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Association Between Delayed Dengue Reporting and Subsequent Dengue Cases in Bangkok

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Fauzan RACHMATULLAH

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Location of practicum:
Unité de Génétique Fonctionnelle des Maladies Infectieuses, Institut Pasteur,
Paris, France

Professional advisor:
Richard Paul, Institut Pasteur, CNRS

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Academic advisor:
Bertrand Lefebvre, EHESP, CNRS, ARENES

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Association Between Delayed Dengue Reporting and Subsequent Dengue Cases in Bangkok

Abstract

Objective: Bangkok is one of the hotspots for dengue transmission with an average annual incidence of 172 cases per 10,000 population from 2003 to 2017. Managing dengue through rapid detection of the symptoms until investigation is crucial in controlling the disease. However, delays might happen along the way, which leads to the main objective of this study, to explore the association of delayed dengue reporting with subsequent dengue cases while also expanding on understanding underlying factors associated with the delay itself.

Methods: Dengue surveillance data at a sub-district level in 2013 from the Bangkok Metropolitan Administration (BMA) and the 2010 census data from National Statistical Office (NSO) were used for this study. A generalised linear model (GLM) and a SatScan™ analysis were done to determine the association between delayed time with socio-economic and demographic factors and subsequent dengue cases respectively. Dengue mapping using QGIS was also done along with the analysis to understand dengue patterns during the time of study.

Results: Delayed time during hospital presentation to data entry was the longest (average of 6.66 days) compared to the delay time from first symptom to hospital manifestation and from data entry to investigation. Various socio-economic, environmental, and demographic factors such as dengue incidence, area size, home ownership and household possessions, nationality, education, gender, and occupation were found to be associated with delayed time during different periods. Dengue clusters were also found in Bangkok with a 14 and 28 days maximum duration, but there was no evidence to believe that delayed reporting is associated with subsequent dengue cases.

Conclusion: Despite finding no evidence of association between delayed reporting and subsequent dengue cases, it would still be relevant to keep improving the surveillance efforts to control dengue in Bangkok. Further studies with different approaches and settings are highly encouraged as this topic is relatively novel.

Key words: Dengue, Delayed Reporting, Investigation, Bangkok

Association entre la déclaration tardive de la dengue et les cas ultérieurs de dengue à Bangkok

Résumé

Objectif : Bangkok est l'un des *hotspot* de la transmission de la dengue avec une incidence annuelle moyenne de 172 cas pour 10,000 habitants entre 2003 et 2017. La gestion de la dengue par la détection rapide des symptômes jusqu'à l'investigation est cruciale pour contrôler la maladie. Cependant, des retards peuvent survenir en cours de route, ce qui conduit à l'objectif principal de cette étude, qui est d'explorer l'association entre la notification tardive de la dengue et les cas de dengue ultérieurs, tout en approfondissant la compréhension des facteurs sous-jacents associés au retard de déclaration à Bangkok.

Méthodes : Les données de surveillance de la dengue au niveau des sous-districts en 2013 de l'Administration métropolitaine de Bangkok (BMA) et les données du recensement 2010 de l'Office national des statistiques (ONS) ont été utilisées pour cette étude. Un modèle linéaire généralisé (GLM) et une analyse SatScan™ ont été réalisés afin de déterminer l'association entre le retard, les facteurs socio-économiques et démographiques et les cas de dengue ultérieurs, respectivement. Une cartographie de la dengue à l'aide de QGIS a également été réalisée en même temps que l'analyse pour comprendre les schémas de la dengue pendant la période d'étude.

Résultats : La déclaration des cas est soumise à des délais importants (6,6 jours en moyenne) au sein des hôpitaux par rapport au délai entre le premier symptôme et la manifestation hospitalière et entre la saisie des données et l'investigation. Divers facteurs socio-économiques, environnementaux et démographiques, tels que l'incidence de la dengue, la taille de la zone, la possession d'une maison et les biens du ménage, la nationalité, l'éducation, le sexe et la profession, ont été associés au retard pendant les différentes périodes. Des clusters de cas de dengue ont également été trouvés à Bangkok avec une durée maximale de 14 et 28 jours, mais les résultats ne permettent d'associer retard de déclaration aux cas de dengue ultérieurs.

Conclusion : Bien qu'il n'y ait pas de preuve d'une association entre la déclaration tardive et les cas de dengue ultérieurs, il serait néanmoins pertinent de poursuivre les efforts de surveillance pour mieux contrôler la dengue à Bangkok. D'autres études avec des approches et sur des contextes différents sont vivement encouragées car ce sujet est relativement nouveau.

Mots clés : La Dengue, déclaration tardive, investigation, Bangkok

List of Abbreviations

ADS	Average Dengue Season
BMA	Bangkok Metropolitan Administration
CATI	Case-Area Targeted Intervention
COVID-19	Corona Virus Disease 2019
DENV	Dengue Virus
DF	Dengue Fever
DHF	Dengue Haemorrhagic Fever
DSS	Dengue Shock Syndrome
GIS	Geographic Information System
GLM	Generalised Linear Model
HDS	High Dengue Season
LDS	Low Dengue Season
MoPH	Ministry of Public Health
NGO	Non-Governmental Organisation
NSO	National Statistical Office
NTD	Neglected Tropical Disease
SD	Standard Deviation

List of Figures and Tables

Table of Contents

1. Introduction

1.1. Dengue

Dengue is an arboviral disease caused by the dengue virus and most commonly transmitted by *Aedes aegypti* or *Aedes albopictus* mosquitoes during a blood meal (1). Infections of dengue virus (DENV) can be asymptomatic or lead to the development of high fever along with other symptoms such as headache, nausea, retro-orbital pain, muscle pain, or rashes (dengue fever, DF) and in some cases more severe symptoms with haemorrhage, Dengue Haemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS) (2). DENV is a single positive stranded RNA virus and part of the Flaviviridae family with four different serotypes, namely DENV 1 – 4 (1). Infection by a specific serotype induces lifelong immunity to that serotype only and not to the other serotypes (3). Subsequent infection with a different serotype can, however, lead to more severe disease (3). This likely occurs through the effects of antibody dependent enhancement, whereby antibodies against the first serotype do not neutralise the virus but aid viral entry into immune cells and enable increased proliferation (4).

Currently, some vaccines have been developed in various clinical phases, but despite recent optimism, there has yet to be any effective vaccines available (5,6). Furthermore, there is no specific treatment for dengue besides keeping the bodily fluids stable and other supportive treatments (7). Thus, early detection in health centres is key to treat dengue infection as it does not only reduce the number of inpatients but also increases the chances of survival (8,9).

1.2. Dengue in Bangkok, Thailand

Dengue has been considered as a Neglected Tropical Disease (NTD) that is estimated to infect approximately 400 million people per year around the world (3). There were nine endemic countries in the 1970 but has grown to more than a hundred endemic countries in 2019 (1). Thailand was one of the first countries where dengue was first detected in the 1950s besides the Philippines and has continued to be one of the hotspot countries with all dengue serotypes, especially in the capital city of Krung Thep Maha Nakhon, or more commonly known as Bangkok (1,10,11). The average annual dengue incidence in Thailand is 115 cases per 100,000 population throughout 2000-2011 (12). Meanwhile, the average annual dengue incidence in Bangkok from 2003-2017 was 172 cases per 100,000 (13). Most of the incidences that occur in Thailand are predominantly aged ≤ 15 years even though it is still common till the age of 24 years old with the cases being either DF or DHF (12). It is estimated that the burden of dengue in Thailand cost approximately 158 (± 33) million USD with 72% of them accounting for the cost of illness and the rest goes to vector control cost (14).

Seasonality is one of the important factors relating to the emergence of cases due to being correlated to high peaks of dengue incidence which commonly occur during the wet season, notably starting from May to October (12,15). Nevertheless, other factors such as socio-economic factors and surveillance system should also be considered for preventive and control measures (15–17). More recently, the COVID-19 pandemic has shown to have reduced the number of dengue incidence by 44.1% worldwide including in Thailand through the implementation of COVID-19 control measures such as closing down schools and the limitation of gatherings (18,19). However, it is important to note that health seeking behaviour and the health system during those times might have been disrupted which impacted the number of cases being recorded (20). Hence, the importance of having a well-built surveillance system.

1.3. Surveillance System and Preventions of Dengue

Surveillance plays a crucial role in public health as it is an ongoing process of collecting, analysing, and interpreting health data for various purposes in public health practices (21–24). Since surveillance revolves around data, its quality should be checked thoroughly to make sure it is complete, accurate, consistent, adequate, and valid (21,24). The data itself could be collected from clinics, hospitals, and primary health centres to name a few which is then stored and used for further purposes (21,24). In a given situation, these data could detect health problems through measuring trends and further develop research questions (21,22).

