ENVIRONMENTAL RISK FACTORS ASSOCIATED WITH PLASMODIUM KNOWLESI IN SABAH, MALAYSIA.

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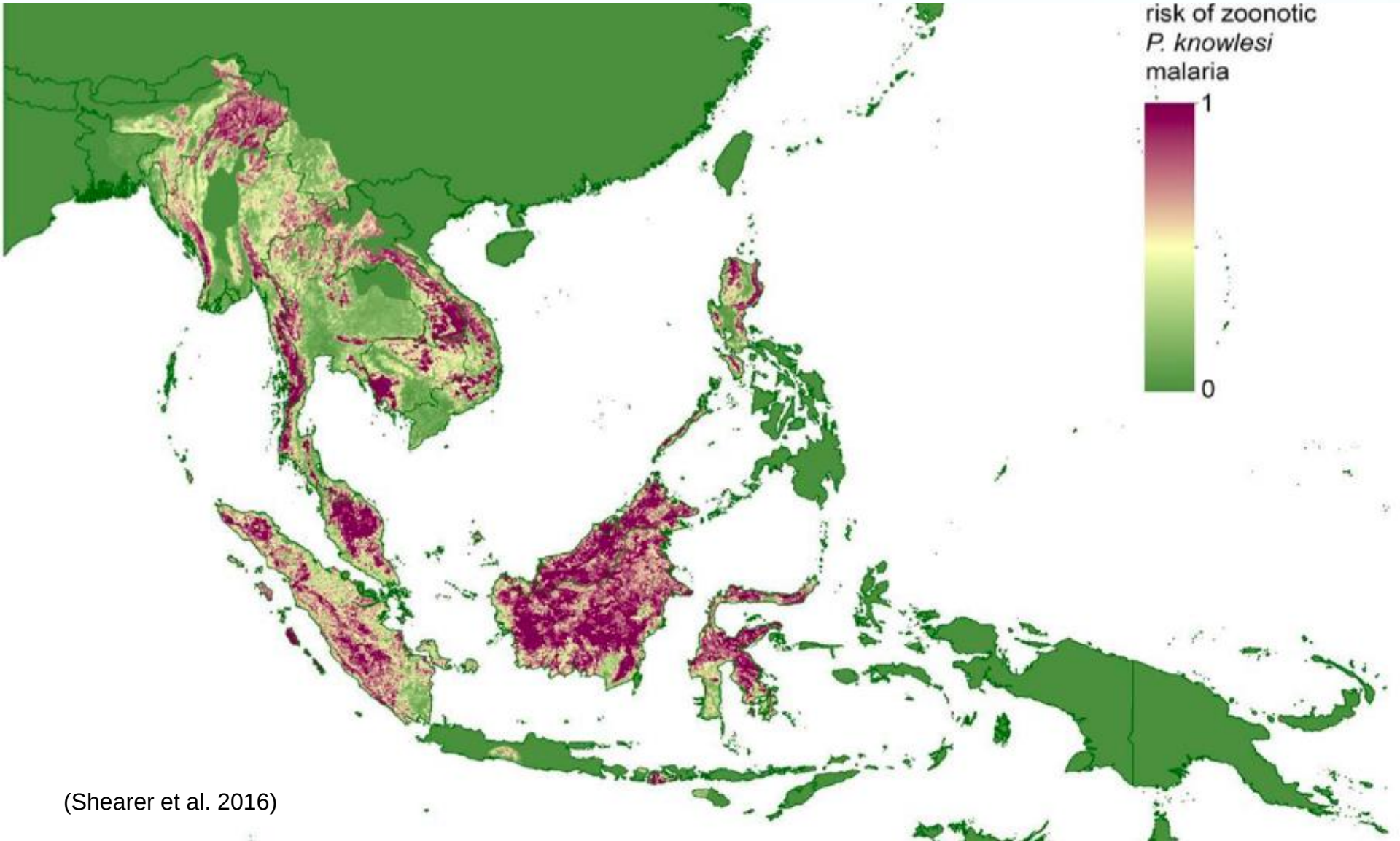
Seminar on climate change 4th May 2017
United Nation University-International Institute for Global Health (UNU-IIGH)

INTRODUCTION

- Malaria is still a major public health concern worldwide.
- WHO estimated 300-500 million malaria cases per year & causing 1 million deaths due to this disease and its complications. (Yusuf et al 2013)
- In Malaysia, the number of malaria cases has declined from 12 thousand to 4 thousand from 2000 to 2012. (MOH, 2014)
  - MOH targets to eliminate malaria by the year 2020.
- Despite the successful malaria control program, the prevalence of *P. knowlesi* cases is still alarming in Sabah. There is still limited studies to identify the environmental risk factors associated with *P. knowlesi* infection in Sabah.
- In 2010-2011, almost half of fatal malaria cases were caused by *P. knowlesi* infection (Rajahram et al. 2016)

DISTRIBUTION *P. KNOWLESI* in SEA



(Shearer et al. 2016)

OBJECTIVE

General Objective :

- To analyze the factors associated with *P. knowlesi* infection for Sabah, Malaysia.

Specific Objective

1. To explore the prevalence and characteristics of *P. knowlesi* cases in Sabah for the year 2013 and 2014.
2. To explore the characteristics of environmental factors (climate factors and non-climate factors) related to the occurrences of *P. knowlesi* cases in Sabah.
3. To evaluate the spatial distribution of malaria density areas in Sabah.
4. To examine the factors associated with *P. knowlesi* density areas in Sabah
5. To develop a model for *P. knowlesi* occurrence for Sabah.

