are twelve divisions and forty districts (Sarawak Government Office, 2022).

3.3 Study duration

The investigation utilised data obtained throughout January 2018 to December 2022. The study was conducted from April 2023 to June 2023.

3.4 Study population

The population of interest for this study is comprised of individuals diagnosed with lymphatic filariasis in the region of Sarawak. The source population for this study

consists of individuals diagnosed with lymphatic filariasis and recorded in the Vekpro online system in Sarawak.

3.5 Subject criteria

3.5.1 Inclusion criterion

All lymphatic filariasis registered in Vekpro online system from 2018 to 2022.

Exclusion criteria are established for imported cases, specifically referring to patients diagnosed with lymphatic filariasis who have stayed in a certain region for a duration of less than six months. Additionally, any incomplete data set, where the required information is absent, is also considered for exclusion.

3.6 Sample size estimation

The calculation of the sample size for determining the incidence of lymphatic filariasis in Sarawak for objective 1 were performed using the single proportion formula, as follows.*:*

$$n = \left(\frac{Z_\alpha}{\Delta}\right)^2 p(1-p)$$

n= numbers of sample

Zα= level significance 95% CI.

P= expected proportion of incidence 39 per100 000 (Aisyah *et al.*, 2022).

Δ= detectable different (precision) is set at 0.0001 in view of small proportion use in this study.

$$n = \left(\frac{1.96}{0.0001}\right)^2 0.00039(1-0.00039)$$

=166 247 (including 10% drop out)

However, the study was used all cases that has been registered in the Vekpro online system; between the years 2018 and 2022.

3.7 Sampling method

The study included all cases of lymphatic filariasis that are recorded in the national registry database through the Vekpro online system between the years 2018 and 2022, who fulfil subject criteria.

3.8 Research tool

The Malaysian Ministry of Health (MOH) created Vekpro Online, an online reporting system, to help with the management of vector-borne and other infectious disease epidemics. The MOH's Division of Disease Control is in charge of its overall administration. Its goal was to monitor the transmission of infectious illnesses using data that had been harmonised for disease control and management. The Assistant Environmental Health Officer is in charge of inputting all data into the Vekpro online system, and the Medical Officer of Health at the district level is in charge of verifying the validity of the information.

To extract data from Vekpro Online, a proforma checklist, as shown in Appendix A, was employed. The variables needed are sociodemographic data such as age, gender, nationality, address, and date of lymphatic filariasis diagnosis. Data on Sarawak's population for 2018 to 2022 was obtained through the Department of Statistics Malaysia (DOSM, 2023).