Dengue surveillance is mainly done to detect and forecast epidemic activities which could then be utilised as an early warning system to notify public health actors to take action (9). Unfortunately, it requires a plethora of data in order to be optimal, including detection of disease cases, laboratory-case and vector surveillance, and monitoring dengue environmental risk factors (9). In most cases, early warning systems for diseases such as dengue primarily depend on meteorological data despite the potential of other types of data mentioned previously to be integrated (25). Besides that, other limitations of the early warning system for dengue are the requirements of highly skilled users and the lack of tools to map transmission levels at a smaller scale (25). Of utmost importance is optimising the surveillance system, without which any data generated can only be treated with caution.

In terms of surveillance, Thailand initiated its first passive surveillance on dengue in 1958, but only to be fully operational in 1974 (26). The transition from post to electronic transmission started from 1999, but it was not mandatory to do so due to limitation for some local level health centres to adapt at the time (12,26). On the other hand, Bangkok has an online operating system called “Epi-net” which collects dengue confirmed cases from hospitals that were reported to the Bangkok Metropolitan Administration (BMA) and Ministry of Public Health (MoPH) (27). Once the dengue case has been notified in the system, an investigation and intervention is carried out within 100 m of the area around the patient’s household, involving environmental clean-up of potential oviposition sites, distribution of larvicides and fumigation of adulticide (27).

Delayed intervention has been one of the major problems for the system in controlling dengue as it relies solely on clinical confirmation of cases and reporting, and necessitates tracing the address of identified cases, which adds to the challenge faced by the system (27). Furthermore, the reporting still relies heavily on patients' health seeking behaviour, physicians' willingness to report and health centre efficiency, which leads to underreporting and delays in reporting even though it is mandatory (10,28). Additionally, lab tests are not mandatory for confirmation, potentially leading to misdiagnosis, and thus misreporting (28). Inaccurate and delayed reporting will affect the response to prevent and control subsequent dengue cases in the neighbouring area of the reported case (15,28).

There have been studies that have tried to tackle the flaws in the reporting system. A notable study by Rotejanaprasert, et al. (2020) tried to correct the delayed reporting system by using a spatiotemporal nowcasting model in order to more accurately predict real-time dengue cases (15). This is based on the data from a previous study that showed approximately 75% of delayed dengue reporting in Thailand could be as long as 6 weeks or more (28). To put it into perspective, dengue in a highly dynamic setting such as Bangkok might pose a huge threat to the public health situation as it is densely populated, along with a high number of commuters coming in and out of the city which could further escalate the spread of the disease. This could lead to direct and indirect economic loss in the country while also risking neighbouring countries from travellers (29,30). Therefore, having good reporting in a surveillance system plays a crucial role in addressing the issue so that it can provide accurate information for better evidence-based dengue intervention and for policy makers to distribute resources effectively (9,31).

1.4. Objectives

General objective: To study the association between delayed dengue case reporting and subsequent dengue case occurrence in Bangkok.

Specific objectives:

- Assess the spatio-temporal variability in time between the steps from symptom onset to intervention actions among sub-districts
- Evaluate if socio-economic and demographic differences among sub-districts contribute to the observed reporting rate variability in health areas.
- Analyse whether reporting delays are associated with subsequent dengue incidences at the sub-district level within the context of the known effects of socio-economic and demographic factors.

2. Methods

2.1. Study Design and Population

This is a semi-ecological study using both individual and aggregated data. The individual case report data and the aggregated sub-district (also known as *Khwaeng*) dengue incidence data were obtained from the Health Department of the Bangkok Metropolitan Administration (BMA) for 2013. A total of 15,046 dengue cases were reported during that year. The case report data were from health centres that coordinate and implement public health programs which are then reported to the BMA. A sample of them are used to represent health areas that consist of several sub-districts (160 sub-districts in total). The data include information on age, gender, whether infection was laboratory confirmed, date of symptom onset, date of clinical presentation, date of reporting and date of intervention, in which 2991 samples were able to be retrieved and mostly used for this study. This data was specifically about dengue intervention, thus collected in a different time than the total cases which resulted in the inability to determine the total number of investigations for 2013.

The dataset with socio-economic and demographic variables was obtained from the 2010 census data conducted by the National Statistical Office ((NSO) of Thailand (32). This dataset included sub-district level aggregated data on a wide range of factors that included education, nationality/immigration, occupation, type and structure of housing, type of water sources, different household amenities, surface area (km^2), number of households, and population characteristics (age, sex, occupation, education level). All these variables were measured in relative percentages except area, number of houses and population density, which were measured in numbers. This study is part of the contribution of human mobilities to dengue diffusion in the Bangkok project which aims to provide evidence for making effective and efficient vector preventive and control measures.

From the available dataset, the variables that are going to be used in this study are summarised in table 1 and table 2:

Table 1. Summary of Used Variables in the BMA Dataset

Variables	Definition
Delay Time (days)	
Symptom Onset to Hospital Presentation	Time needed for a person to seek medical attention after experiencing symptoms
Hospital Presentation to Data Entry	Time needed for hospitals to input cases to the system
Data Entry to Intervention	Time needed for health centres to investigate cases after receiving report from the system

Table 1. Cont.

Variables	Definition
Age (years)	Age of presenting cases
Season Type	Different type of dengue seasons (low, average, high)*
Dengue Incidence	Overall dengue incidence per sub-district during 2013

*Refer to the next subsection

Table 2. Summary of Used Variables in the NSO Dataset

Variables	Definition
Area (km^2)	Total area of a sub-district
Population Density	Total number of populations divided by the total area in a given sub-district
Religion	Percentage of population with a belief of either Buddhism, Christian, Confucius, Islam, or Hinduism
Nationality	Percentage of population with a national background of either Burmese, Chinese, Cambodian, Lao, Thai, or other foreigners
Occupation	
Agriculture	Percentage of population working in the field of agriculture, forestry, and fishery
Manual Labour	Percentage of population that works to provide manual labour such as construction and mining
Education	
No Education	Percentage of population that has no education
Primary	Percentage of population that completed primary education
Secondary	Percentage of population that completed secondary education
Higher Education	Percentage of population that completed higher secondary education
Undergraduate	Percentage of population that completed bachelor’s degree
Postgraduate	Percentage of population that completed Postgraduate or above
Home Ownership and Household Possessions	Percentage of population that has certain type of possession such as houses (condominium, town house, row house, detached house, flats, wood houses, cement/brick houses, recycled material), Air condition, ground water/well, motorcycle, car, washing machine, internet, cable TV, and cooking fuel (electricity, gas, charcoal/wood)

Table 2. Cont.

Variables	Definition
Migration Status	Percentage of population that has moved into Bangkok in the last 5 years from abroad or cities outside of Bangkok

Something to point out from this list is the home ownership and household possessions. With limited variables available in the dataset, this study uses these variables to reflect the population's affluence. This is based on the assumption that having certain types of possession such as car, internet, cable TV, or condominium represents a population with a degree of higher income, considering that the data was collected for the 2010 census where it may have not been as common to have as today.

2.2. Descriptive Analysis

Descriptive data analysis was done using the RStudio (version 2021.09.1) and Microsoft Excel 2021. Descriptive analysis of delayed reporting (symptom onset, hospitalisation, data entry, and intervention), study population socio-demographic characteristics, and dengue incidence will be presented in the form of graphs and tables which consists of standard deviation (SD), mean ($\bar{x}$), and percentages, depending on the type of data.

In this study, the seasons are going to be split up into low, average, and high seasons that is obtained through the following calculations:

$$Low\ Dengue\ Season\ (LDS) \leq \bar{x} - SD$$

$$High\ Dengue\ Season\ (HDS) \geq \bar{x} + SD$$

$$LDS > Average\ Dengue\ Season\ (ADS) < HDS$$

The $\bar{x}$ and SD is obtained by using the data from the total Bangkok 2013 dengue incidence. This time period was used due to being the year with the highest dengue incidence compared to other years in the dataset. Based on the calculation used to categorise dengue seasons, the results are as follows:

Table 3. Dengue Season Categorisation

Seasons	Weeks (Biweekly)
Low Dengue Seasons	Week 5 ~ 11
Average Dengue Seasons	Week 1 ~ 4, Week 12 ~ 14, Week 19 ~ 21, Week 23 ~ 26
High Dengue Seasons	Week 15 ~ 18, week 22

Biweekly was the chosen time frame for this study with the consideration of the average time for an infected person to infect a mosquito and for the virus then to complete its development within the mosquito (extrinsic incubation period) and for the virus to become patent in a newly infected person (i.e. after the latent period within the infected human). These incubation periods last 7-10 days and 5-7 days in mosquitoes and humans respectively (33,34). The categorisation will be the basis for further analysis when trying to explore spatio-temporal variability throughout different dengue seasons.