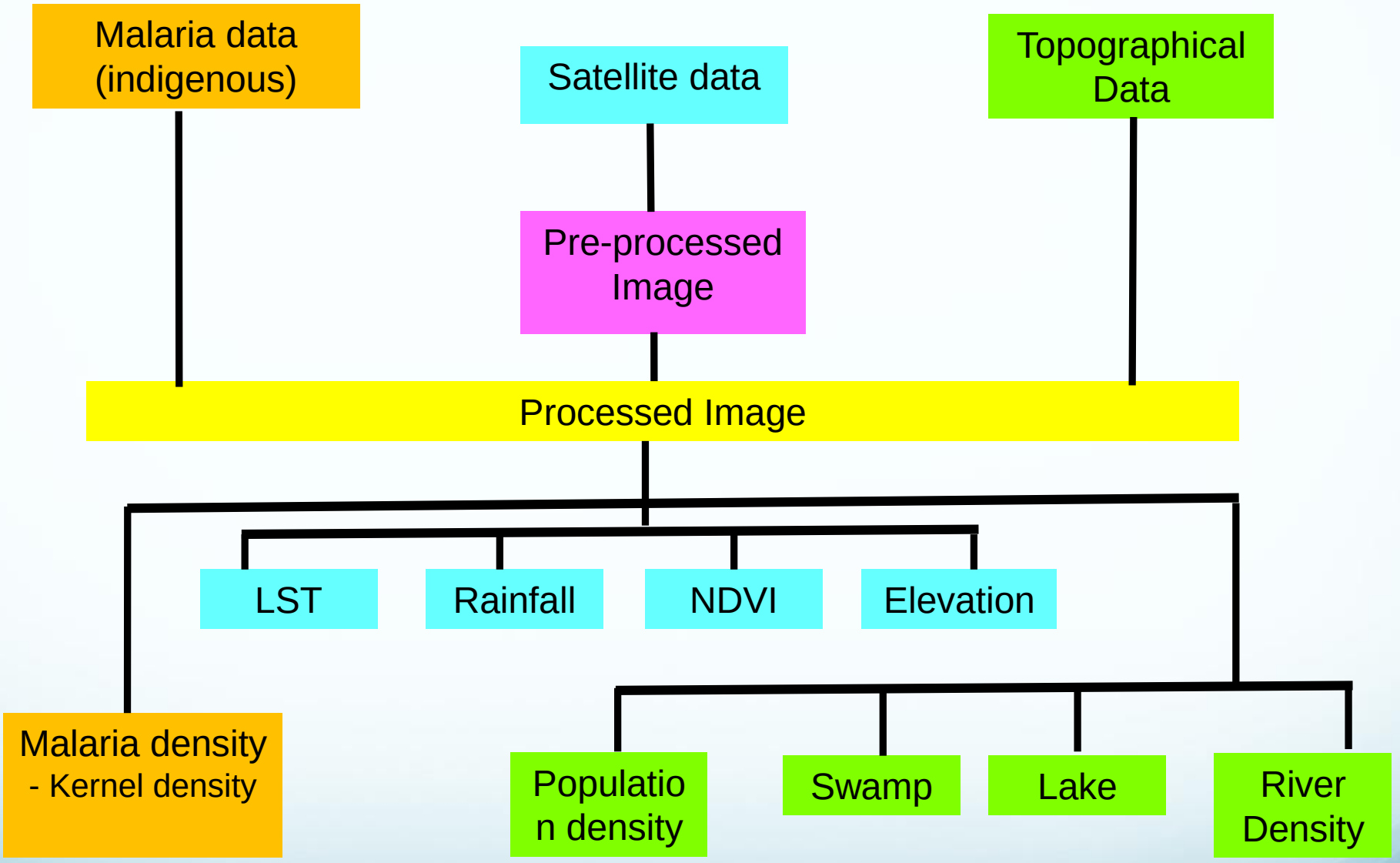
METHODOLOGY

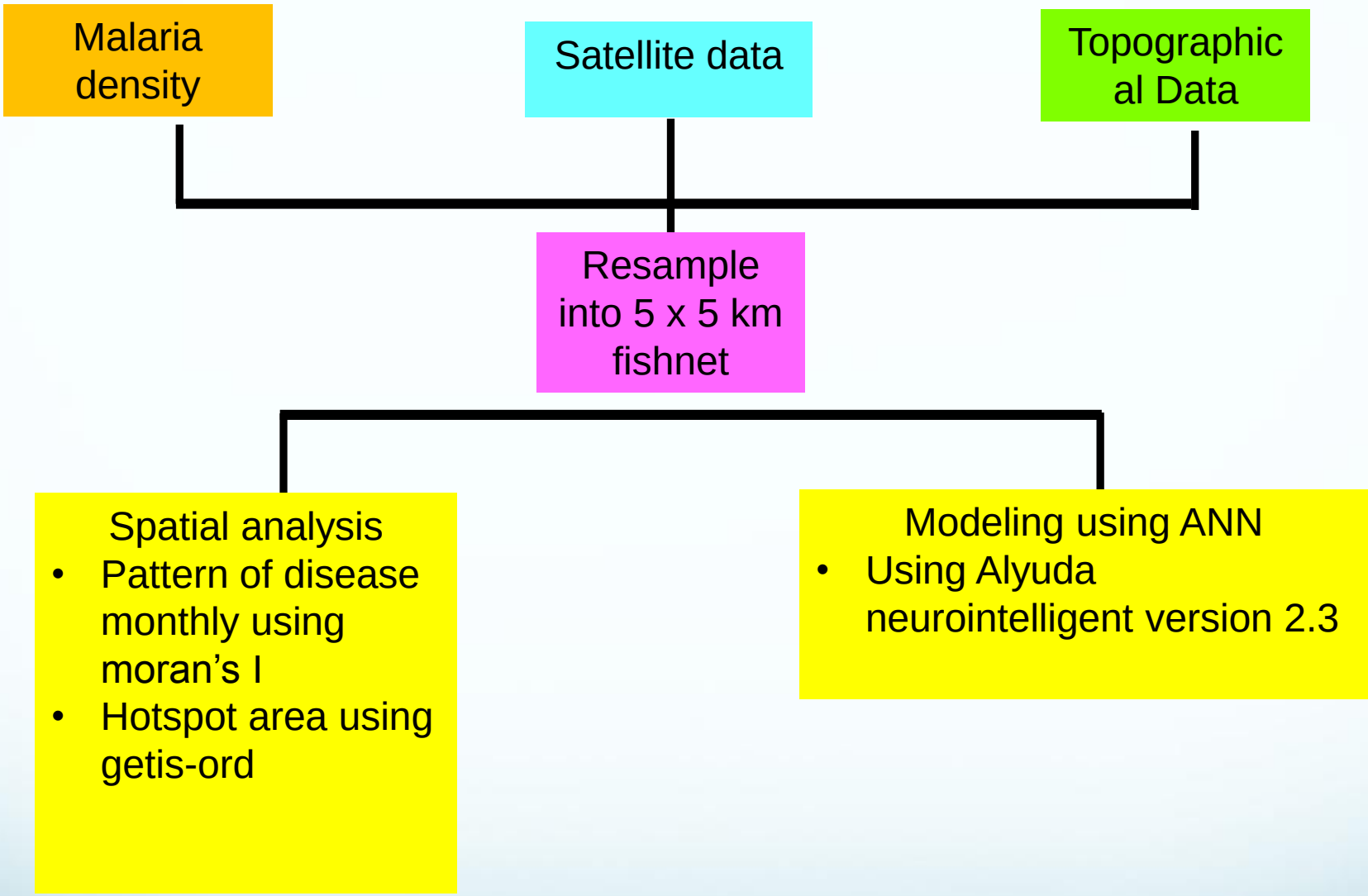
Latitudes of 4º to 7º north of the equator and longitudes of 115º to 119º east.

METHODOLOGY

- Study Design
  - Retrospective, ecological study from the period of 01 January 2013 – 31 December 2014.
- Study subject
  - Districts in Sabah

	VARIABLE	SOURCE OF DATA	RESOLUTION	FREQUENCY	NUMBER OF IMAGES
1.	**Malaria**	**Vekpro, MOH**		**Daily**	**104 images**
2	**Satellite data**				
	LST	MOD11A	1 km	Every 6 days	90 images
	Rainfall	TRMM	30 km	Daily	730 images
	NDVI	Landsat 8	250 m	Weekly	137 images
	Elevation	STRM	1 km		12 images
3	**Topographical data**				
	Population density	ESRI Malaysia			1 images
	River density	JUPEM	1;50,000		1 images
	Swamp	JUPEM	1;50,000		1 images
	Lake	JUPEM	1;50,000		1 images
				TOTAL IMAGES	1077 images


Malaria data (indigenous)
Satellite data
Topographical Data
Pre-processed Image
Processed Image
LST
Rainfall
NDVI
Elevation
Malaria density - Kernel density
Populatio n density
Swamp
Lake
River Density


Malaria density
Satellite data
Topographical Data
Resample into 5 x 5 km fishnet
Spatial analysis
• Pattern of disease monthly using moran's I
• Hotspot area using getis-ord
Modeling using ANN
• Using Alyuda neurointelligent version 2.3

Run analysis for 8 parameter

- Feature selection: Stepwise
- Select best fit model
  - 6 parameter fit model

Pre-processing- scaling of data

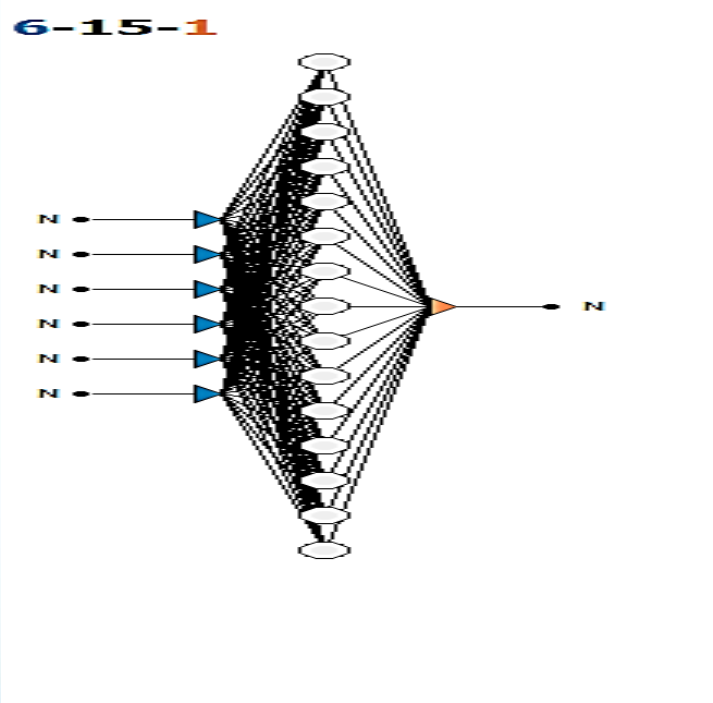
Model design

- best fit design(6-15-1) (fitness:4852)

Training the data

- Test selected : Quick propagation
- Correlation 0.70

Testing result-paired sample t-test between observed & predicted

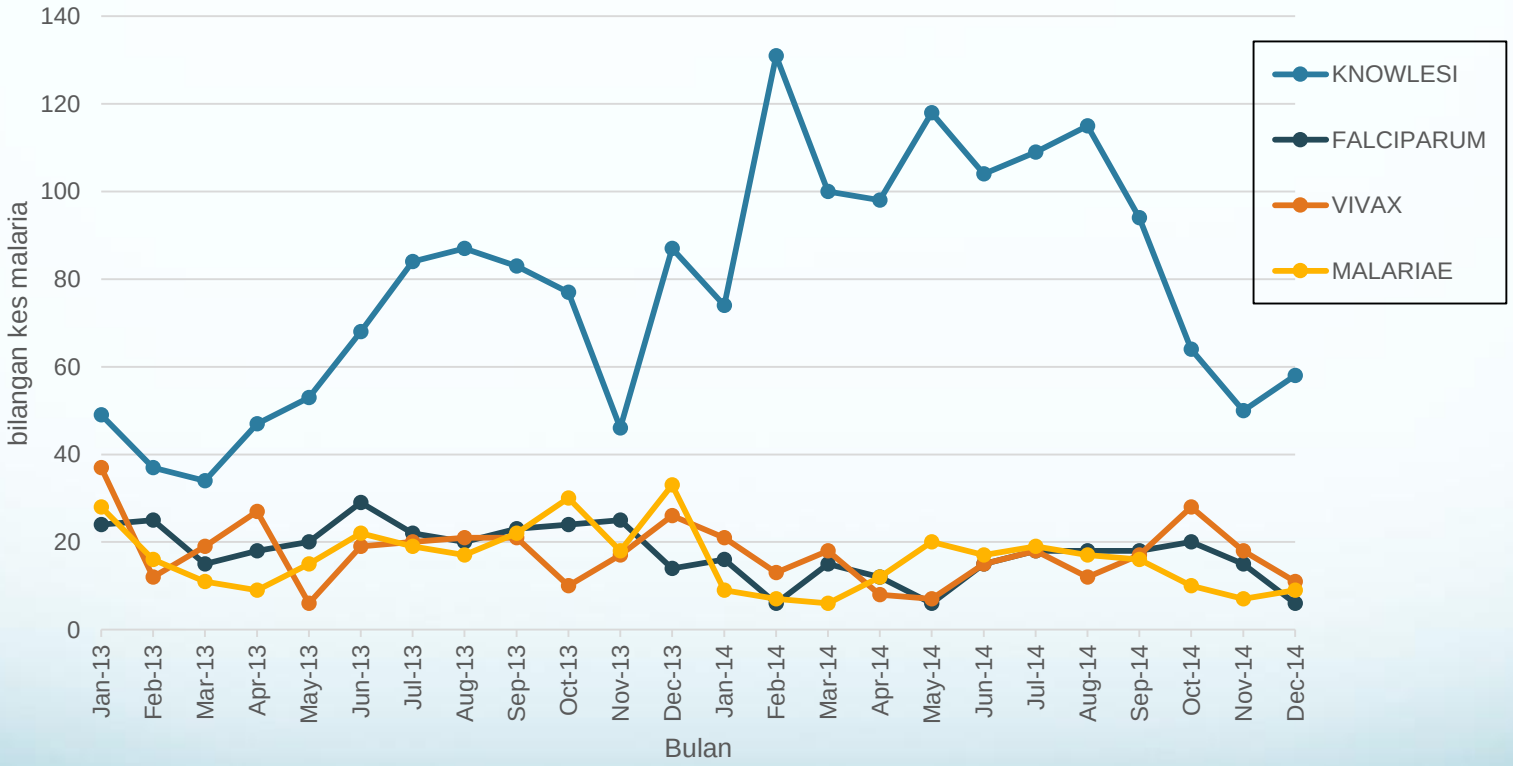


RESULTS AND DISCUSSION

Characteristics of malaria cases in Sabah, 2013-2014

		2013	2014	Total
1.	Total no. of cases	1608 (47.48%)	1779 (52.52%)	3387
2.	Case classification	1513 (46.9%)	1712 (53.1%)	3225
	Indigenous	**88 (57.9%)**	**64 (42.11%)**	**152**
	Imported	3 (100%)	0 (0.0%)	3
	Induced	1 (50%)	1(50%)	2
	Introduced	1 (33.3%)	2(66.77%)	3
	Relapse	1513 (46.9%)	1712 (53.1%)	3225

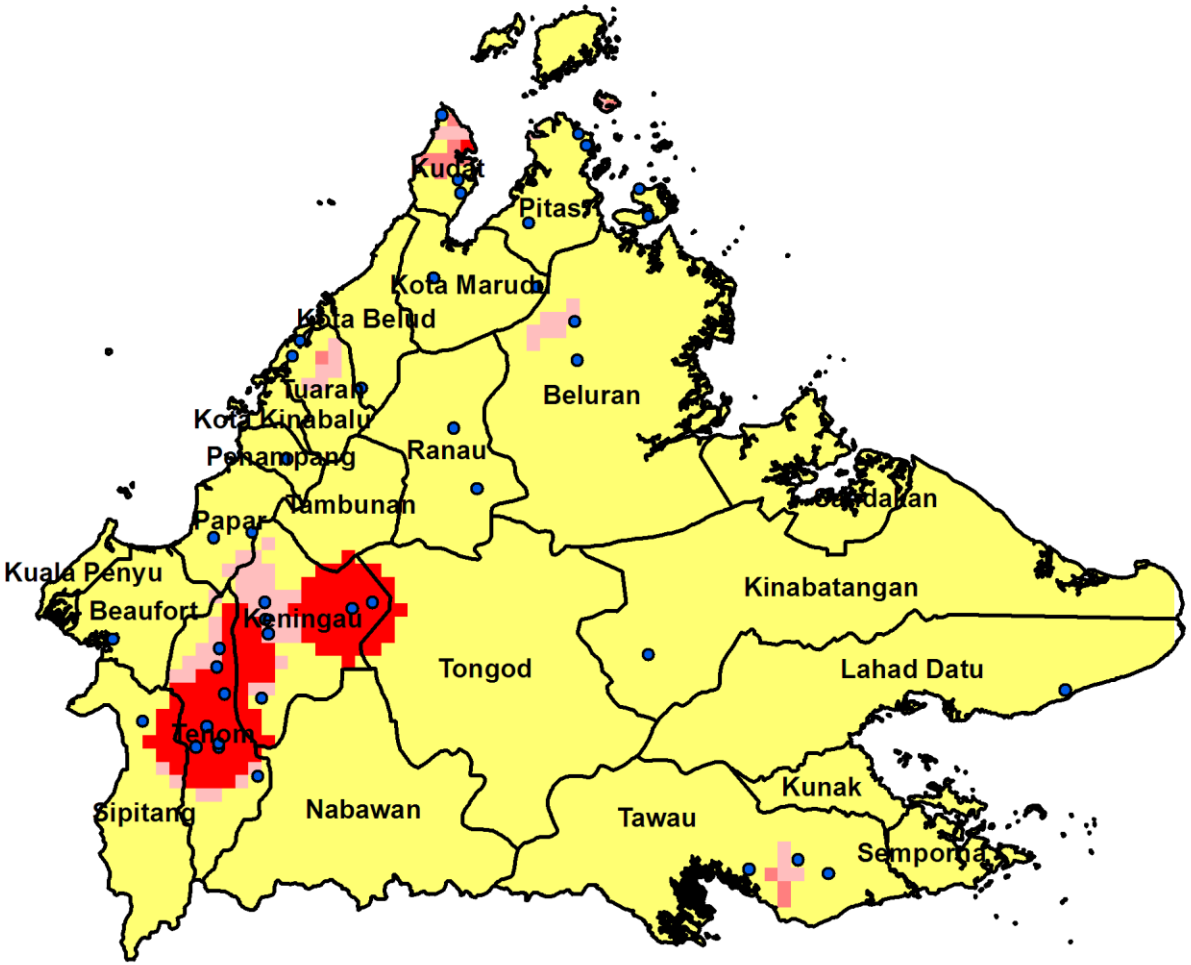
Distribution of malaria species in Sabah,2013-2014



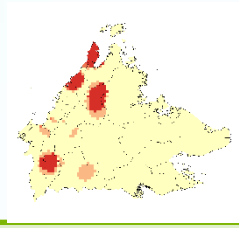
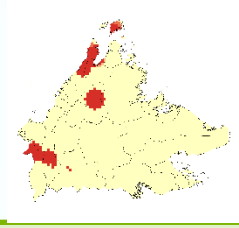
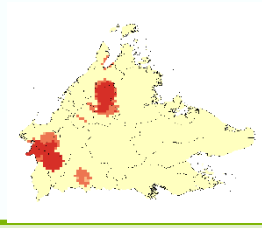
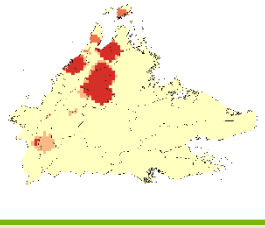
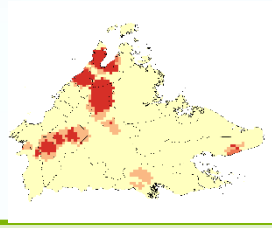
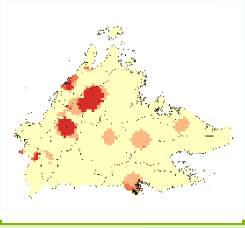
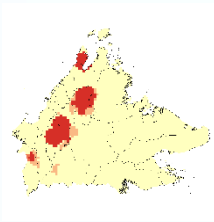
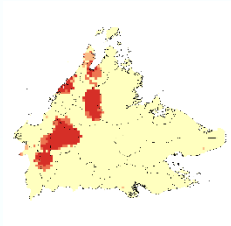
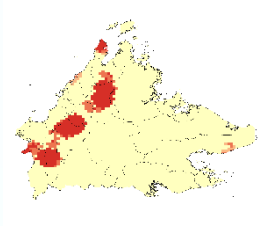
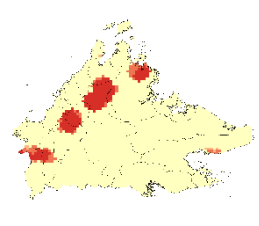
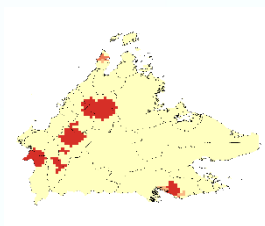
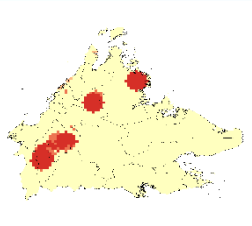
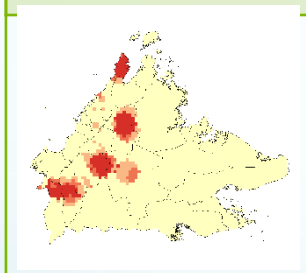
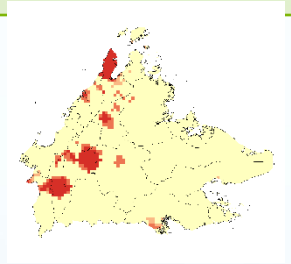
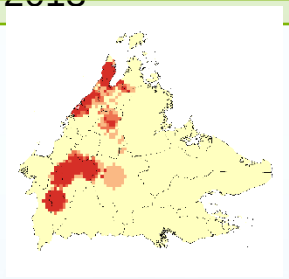
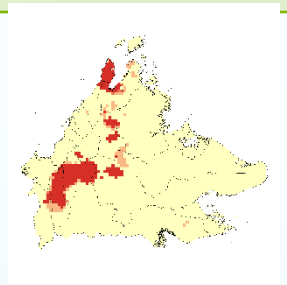
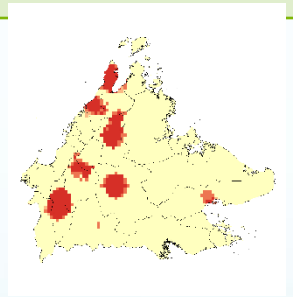
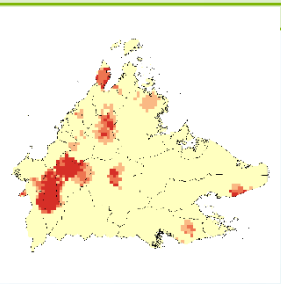
Characteristics of *P. knowlesi* cases

- **Males** (83.5%), **mean age** 36 years old, **Malaysians**, **Bumiputera** Sabahans (82.3%).
- **Agricultural sector** contributes the highest no. of cases (82.2%), followed by forest-related activities such as lodging and collection of forest products (17.5%).

- Moran's I – *P. knowlesi* cases occur in clusters.
  - Moran index is between 0.22 - 0.24
  - Z-score 15-16
  - P-value is significant (<0.001)