2.3. Spatial Analysis

Geographic Information System (GIS) is a spatial system which is capable of creating, managing, analysing, and mapping data (35,36). GIS could help understand patterns, relationships, and geographical context, thus improving communication, management, and decision making (35,36). For this study, QGIS (version 3.16.13) was used to map dengue incidence rate and investigation ratio in the sub-district level throughout the different dengue seasons in 2013. Dengue incidences rate was calculated based on the number of cases divided by the population in the sub-district and adjusted by 10,000 population. Meanwhile, investigation ratios were calculated using the number of investigated cases of each sub-district divided by the total number of dengue cases of the same sub-district, then turned it into percentage. Following that, dengue data in the excel were joined using the join layer feature with the shapefile (shp.) using the software by matching variable "GEOCODE" in the shapefile with variable "CODE160" from the excel sheets. All missing data were coded into a unique code and labelled accordingly.

2.4. Statistical Analysis

To assess the significance of association of variables with delay times, a generalised linear model (GLM) with poisson distribution was fitted. A dispersion parameter was estimated to account for any overdispersion of the data. Firstly, a univariable analysis was performed for each variable and a P-value threshold of P = 0.2 was taken for use of the variable in the multivariable analysis. Because many variables within the same category type (e.g. Religion, nationality, income, education level) were correlated, multivariable analyses were first performed within the category prior to the final multivariable analysis. Only those variables at P-value ≤ 0.05 from the "within" category multivariable analysis were included in the final multivariable analysis. All such variables were fitted in the full model, which was then simplified by backward elimination of non-significant variables. Socio-economic and demographic variables were selected as those being most appropriate as previously described in the literature. To note that the variables age and gender reflect the actual information of the person presenting at the hospital. All the other variables represent a sub-district aggregated classification.

2.5. SaTScan™ Analysis

In order to explore whether the data are randomly distributed over space and time and detect clusters, further spatio-temporal analysis was used using SaTScan™. Besides detecting clusters, this analysis could also be used to perform geographical surveillance of diseases and identify areas with high and low rates of that particular disease. The results will be shown as cartesian coordinates with circles which indicate the clusters that have their own likelihood ratios based on the number of observed and expected cases within and outside the circle. Maximum likelihood is also calculated over all possible circles called scan statistics.

The standard purely spatial scan statistic imposes a circular window on the cartesian coordinates. The window is in turn centred on each of several possible grid points positioned throughout the study region (37). For each grid point, the radius of the window varies continuously in size from zero to some upper limit specified by the user. In this way, the circular window is flexible both in location and size (37). In total, the method creates an infinite number of distinct geographical circles with different sets of neighbouring data locations within them. Each circle is a possible candidate cluster (37). The space-time scan statistic is defined by a cylindrical window with a circular geographic base and with height corresponding to time. The base is defined exactly as for the purely spatial scan statistic, while the height reflects the time period of potential clusters (37). The cylindrical window is then moved in space and time, so that for each possible geographical location and size, it also visits each possible time period (37). In effect, we obtain an infinite number of overlapping cylinders of different size and shape, jointly covering the entire study region, where each cylinder reflects a possible cluster (37).

For the Poisson model, the expected number of cases in each area under the null hypothesis is calculated using indirect standardisation (37). Without covariate adjustment the expected number of cases in a location is:

$$\mathrm{E[c]} = \mathrm{p} * \frac{\mathrm{C}}{\mathrm{P}}$$

where *c* is the observed number of cases and p the population in the location of interest, while *C* and *P* are the total number of cases and population respectively (37).

To include covariates, *ci*, *pi*, *Ci* and P*i* are defined in the same way, but for covariate category i. The indirectly standardised covariate adjusted expected number of cases (spatial analysis) is:

$$\mathrm{E}[c] = \Sigma i\, E[ci] = \Sigma i\, pi * \frac{Ci}{Pi}$$

For the spatio-temporal analysis, the Discrete Poisson model was used, where the expected number of cases in each area is proportional to its population size. The maximum temporal window for a hotspot cluster was set to 14 or 28 days. The maximum spatial window was set to 10%, reflecting the overall incidence rate of dengue across Bangkok. Only clusters with no geographical overlap were allowed and a significant P value threshold was set to P<0.012 to account for the four analyses (i.e. 0.05/4).

3. Results

3.1. Defining the Data Through Descriptive analysis

Table 4. Distribution of Delay Time and Dengue Related Variables in Bangkok 2013

Variables	N = 2998[1]
Delay Time (days)	
Symptom Onset to Hospital Presentation	2.15 (2.10)
Hospital Presentation to Data Entry	6.66 (7.07)
Data Entry to Intervention	0.64 (2.28)
Age (years)	23.34 (14.91)
Dengue Incidence per Sub-district	94.04 (93.96)
[1]Mean (SD)	

Based on table 4, dengue incidence during 2013 in Bangkok has an average of 94 cases with the average age of infection around 23 years old. Furthermore, among the delayed time categories, hospital presentation to data entry has the highest average delay time of 6.66 days (7.07) which is three times longer than the symptom onset to hospital presentation and even longer if compared to the data entry to intervention delay time.

Table 5. Distribution of Socio-Economic and Demographic Variables in Bangkok

Variables	N = 160[1]
Area (km^2)	9.89 (11.95)
Population Density (pop/km^2)	10,202.90 (6,272.29)
Religion (%)	
Buddhism	91.51 (12.79)
Christian	1.86 (4.47)
Confucius	0.21 (2.09)
Islam	5.42 (11.30)
Hinduism	0.39 (1.31)
Nationality (%)	
Lao	0.53 (1.37)
Burmese	2.51 (3.03)
Chinese	1.20 (1.71)
Other Foreigners	3.74 (10.82)
Thailand	91.08 (15.09)
Migration Status (%)	9.96 (8.02)
Occupation (%)	
Agriculture	1.10 (2.88)
Manual Labour	21.66 (10.60)
[1]Mean (SD)	

Table 5. Cont.

Variables	N = 160[1]
Education (%)	
No Education	4.82 (2.17)
Primary	19.37 (5.31)
Secondary	18.36 (4.14)
Higher Secondary	22.28 (5.17)
Undergraduate	23.92 (6.05)
Postgraduate	5.48 (3.03)
Home Ownership and Household	
Possessions (%)	5.86 (7.93)
Condominium	11.14 (13.26)
Town House	29.42 (22.85)
Row House	33.93 (21.49)
Detached House	18.16 (15.95)
Flats	14.11 (9.85)
Wood House	10.60 (6.65)
Cement/Brick House	0.06 (0.25)
Recycled Material House	46.21 (13.89)
Air Conditioner	0.05 (0.10)
Ground water/well	40.62 (12.05)
Motorcycle	44.37 (11.86)
Car	61.06 (11.29)
Washing Machine	36.54 (10.20)
Internet	31.26 (14.87)
Cable TV	
Cooking Fuel	8.52 (7.85)
Electricity	79.75 (12.86)
Gas	0.59 (0.56)
Charcoal/wood	

[1]Mean (SD)

Across 160 sub-districts, Bangkok has an average population density of 10,202.90 population/km^2 (6,272.29) with Buddhism (91.51%) being the dominant faith, followed by Islam (5.42%). Meanwhile, most of the population residing in Bangkok have Thai nationality (91.08%), with other nationality such as Burmese (2.51%) making up most of the minority. Additionally, Undergraduate (23.92%) and Higher secondary school (22.28%) make up most of the population's education background. In terms of Income, people mostly live in detached houses and row houses with an average of 33.93% and 29.42% respectively. Out of all the other possessions, washing machine (61.06%) and air conditioner (46.21%) are the most common items that the people in Bangkok own. Meanwhile gas seems to be the most used for cooking fuel with an average of 79.75%.