DECEMBER 2014

					
January 2013	February 2013	Mac 2013	April 2013	May 2014	June 2014
					
July 2014	August 2013	September 2013	October 2013	November 2013	December 2013
					
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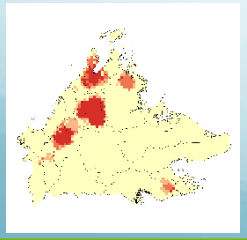	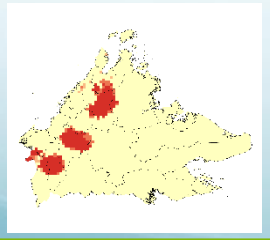	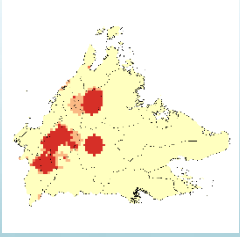	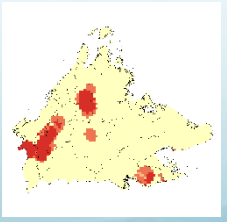	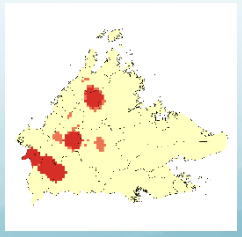	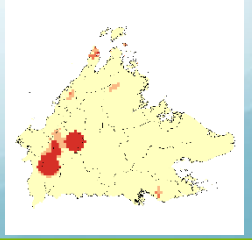
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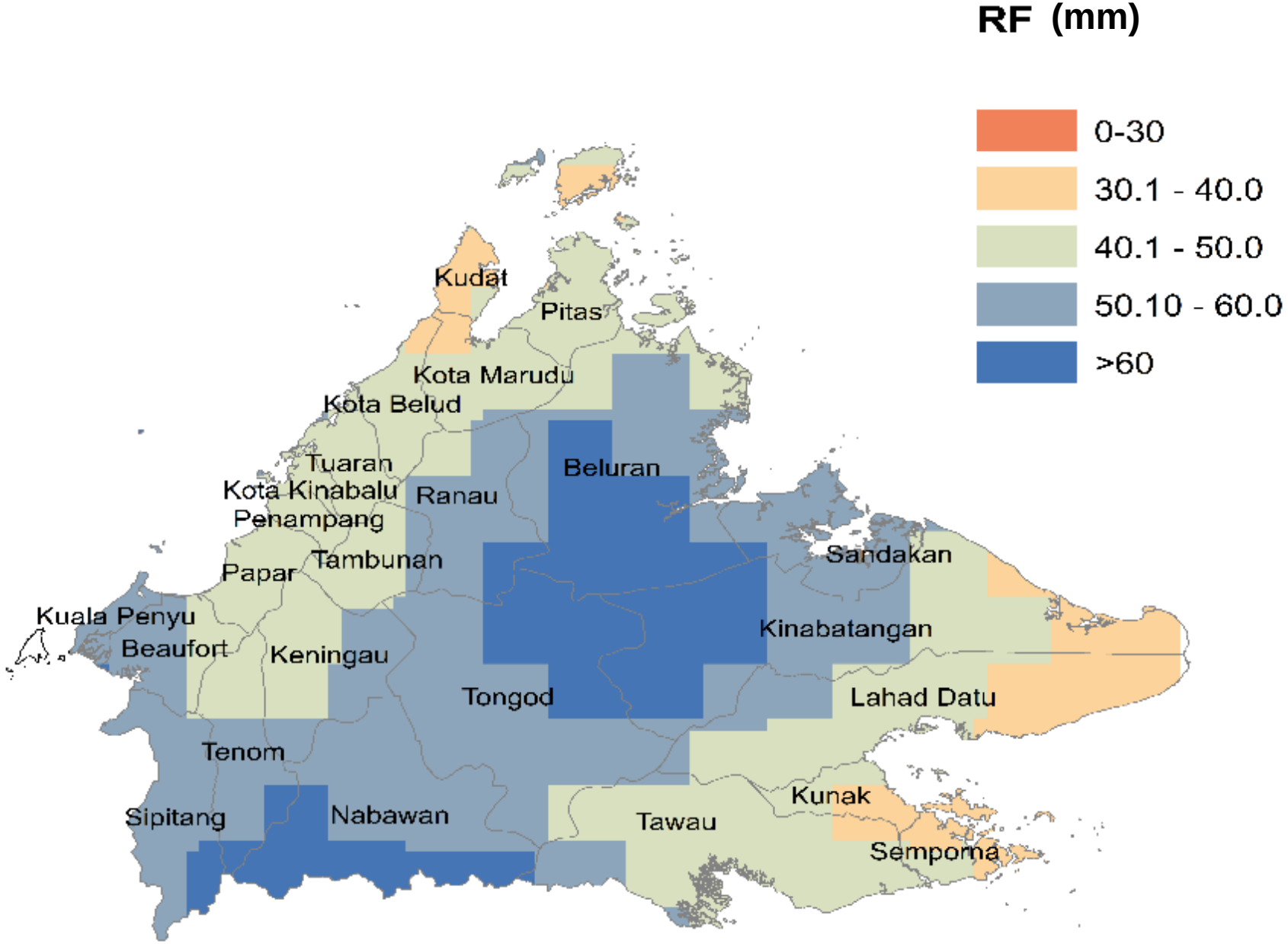
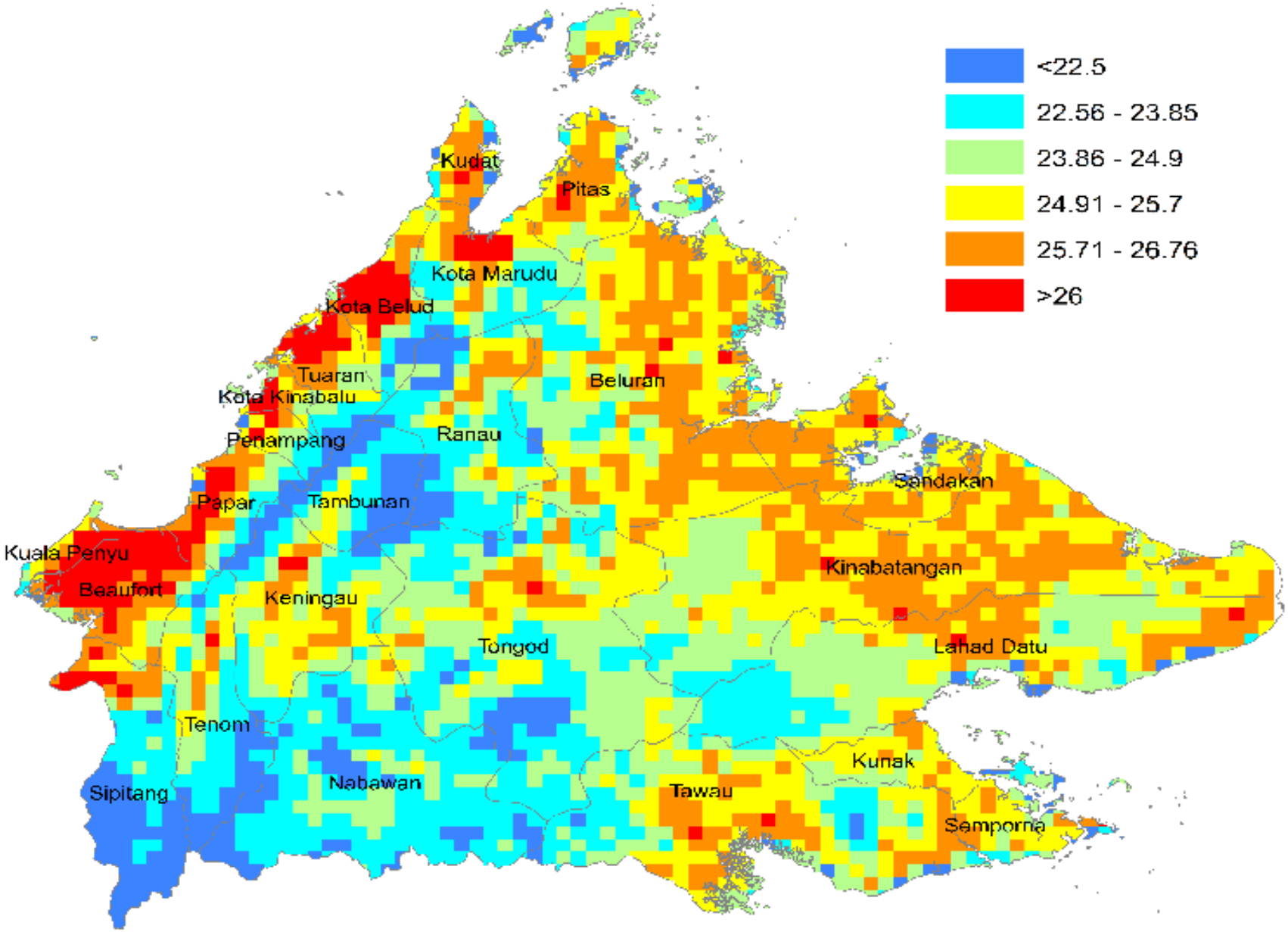

RF (mm)
0-30
30.1 - 40.0
40.1 - 50.0
50.10 - 60.0
>60
Kudat
Pitas
Kota Marudu
Kota Belud
Tuaran
Kota Kinabalu
Penampang
Ranau
Beluran
Sandakan
Papar
Tambunan
Kuala Penyu
Beaufort
Keningau
Kinabatangan
Tongod
Lahad Datu
Tenom
Kunak
Sipitang
Nabawan
Tawau
Semporna


LST (°C)
<22.5
22.56 - 23.85
23.86 - 24.9
24.91 - 25.7
25.71 - 26.76
>26
Kudat
Pitas
Kota Marudu
Kota Belud
Tuaran
Kota Kinabalu
Penampang
Ranau
Beluran
Sandakan
Papar
Tambunan
Kuala Penyu
Beaufort
Keningau
Kinabatangan
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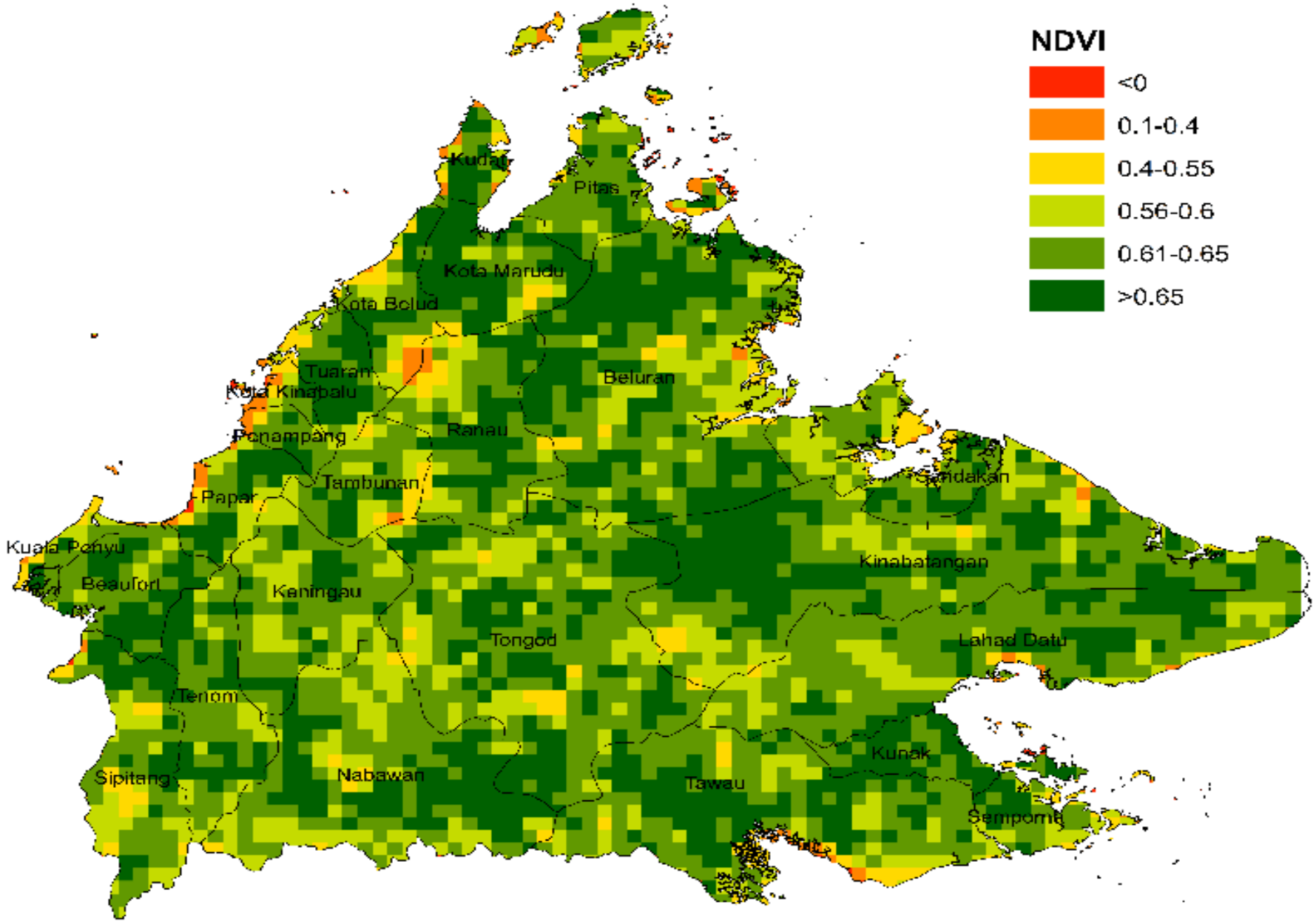
Lahad Datu
Tenom
Kunak
Nabawan
Sipitang
Tawau
Semporna


NDVI
<0
0.1-0.4
0.4-0.55
0.56-0.6
0.61-0.65
>0.65
Kudat
Pitas
Kota Marudu
Kota Belud
Tuaran
Kota Kinabalu
Penampang
Ranau
Beluran
Tambunan
Papar
Sandakan
Kuala Penyu
Beaufort
Keningau
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Lahad Datu
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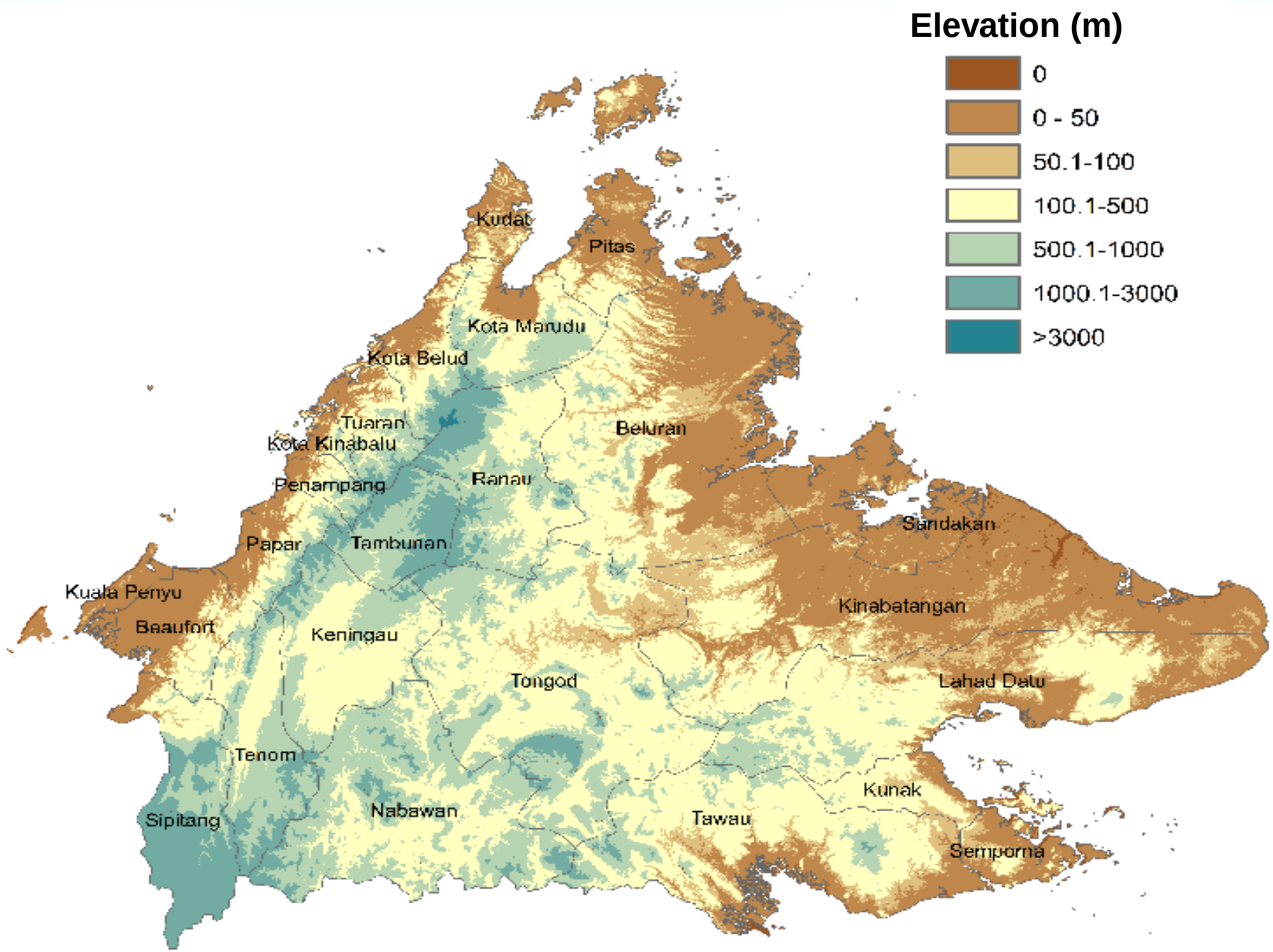
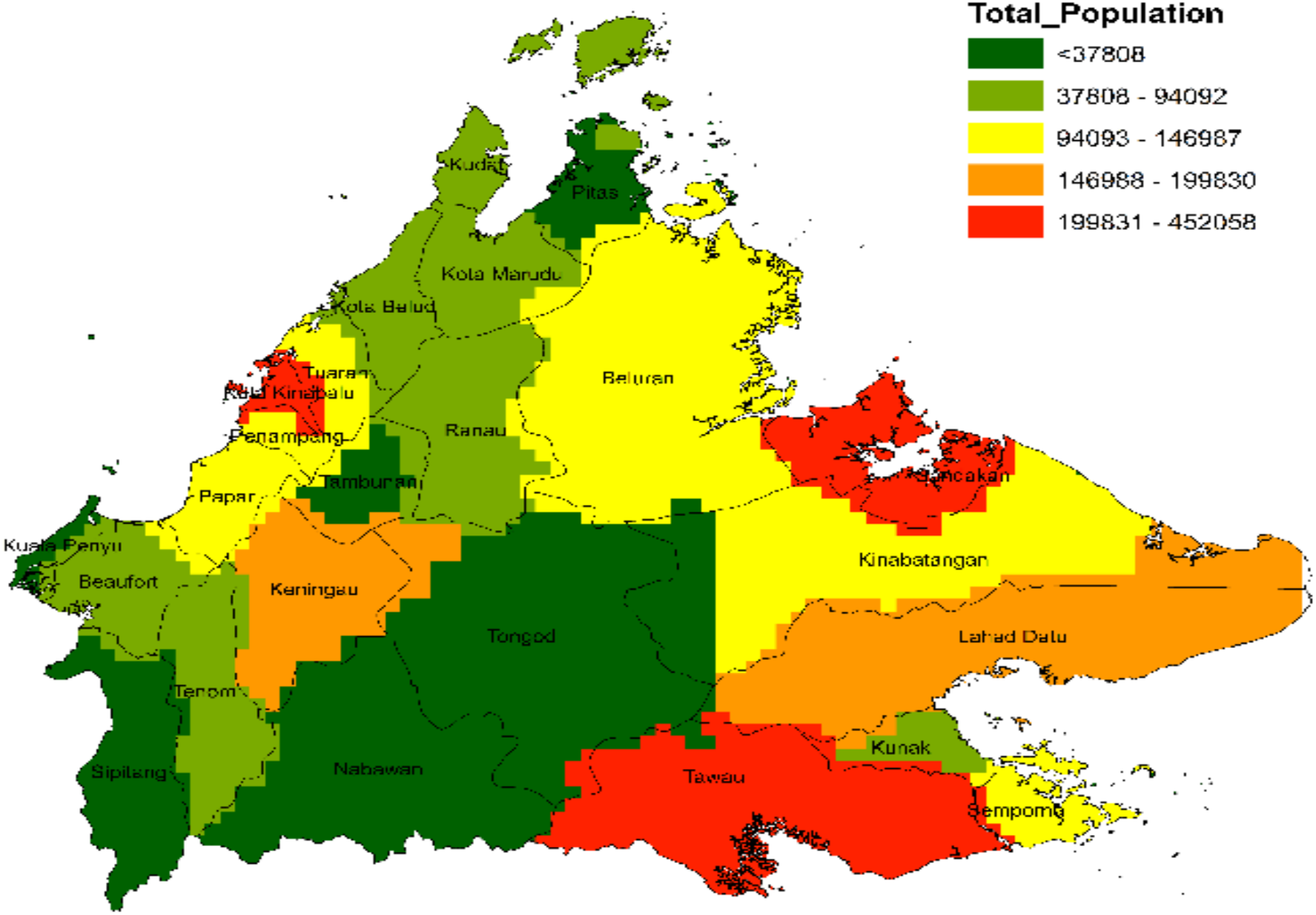
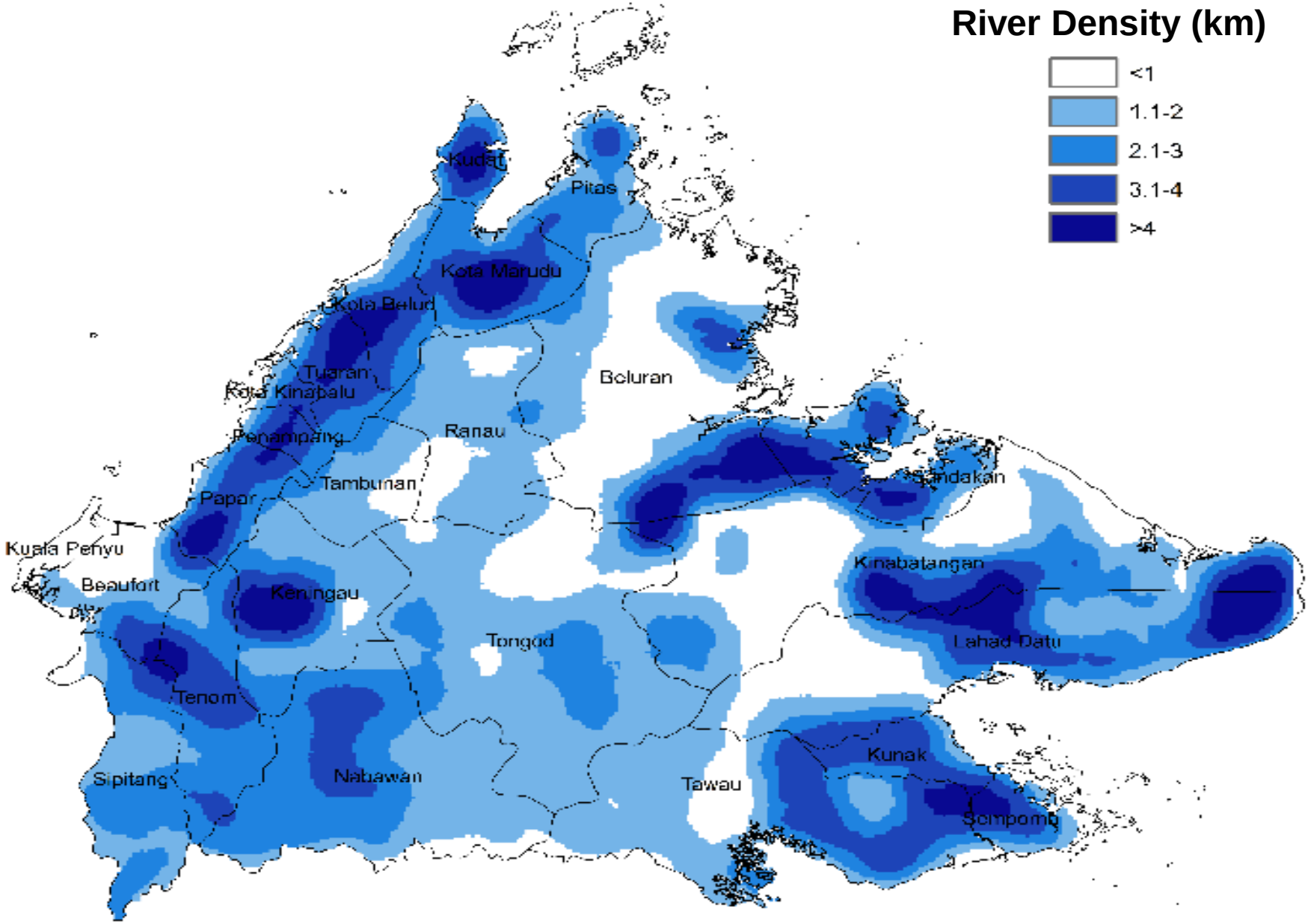
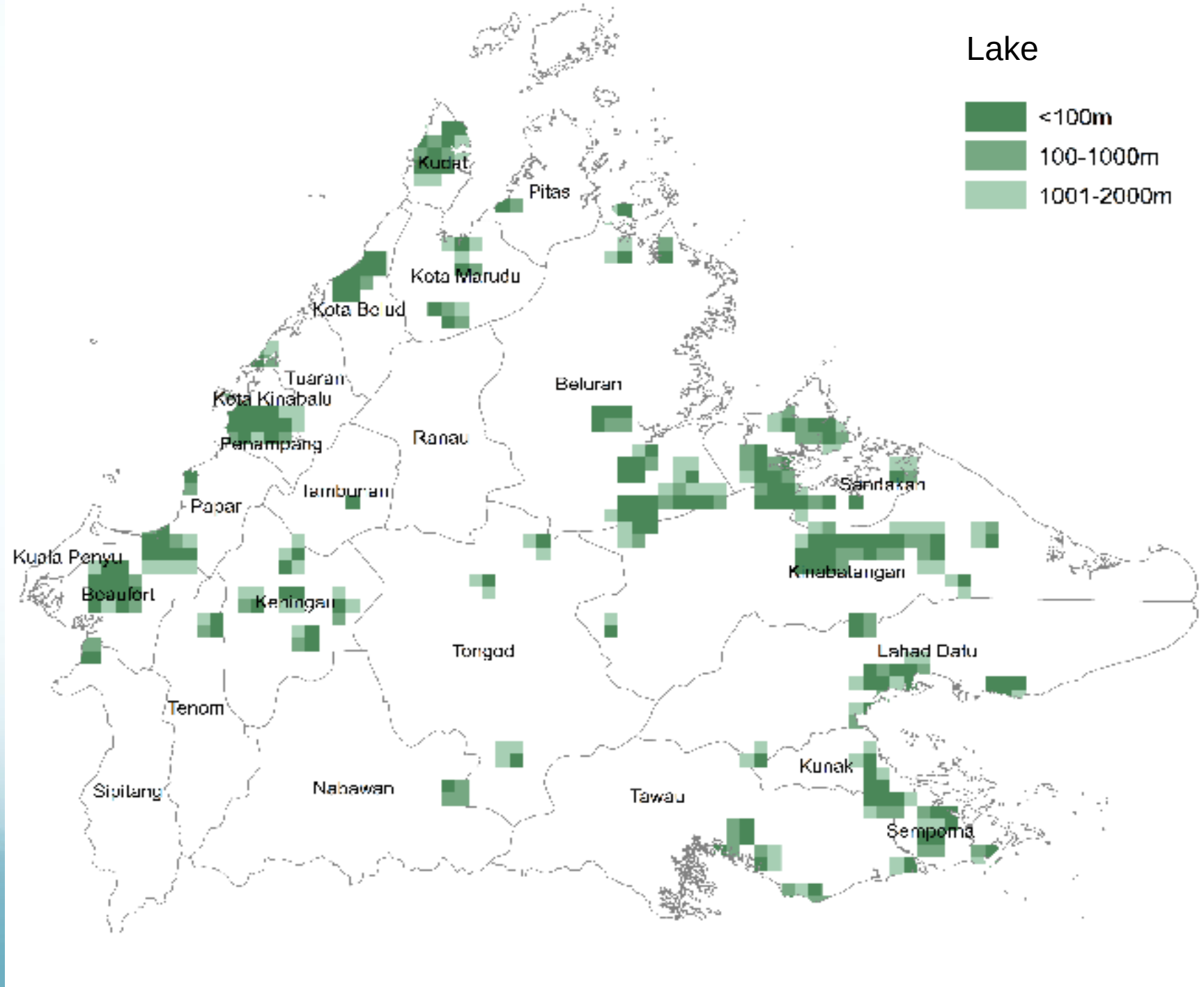
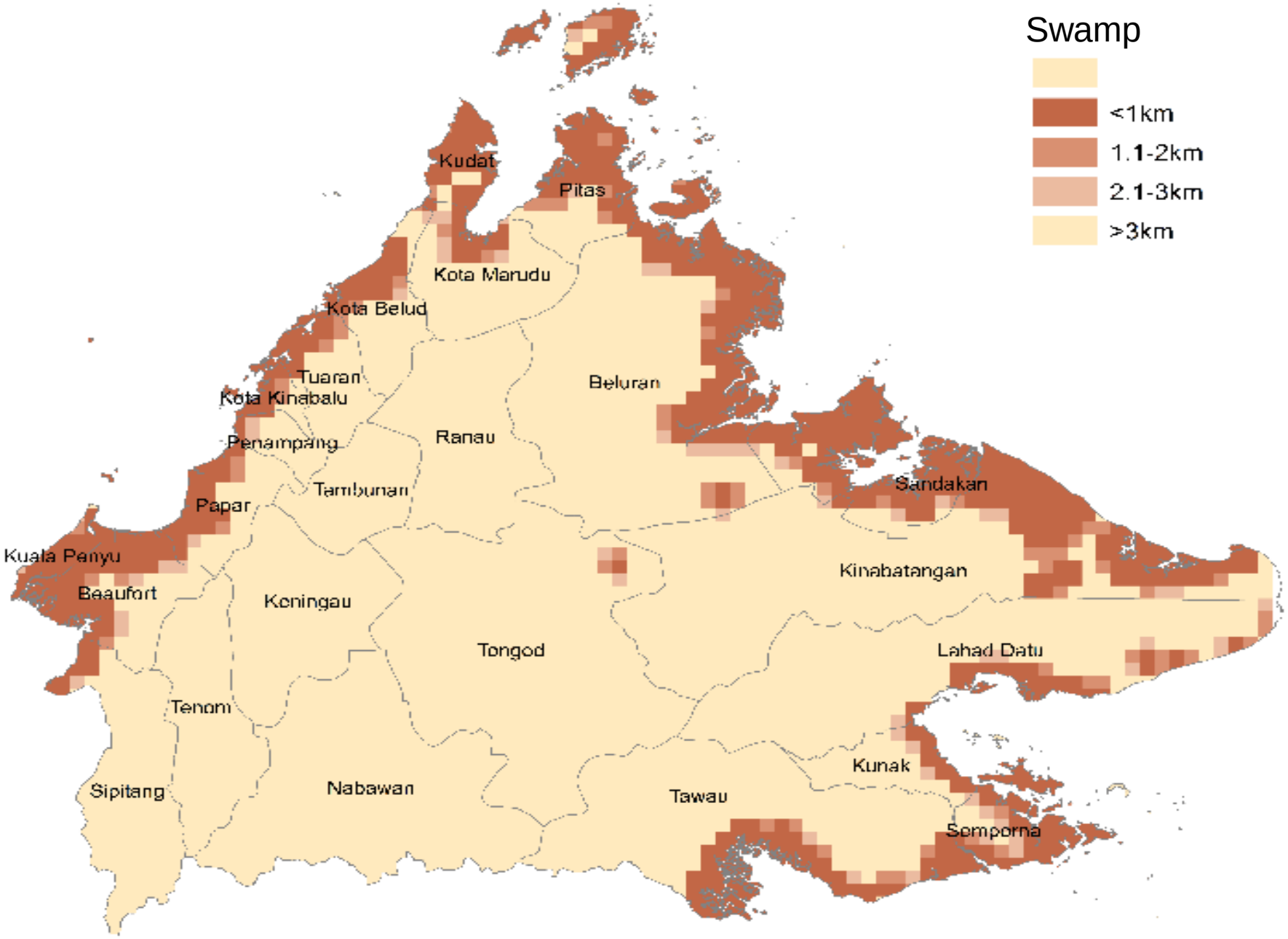
Nabawan
Tawau
Semporna