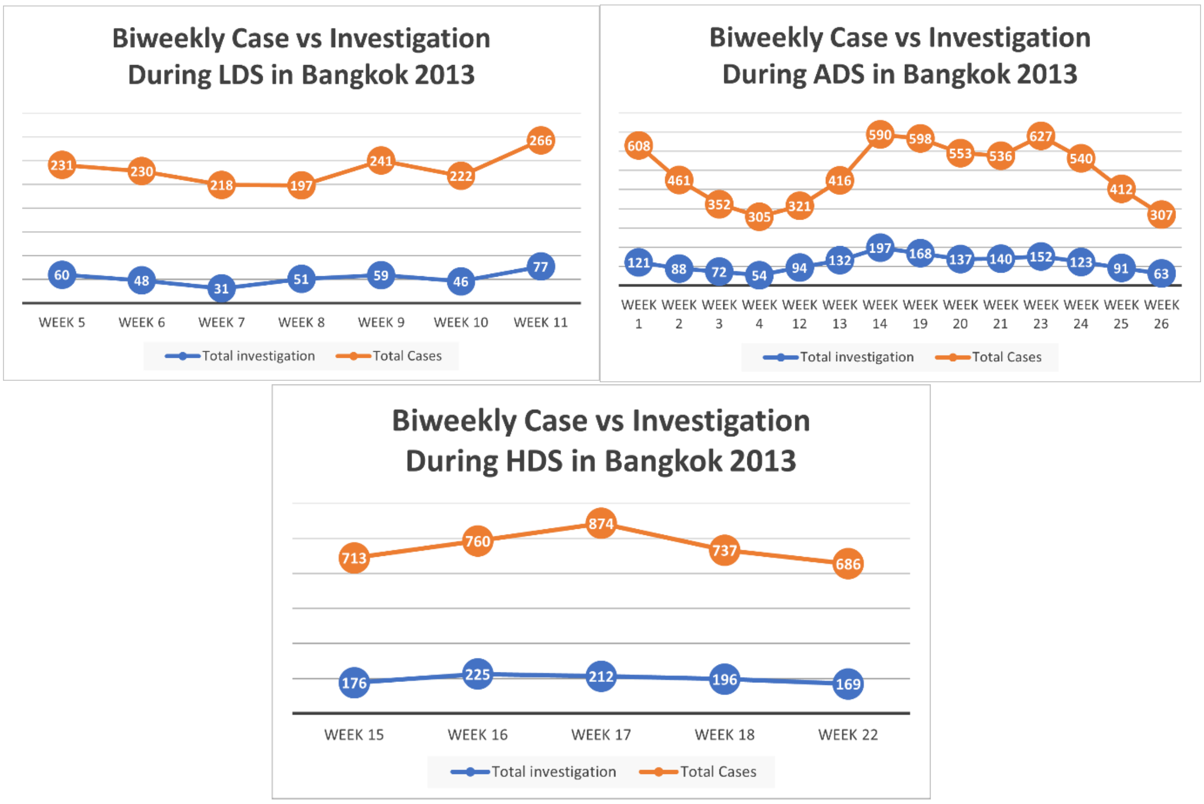

Figure 1. Biweekly Cases Compared to Number of Investigation During Different Dengue Seasons in Bangkok 2013

Investigations of dengue in Bangkok generally follow a similar trend as the number of cases present during a particular time throughout different dengue seasons in 2013. If there is an increase in dengue incidence, there would generally be an increase in investigation number. However, the increase or decrease in the number of cases during LDS or HDS were not as extreme as the increase during ADS from week 12 to 14, as well as the decrease from week 23 to 26 which is shown in figure 1.

3.2. Dengue Mapping in Bangkok

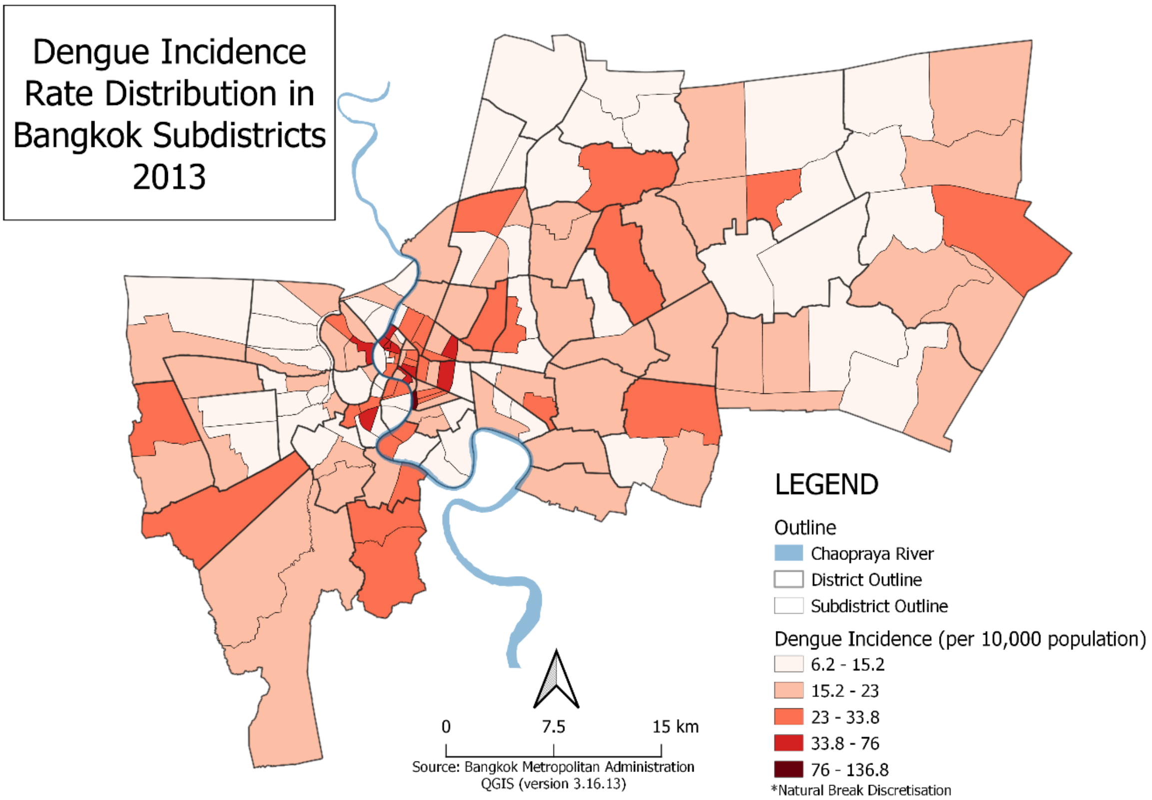

Figure 2. Dengue Incidence Rate in Bangkok Subdistricts 2013

In the span of a year in 2013, the mean dengue incidence rate of 2013 was 20.81/10,000 population with the highest incidence rate being 136.8/10,000 population. As seen in figure 2, high dengue incidence rate is more concentrated in the centre of Bangkok. In contrast, lower incidence rates are usually more spread out across the city with the lowest being 6.18/10,000 population.

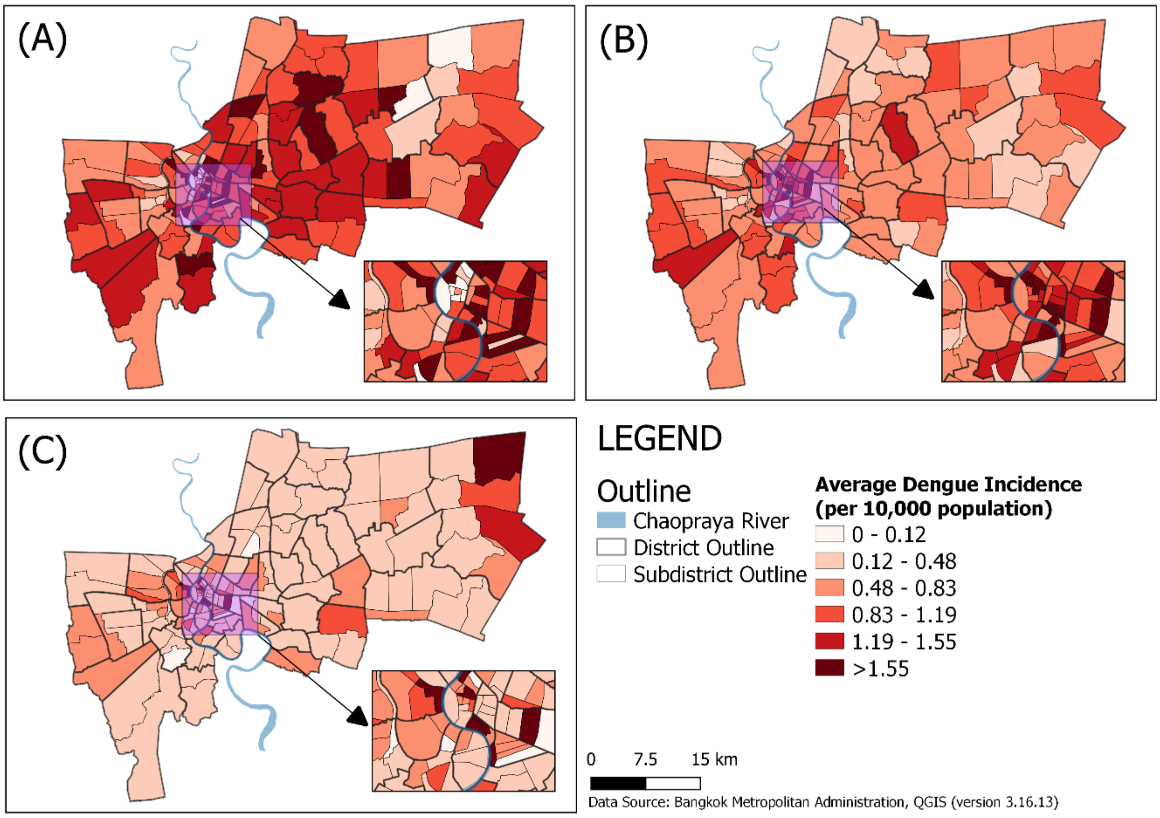

Figure 3. Average Dengue Incidence Rate Across Different Dengue Seasons
(A) High Dengue Season, (B) Average Dengue Season, (C) Low Dengue Season