Elevation (m)
0
0 - 50
50.1-100
100.1-500
500.1-1000
1000.1-3000
>3000
Kudat
Pitas
Kota Marudu
Kota Belud
Tuaran
Kota Kinabalu
Penampang
Ranau
Beluran
Sandakan
Papar
Tambunan
Kuala Penyu
Beaufort
Keningau
Kinabatangan
Tongod
Lahad Datu
Tenom
Kunak
Sipitang
Nabawan
Tawau
Semporna


Total_Population
<37808
37808 - 94092
94093 - 146987
146988 - 199830
199831 - 452058
Kudat
Pitas
Kota Marudu
Kota Belud
Tuaran
Kota Kinabalu
Penampang
Ranau
Beluran
Tamburan
Papar
Kuala Penyu
Beaufort
Keningau
Tongod
Kinabatangan
Lahad Datu
Tenom
Sipitang
Nabawan
Tawau
Kunak
Semporna


River Density (km)
<1
1.1-2
2.1-3
3.1-4
>4
Kudat
Pitas
Kota Marudu
Kota Belud
Tuaran
Kota Kinabalu
Penampang
Papar
Kuala Penyu
Beaufort
Keningau
Tambunan
Ranau
Beluran
Sandakan
Kinabatangan
Lahad Datu
Tongod
Tenom
Sipitang
Nabawan
Tawau
Kunak
Semporna


Lake
<100m
100-1000m
1001-2000m
Kudat
Pitas
Kota Marudu
Kota Belud
Tuaran
Kota Kinabalu
Penampang
Ranau
Beluran
Sandakan
Papar
Tamburan
Kuala Penyu
Beaufort
Keningau
Kinabatangan
Tongod
Lahad Datu
Tenom
Kunak
Sipitang
Nabawan
Tawau
Semporna


Swamp
<1km
1.1-2km
2.1-3km
>3km
Kudat
Pitas
Kota Marudu
Kota Belud
Tuaran
Kota Kinabalu
Penampang
Ranau
Beluran
Tambunan
Papar
Sandakan
Kuala Penyu
Kinabatangan
Beaufort
Keningau
Tongod
Lahad Datu
Tenom
Kunak
Sipitang
Nabawan
Tawau
Semporna

MODELING USING ANN

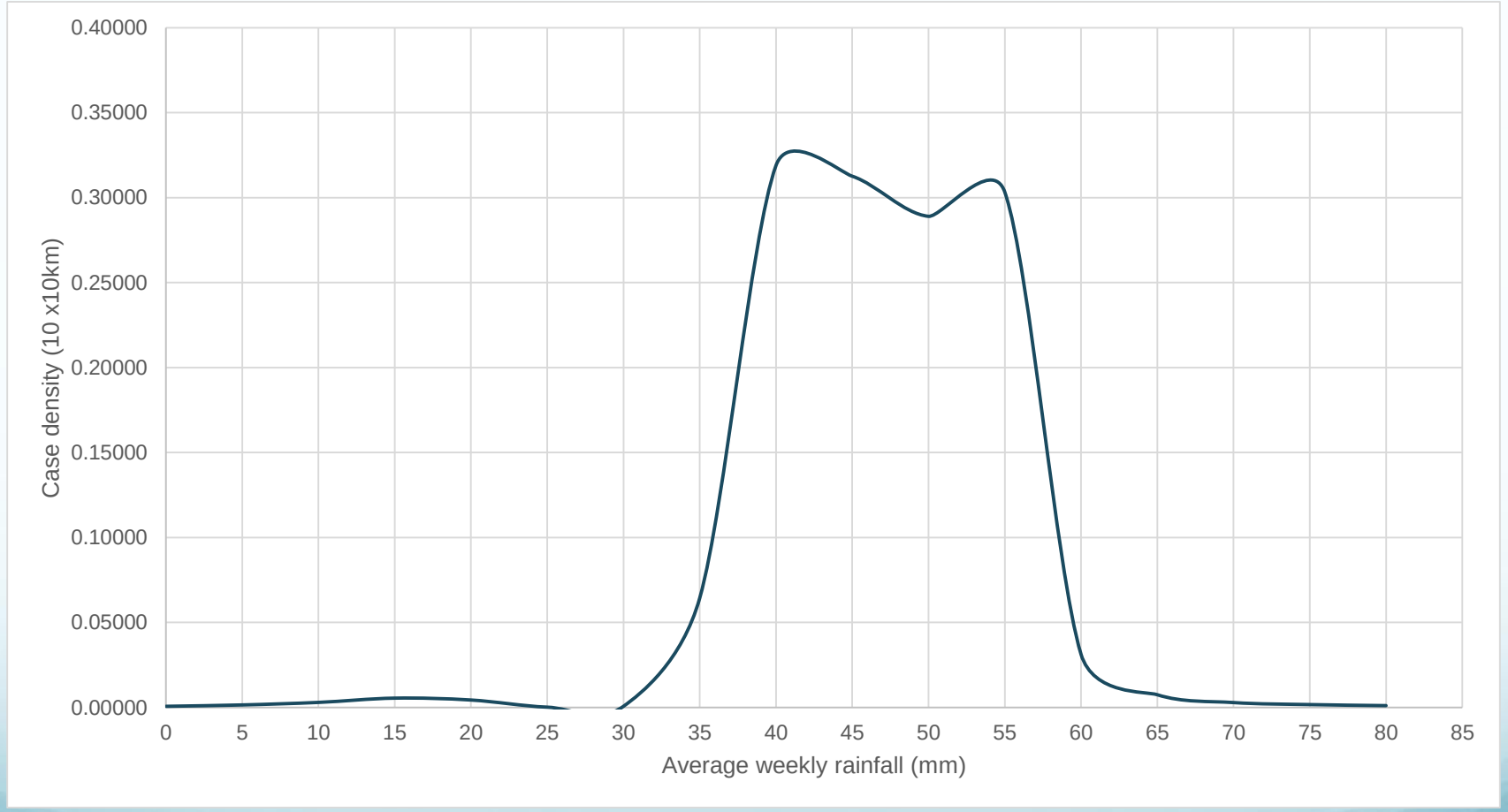
- Alyuda neurointelligent 2.2 software was used.
- Based on feature selection; forward stepwise model with a smoothing factor of 0.1 was selected.
  - 6 predicted factors were selected based on the best fit model
    1. Rainfall
    2. LST
    3. NDVI
    4. Elevation
    5. River
    6. Population density
  - Neuron 6-15-1 design was selected.

	Mean(SD)	R	p	Paired sample t-test	p
Actual case	0.000226(0.00045)	0.70	<0.001	0.975	**0.329**
Predicted case	0.000219(0.00031)				

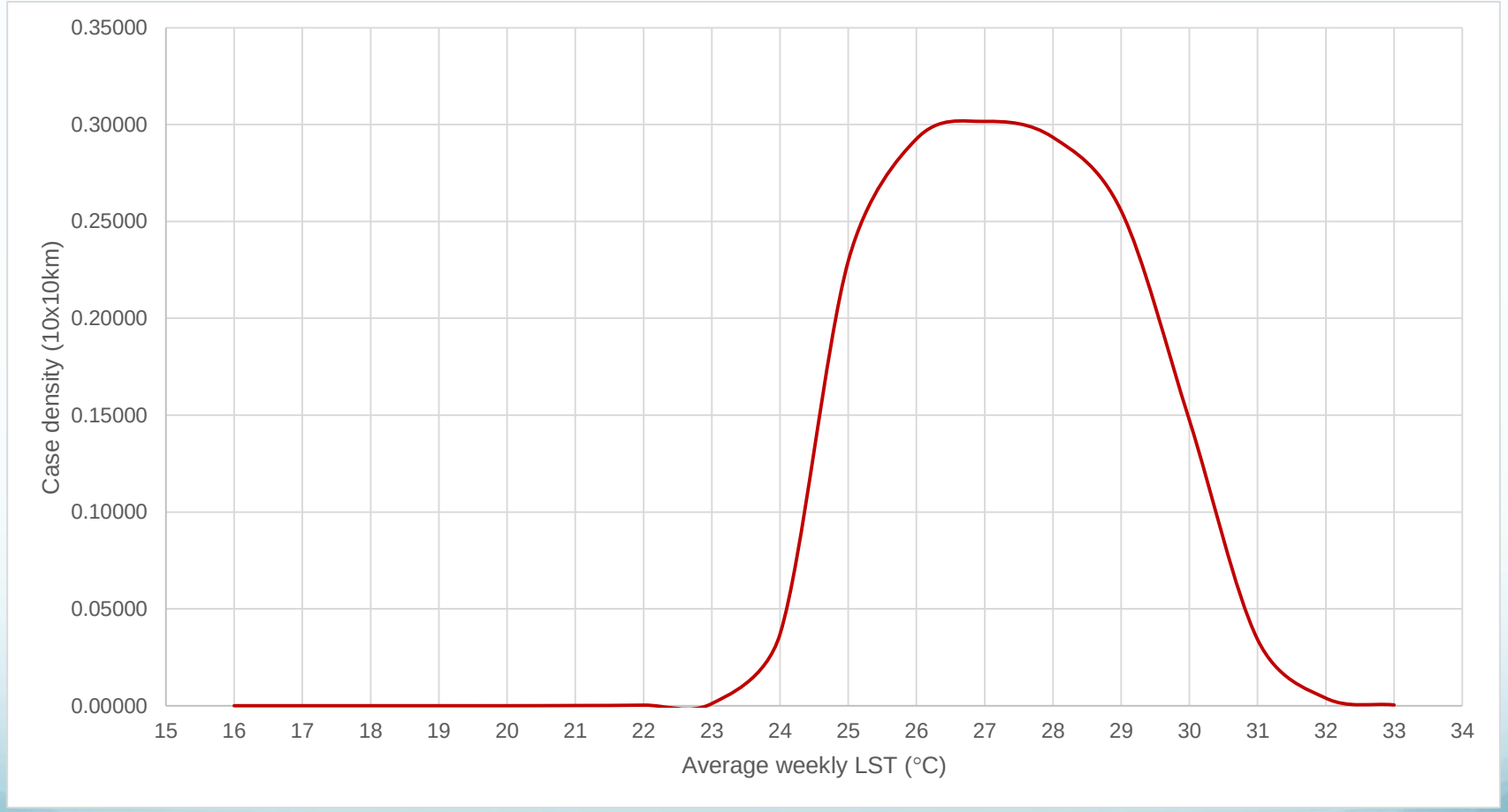
- Based from the model, 6 out 8 parameters were used to predict the occurrence of malaria in Sabah.

- From the model, the p value of paired sample-t test shows no significance, which explained that there was no difference between the mean observed and predicted malaria cases.