In comparison with the previous map, figure 3 compares the average incidence rate of dengue across different dengue seasons in Bangkok sub-districts. It uses an average of the incidence rate since each dengue season comprises varying number of weeks which might cause bias when comparing them without any standardisation. Based on figure 3, it can be seen that there is a big contrast in the average dengue incidence rate in the LDS compared to both HDS and ADS. However, high dengue incidence rate is rather similar in the centre of Bangkok across all maps. The highest average incidence rates are 4.07 cases/10,000 population, 6.02 cases/10,000 population, and 8.44 cases/10,000 population for LDS, ADS, and HDS respectively.

Moving further into the study, dengue investigation is an important component to understand since it is closely related to the responsiveness of health centres in that particular area when an outbreak occurs. Figure 4 visualises the ratio of investigation in each sub-district and compares them across different dengue seasons.

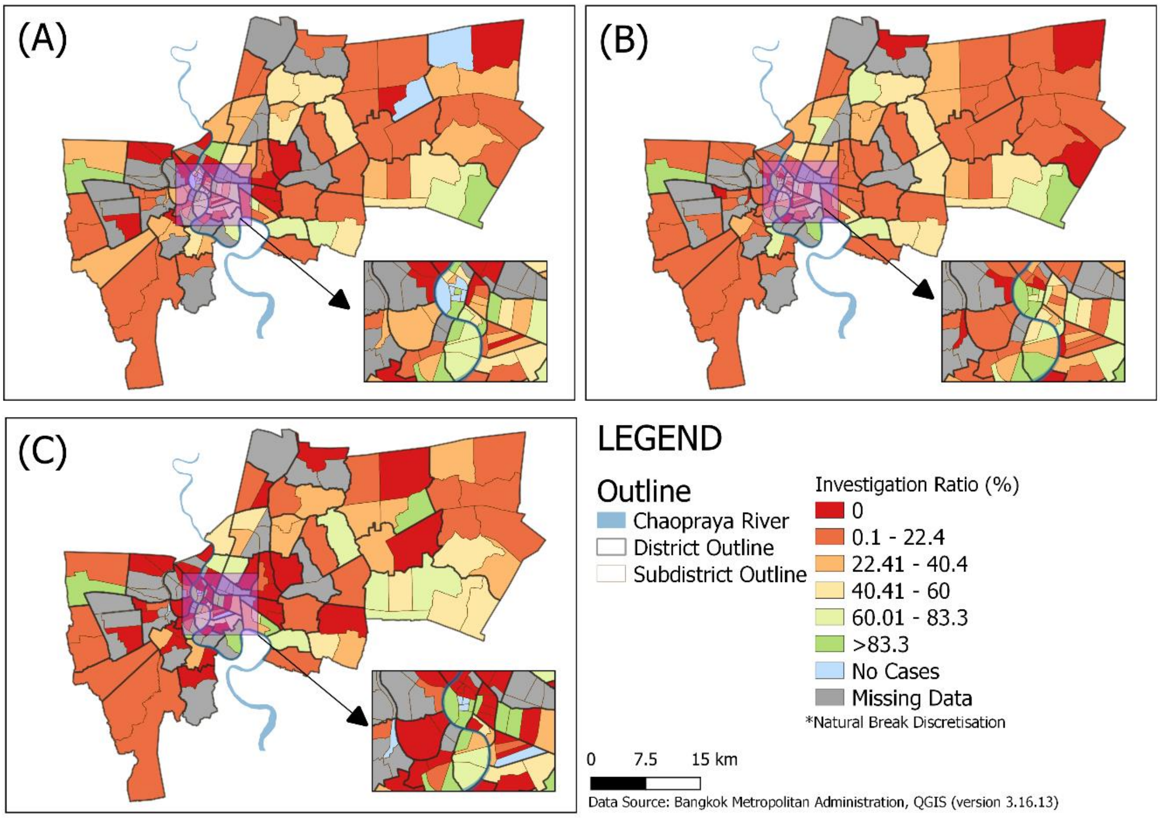

Figure 4. Dengue Investigation Ratio Across Different Dengue Seasons.
(A) High Dengue Season, (B) Average Dengue Season, (C) Low Dengue Season

Among the total of 160 sub-districts in Bangkok, there were 37 sub-districts that lacked reports on their dengue investigation activities and are considered as missing data. In terms of investigation ratio, there are 23 sub-districts during the LDS and ADS that have an investigation ratio of >60%, while the HDS has a lower number of 22 sub-districts.

3.3. Socio-economic, Environmental, and Demographic Variables Associated with Delayed Reporting

Table 6. Final Multivariable Model of Symptom Onset to Hospital Presentation

Variable	RR (95% CI)	P-value
Dengue Incidence	-	0.236
Season Type	-	0.153
Religion		
Islam	-	0.767
Home Ownership and Household Possessions		
Condominium	1.011 (1.003 – 1.020)	0.011*
Ground water/well	0.099 (0.038 – 0.260)	<0.001*
Nationality		
Lao	-	0.07
Occupation		
Agriculture	-	0.131

*Significant P-value (≤ 0.05), **R^2 = 4.7%

Table 6. Cont.

Variable	RR (95% CI)	P-value
Education		
Postgraduate	-	0.592

*Significant P-value (≤ 0.05), **R^2 = 4.7%

In the final analysis shown in table 6, only percentage coverage of wells/ground water and condominium housing were found to be associated with the delay time within the period of symptom onset and hospital presentation. Increased percentage of condominiums increase the delay with a Relative Risk (RR) of 1.011 for every percentage increase. Percentage groundwater, by contrast, led to a decrease in risk (RR=0.099) for every percentage increase in groundwater coverage. The final adequate model explained only 4.7% of the variation in delay time.

Table 7. Final Multivariable Model of Hospital Presentation to Data Entry

Variable	RR (95% CI)	P-value
Dengue Incidence	1.04 (1.02 – 1.07)	0.002*
Gender	1.14 (1.01 – 1.27)	0.03*
Education		
Higher Secondary Education	1.007 (1.001 – 1.012)	0.024*
Home Ownership and Household Possessions		
Condominium	0.985 (0.974 – 0.995)	0.004*
Ground water/well	-	0.079

*Significant P-value (≤ 0.05), **R^2 = 2.5%

Table 7 shows the findings of the univariable and multivariable analyses. In the final analysis, the overall number of cases led to an increased delay in the delay to data entry. Surprisingly, there was a small but significant increase in the delay time when the individual was male as compared to female. In contrast to the delay time from symptom onset to hospital presentation, individuals living in sub-districts with a higher percentage of condominiums and affluent housing were associated with a shorter entry delay. There was additionally a small association with the percentage of higher secondary education and slower data entry; given the very small P value, this is likely a spurious result. The final adequate model explained only 2.5% of the variation in delay time.

Table 8. Final Multivariable Model of Data Entry to Investigation

Variable	RR (95% CI)	P-value
Dengue Incidence	0.95 (0.91 – 0.99)	0.017*
Area (km^2)	1.4 (1.33 – 1.47)	<0.001*
Population Density	-	0.984
Religion		
Confucius	$4x10^{-6}$ ($1.7x10^{-7}$ – $1.1x10^{-4}$)	<0.001*

*Significant P-value (≤ 0.05), **R^2 = 34%

Table 8. Cont.

Variable	RR (95% CI)	P-value
Nationality		
Lao	0.81 (0.70 – 0.95)	0.008*
Burmese	-	0.231
Chinese	1.17 (1.06 – 1.29)	0.002*
Other Foreigners	0.46 (0.35 – 0.61)	<0.001*
Thailand	-	0.984
Age	0.992 (0.986 – 0.998)	0.009*
Occupation		
Agriculture	0.56 (0.50 – 0.64)	<0.001*
Manual Labour	-	0.153
Education		
No Education	1.28 (1.14 – 1.44)	<0.001*
Primary	-	0.262
Home Ownership and Household Possessions		
Condominium	-	0.353
Ground water/well	-	0.726
Detached House	-	0.708
Flats	-	0.353

*Significant P-value (≤ 0.05), **R^2 = 34%

In the analysis of variables associated with time delay from data entry to intervention, a number of variables were found to be significantly associated and the final model explained 34% of the variation in this time delay, contrasting with the model fit for the previous time delays. Of particular note were the associations with nationality and religious beliefs. Sub-districts with higher Lao or foreign populations had a shorter delay time to intervention (Table 8). This was also the case for sub-districts with higher percentage of Confucius adepts, although higher Chinese populations led to longer delay times. These two variables were correlated (r=0.18) but not to a strong extent and thus the observed differences may reflect different populational aspects impacting delay times. Sub-districts covering a larger area led to longer delays, whereas agricultural areas led to shorter delays. Sub-districts with a higher degree of lack of education were associated with longer delays. Finally, there were very small associations with both age and overall dengue incidence and a smaller delay; these effects were very marginal and potentially spurious, arising from model overfitting. Indeed, removal of the Chinese variable led to significant re-enforcing of the faster response time in the Confucius, Foreigner and Lao sub-districts and a loss of significance of both age and overall dengue incidence with little loss in explanatory power of the model.

3.4. Dengue Clusters in Bangkok

To assess the impact of time delays (hospital presentation to data entry and then to intervention), a spatio-temporal cluster analysis was performed on all the sub-districts that had

>60% of the total number of cases occurring (in the large dataset) that also had an investigation performed.

SatScan TM was used for the cluster analysis and a discrete Poisson model was fitted restricting the maximum population size that could occur within a cluster to 10% of the population and the maximum duration of the cluster to 14 or 28 days. These time lengths were chosen to increase the probability that the cases might be related and thus enabling us to test whether delay in time to entry and intervention impacted upon the subsequent dengue cases in the area.

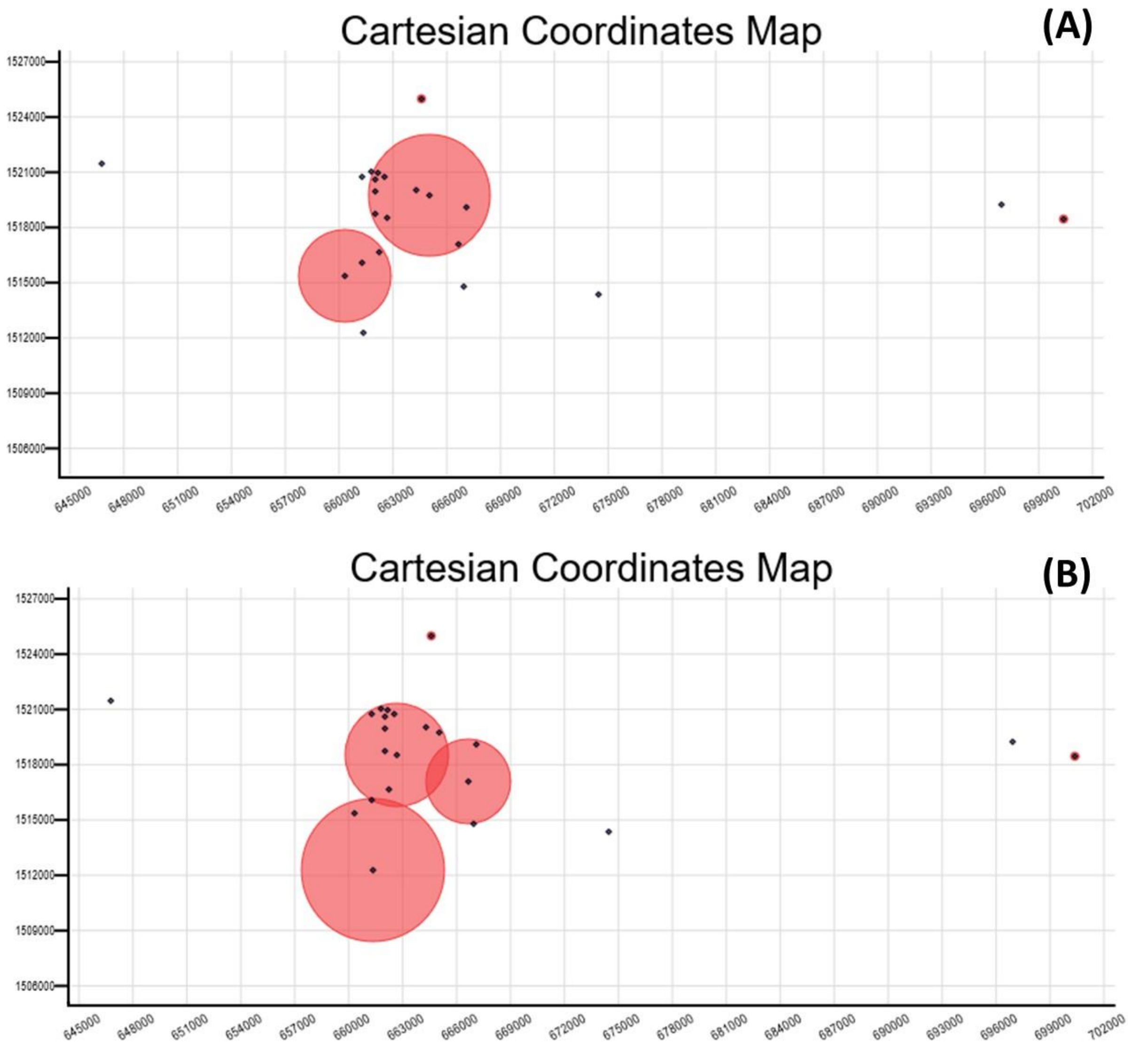

Figure 5. SatScan Model. (A) 14 Days Max Duration of Cluster with No Covariate, (B) 28 days Max Duration of Cluster with No Covariate

The models were first fitted without any covariates to detect the presence of any clusters of dengue. Then the models were fitted including delay time to data entry or delay time to intervention as a covariate. Few clusters were identified as shown in Figure 5, encompassing a variable number of sub-districts, dates and numbers of cases (Table 9).

Table 9. SatScan Models in Numbers

Cluster number	Number of *Khwaeng*	Number of Cases	Dates	P-value	Risk Ratio (RR)	Log Likelihood Ratio (LLR)
A. 14 Days max duration of cluster (No Covariate)						
1	10	25	12–23/8	$2x10^{-10}$	9.17	32.8
2	3	14	4–17/8	0.0012	7.05	15.2
3	1	4	15–23/8	0.0069	74.5	13.3
B. 14 Days with hospital to entry delay as covariate						
1	10	21	12–23/8	$7x10^{-9}$	9.42	28.1
2	3	14	4–17/8	0.0012	6.92	15
3	1	4	15–23/8	0.0069	73.9	13.3
C. 14 Days with hospital to intervention delay as covariate						
1	10	21	12–23/8	$5x10^{-9}$	9.54	28.4
2	3	14	4–17/8	$2.6x10^{-3}$	6.42	14.1
3	1	4	15–23/8	$6.7x10^{-3}$	71.11	13.1
D. 28 Days max duration of cluster (No Covariate)						
1	9	42	11/11 – 8/12	$3.6x10^{-15}$	7.12	45.6
2	2	13	12-22/8	$8.6x10^{-6}$	12.76	21
3	1	6	31/7 – 23/8	$4.5x10^{-4}$	41.98	16.5
4	3	17	5-19/8	$7.4x10^{-3}$	4.89	13.4
E. 28 Days with hospital to entry delay as covariate						
1	9	42	11/11 – 8/12	$4.0x10^{-13}$	6.37	41.7
2	1	9	12-22/8	$4.9x10^{-6}$	31.45	22.3
3	1	6	31/7 – 23/8	$6.5x10^{-4}$	41.5	16.5
4	3	17	5-19/8	0.012	4.87	13.3
F. 28 Days with hospital to intervention delay as covariate						
1	9	42	11/11 – 8/12	$7.7x10^{-13}$	6.28	41.2
2	1	9	12-22/8	$2.4x10^{-6}$	30.8	22.1
3	1	6	31/7 – 23/8	$4.6x10^{-4}$	40.08	16.3

As can be seen in Table 9, fitting the covariates made very little difference to the number, size and timespan of the clusters. The clusters in the model fit without covariates had the highest log likelihood ratios and thus can be considered the best model fit. Thus, inclusion of delay covariates does not improve the model and so, with the limits of the current analyses and data, there is no evidence to believe that delay time impacts upon subsequent dengue incidences.

4. Discussion

4.1. Limitations and Strengths

Before going further into the discussion of the results, it is important to acknowledge that some limitations were present in this study. There were 37 out of 160 sub-districts (23%) with missing data on dengue investigations which leads to a lower number of samples that could have been collected during 2013 in Bangkok. There is also the fact that investigation data from surveillance could only represent a fraction of the total cases occurring. Moreover, the nature of ecological study should be considered carefully when interpreting the result as ecological fallacy might occur by using aggregated data which does not account for individual risk factors (38). In addition to that, the socio-economic and demographic data were not collected specifically for this study which resulted in a limited number of variables that can be included for analysing the effect on delay time throughout different time frames. Individual and health centre data would have been able to provide a more obvious association between the covariates and the outcome. Knowing all this, utilising investigation data with a long span of time or on a larger scale might have given a more robust result.

Despite the limitations, this study has its positives, notably using sub-district level data as compared to data from the district or city level. This provides a more detailed view on the dengue spatial dynamics when interacting with other variables on a smaller scale. Moreover, this study could be considered as relatively novel because previous studies usually explore certain factors that affect data entry in specific health care settings, trying to improve dengue forecasting through mathematical models, but this study tries to explore the potential impact of delay time on subsequent dengue cases (15).

4.2. Dengue Dynamic, Delay Time, and Public Health Implications

Dengue has always been known for being an endemic disease in Thailand, especially Bangkok. Being a metropolitan city, it is susceptible to the disease as dengue is often associated with being prevalent in a more densely populated area since transmission is generally easier because people are in close proximity and having a more suitable environment for mosquitoes to reproduce (39). It is shown through the high average number of dengue incidence throughout 2013 in the sub-districts. This creates an urgency for health authorities to act swiftly and efficiently. Unfortunately, delays could happen and might affect the efforts in handling the situation which was explored in this study.

The first delay that could occur during a dengue outbreak is from the individual report to health centres. In this stage, individual health seeking behaviour plays a huge role in treating the disease and recording the actual number of diseases happening in an area. This study found that sub-districts that have a higher percentage of condominiums show higher risk albeit only a slight increased risk in delay. Higher number of condominiums could suggest that the area is affluent, but it is also important to take into account the actual distribution of other types of housing as it might have been only a fraction of the total type of housing. In other studies, people with higher capacity to afford healthcare are usually more likely to seek medical attention which might explain why the risk ratio was small (40,41). In contrast, condominium have a lower risk of delay during the hospital presentation and data entry period. This goes in line with other studies that found people with higher income have better access to healthcare and chose private to healthcare centres due having better reported timeliness and service towards patients (42–45).

Another factor found to be associated with risk of delay is owning groundwater/well. This factor however has a protective effect compared to the previous factor. There are no clear reasons for this matter, but households using groundwater/well have less risk to be a breeding ground for mosquitoes as it is usually inaccessible as compared to households using rain harvested waters (46). This might also reflect the knowledge and awareness of the area regarding dengue which is shown to have a tendency to seek medical attention the higher their knowledge and awareness (47,48).

It is known from this study that delay time from hospital to data entry has the longest average delay reaching close to 7 days. This is commonly caused by managerial and human resources factors within the hospital or other health centres. Employee training, satisfaction, and adequate tools are some of the factors that are usually associated with the delay. Whereas this study with its variable limitations found that dengue incidence, gender, and condominiums were associated with the delay.

We assume that higher dengue incidence might cause a delay in data entry due to an abundance of cases coming at the same time within a time period which could hinder the ability to quickly input the data into the system. The COVID-19 pandemic can be an example where healthcare services and workers experience being disrupted due to the abundance of cases and being a novel disease (49,50). With that in mind, strengthening the healthcare system and having protocols during outbreaks in health centres should enable healthcare workers to better deal with the situation. Consequently, higher dengue incidence could also trigger investigations to be done earlier, as found in this study. Previous studies mentioned that a lot of dengue cases might not have been detected due to people having undifferentiated fever even with surveillance taking place which suggest that there might be more cases than what was reported, prompting a quicker response (51,52).

Additionally, it was surprising to find that male have a higher risk of delay compared to females in comparison to other studies that found females are more likely to be neglected when it comes to access to healthcare (53,54). In this case, previous studies reported that excess cases of dengue are usually skewed towards male which we assume that when females are admitted to a healthcare centre, it is considered a rare case, thus prompting rapid reporting from healthcare personnel (55,56). However, more evidence is needed to determine its association through direct observation in the healthcare settings instead of relying only on aggregated data.

Delay could also happen between the data entry and investigation period. Larger areas, Chinese nationality, and having no education are shown to be associated with experiencing longer delay in this matter. Areas with higher percentage of people with no education could suggest less receptivity of people towards investigation from outside their community and less involvement in dengue prevention practices which might lead to delayed investigation (57,58). There are no clear explanations on how nationality could affect the delay in intervention. However, we speculate that it might also be related with receptivity towards investigation from authorities. Some of the population from other nationalities might be reluctant to interact with the authorities due to language barriers, illegal migration status, or other possible explanations that need to be explored further. On the other hand, this could also be said for the Lao nationalities or other foreigners that have the opposite risk compared to Chinese nationality. Another peculiar case is regarding Confucianism which has a protective risk from delayed intervention. There is no clear evidence from literature related to religion and dengue, but the number of Confucianism is small in Thailand, and it might be by chance that the population with those beliefs was distributed in areas with rapid response for investigation, thus creating a bias in the result. Nonetheless, it would be interesting to investigate further regarding the association between socio-cultural variables with different aspects of dengue transmission and intervention.

Beyond area size, specific issues concerning the city itself may create difficulties for on-field investigations. Larger areas usually need more time to prepare in order to cover all the areas needed for investigation. Unfortunately, there was no study found specifically about area and delayed intervention, but case-area targeted interventions (CATI) are usually used to maximise the effect of the investigation, although increased base transmission or reduced case detection rates could reduce its effectiveness (59). CATI itself focuses the intervention on a certain radius around the house of the patients (usually within 100m radius) and would be more effective in a low-density area, although implementing it in Bangkok might be challenging as it is a high-density area (59). Furthermore, there is an added challenge of finding the right address of the patient during the investigation, as the address is not always easily identified. It would be a different case for agricultural areas as they are usually less densely populated and not the preferred environment for *Aedes aegypti* mosquitoes to reproduce resulting in lower chance of transmission overall (60). This might suggest that CATI would be more effective to implement and require less time to prepare if cases were low in number.

Finally, even though there was no evidence found to believe that delayed time is associated with subsequent dengue cases in this study, it is important to note that a timely case report could provide assistance for making better informed decisions (15,61). This can be achieved through correcting reporting delays, better data management, and collaboration between healthcare service providers, government agencies, NGOs, or other potential stakeholders to further enhance the surveillance system (15,61–63). With the latest disruption caused by the COVID-19 pandemic, it is even more important to mend the drawbacks experienced from it.

5. Conclusion

Dengue remains as a persistent issue in Bangkok and the rest of Thailand over the years. Delays that were present during the time between symptom manifestation and hospital presentation, data entry, and investigation, along with the underlying factors highlights the need for further improvement. Although there was no evidence to believe that delay time has any correlation with subsequent dengue cases in this study, increasing surveillance efforts will remain relevant. Not only that, gaining a deeper understanding of socio-economic and demographic factors associated with delay time can prove to be beneficial for future endeavours in better controlling the disease. Considering that this study was fairly novel, conducting further research utilising different methodologies in a variety of settings is highly encouraged.

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Annexes

A. Ethical Clearance

The University Of Sheffield.

Downloaded: 08/06/2022
Approved: 12/04/2022

Fauzan Rachmatullah
Registration number: 200223272
School of Health and Related Research
Programme: European Public Health

Dear Fauzan

PROJECT TITLE: Association Between Delayed Dengue Reporting and Subsequent Dengue Cases in Bangkok
APPLICATION: Reference Number 046163

This letter confirms that you have signed a University Research Ethics Committee-approved self-declaration to confirm that your research will involve only existing research, clinical or other data that has been robustly anonymised. You have judged it to be unlikely that this project would cause offence to those who originally provided the data, should they become aware of it.

As such, on behalf of the University Research Ethics Committee, I can confirm that your project can go ahead on the basis of this self-declaration.

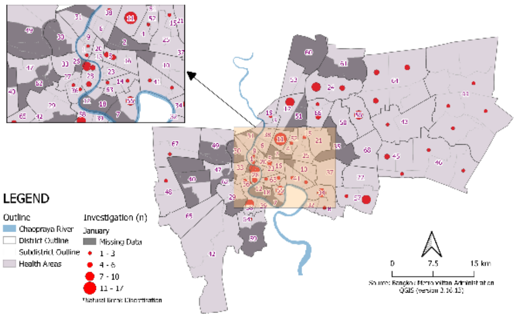
If during the course of the project you need to deviate significantly from the above-approved documentation please inform me since full ethical review may be required.

Yours sincerely

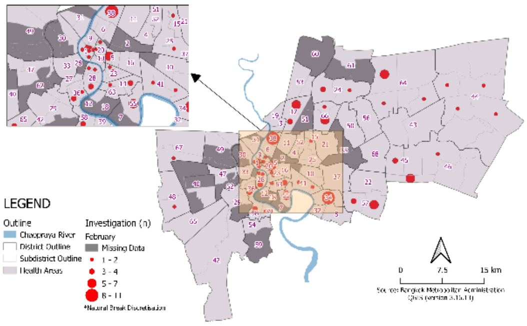
Devianee Keetharuth
Departmental Ethics Administrator

B. Number of Dengue Investigation Maps per month

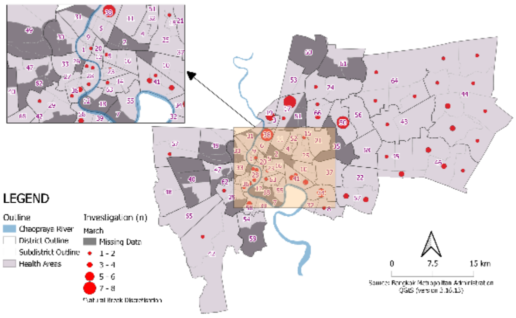
Number of Dengue Investigation in Bangkok Subdistricts, January 2013



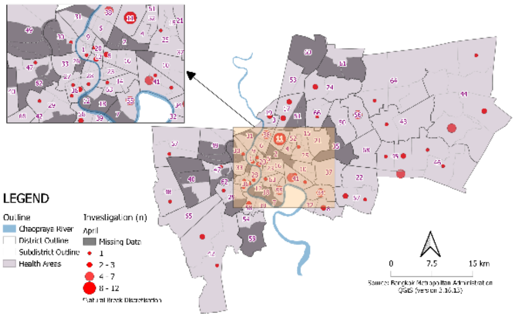
Number of Dengue Investigation in Bangkok Subdistricts, February 2013



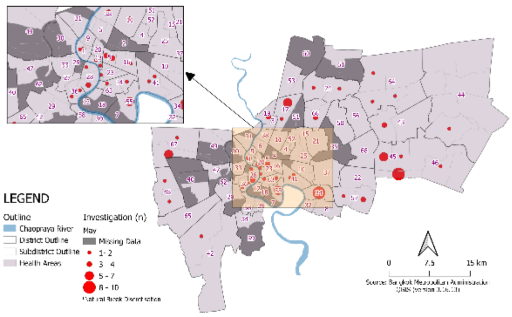
Number of Dengue Investigation in Bangkok Subdistricts, March 2013



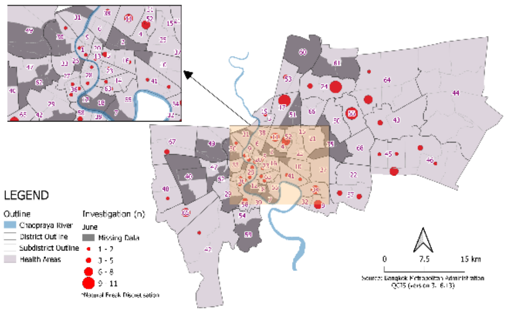
Number of Dengue Investigation in Bangkok Subdistricts, April 2013



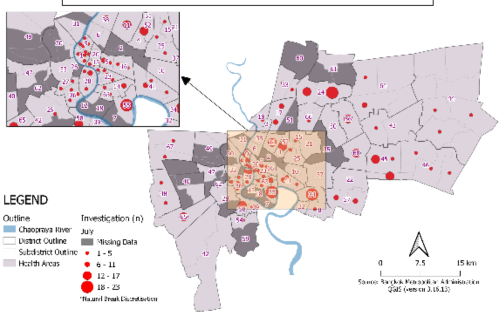
Number of Dengue Investigation in Bangkok Subdistricts, May 2013



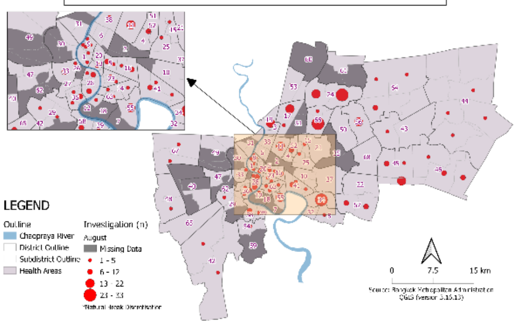
Number of Dengue Investigation in Bangkok Subdistricts, June 2013

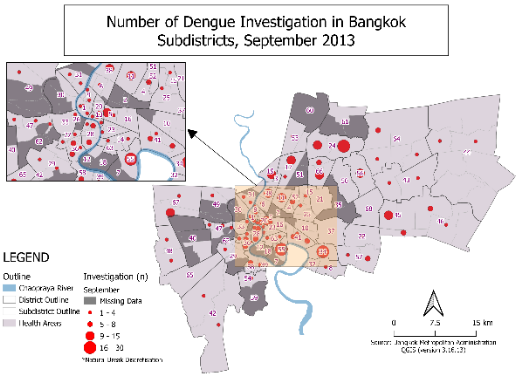


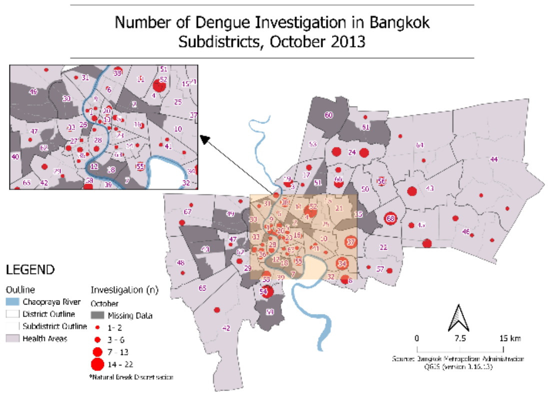
Number of Dengue Investigation in Bangkok Subdistricts, July 2013

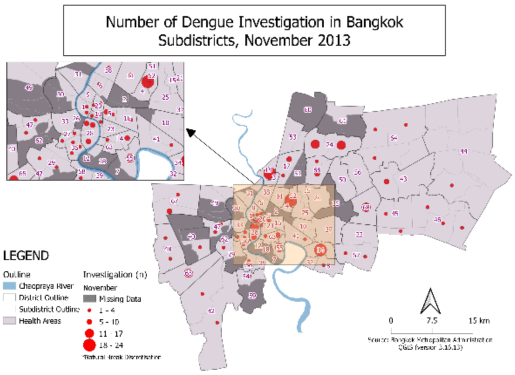


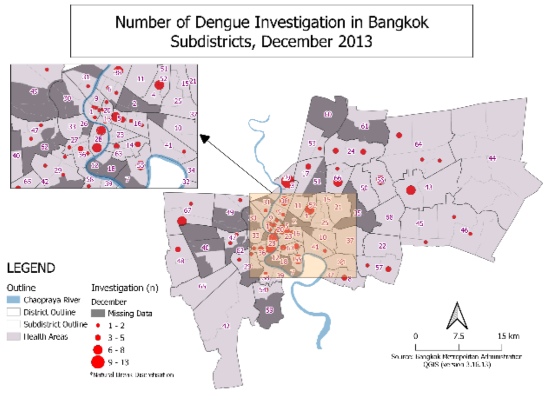
Number of Dengue Investigation in Bangkok Subdistricts, August 2013




Number of Dengue Investigation in Bangkok
Subdistricts, September 2013
LEGEND
Outline
Chaopraya River
District Outline
Subdistrict Outline
Health Areas
Investigation (n)
September
Missing Data
1 - 4
5 - 8
9 - 15
16 - 30
0
7.5
15 km


Number of Dengue Investigation in Bangkok
Subdistricts, October 2013
LEGEND
Outline
Chaopraya River
District Outline
Subdistrict Outline
Health Areas
Investigation (n)
October
Missing Data
1 - 2
3 - 6
7 - 13
14 - 22
*Natural Break Discretisation
0
7.5
15 km


Number of Dengue Investigation in Bangkok
Subdistricts, November 2013
LEGEND
Outline
Chaopraya River
District Outline
Subdistrict Outline
Health Areas
Investigation (n)
November
Missing Data
1 - 4
5 - 10
11 - 17
18 - 24
0
7.5
15 km


Number of Dengue Investigation in Bangkok
Subdistricts, December 2013
LEGEND
Outline
Chaopraya River
District Outline
Subdistrict Outline
Health Areas
Investigation (n)
December
Missing Data
1 - 2
3 - 5
6 - 8
9 - 13
0
7.5
15 km