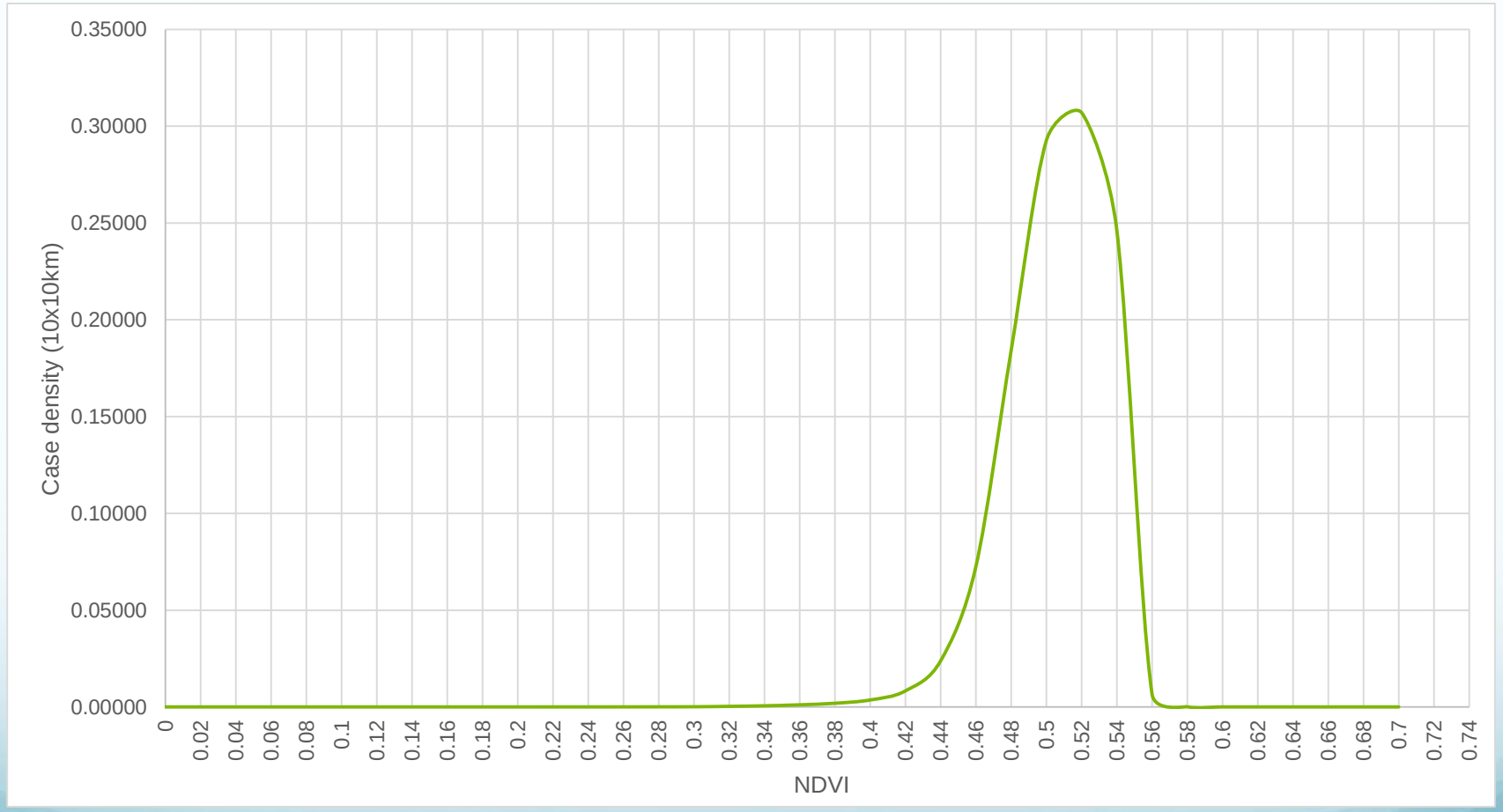
Rainfall


0.40000
0.35000
0.30000
0.25000
0.20000
0.15000
0.10000
0.05000
0.00000
Case density (10 x10km)
0
5
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
85
Average weekly rainfall (mm)

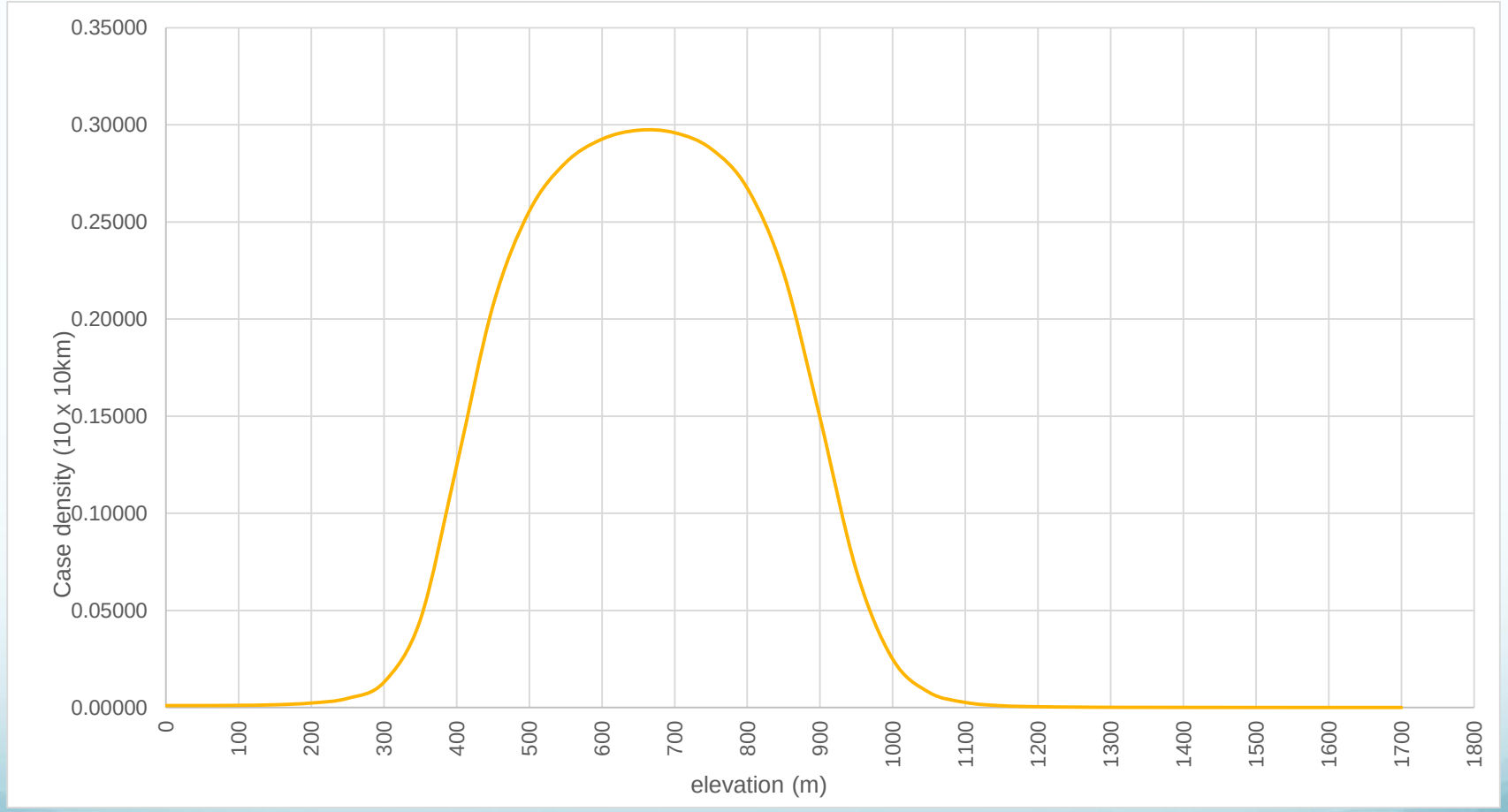
LST


0.35000
0.30000
0.25000
0.20000
0.15000
0.10000
0.05000
0.00000
Case density (10x10km)
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
Average weekly LST (°C)

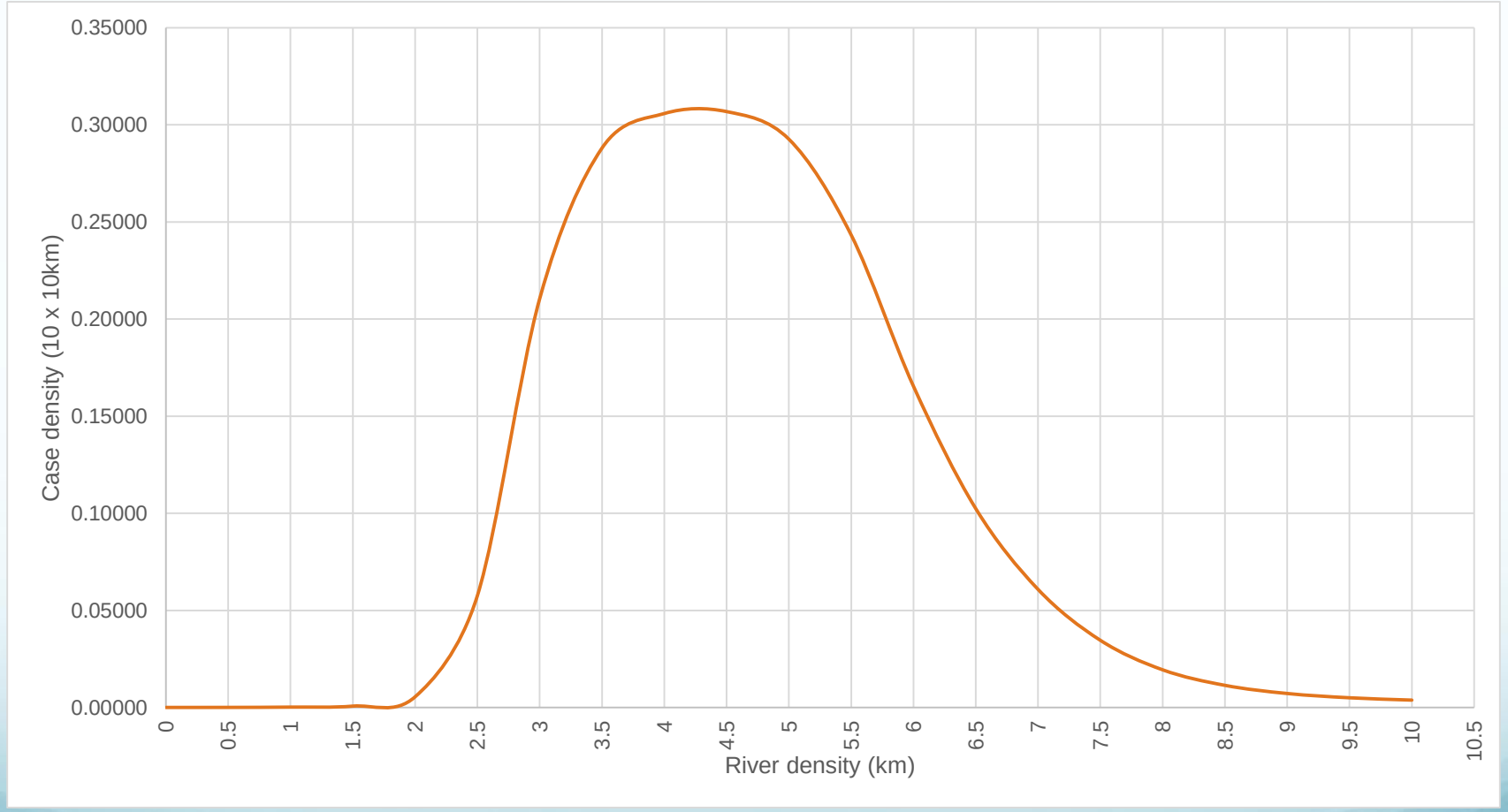
NDVI


0.35000
0.30000
0.25000
0.20000
0.15000
0.10000
0.05000
0.00000
Case density (10x10km)
0
0.02
0.04
0.06
0.08
0.1
0.12
0.14
0.16
0.18
0.2
0.22
0.24
0.26
0.28
0.3
0.32
0.34
0.36
0.38
0.4
0.42
0.44
0.46
0.48
0.5
0.52
0.54
0.56
0.58
0.6
0.62
0.64
0.66
0.68
0.7
0.72
0.74
NDVI

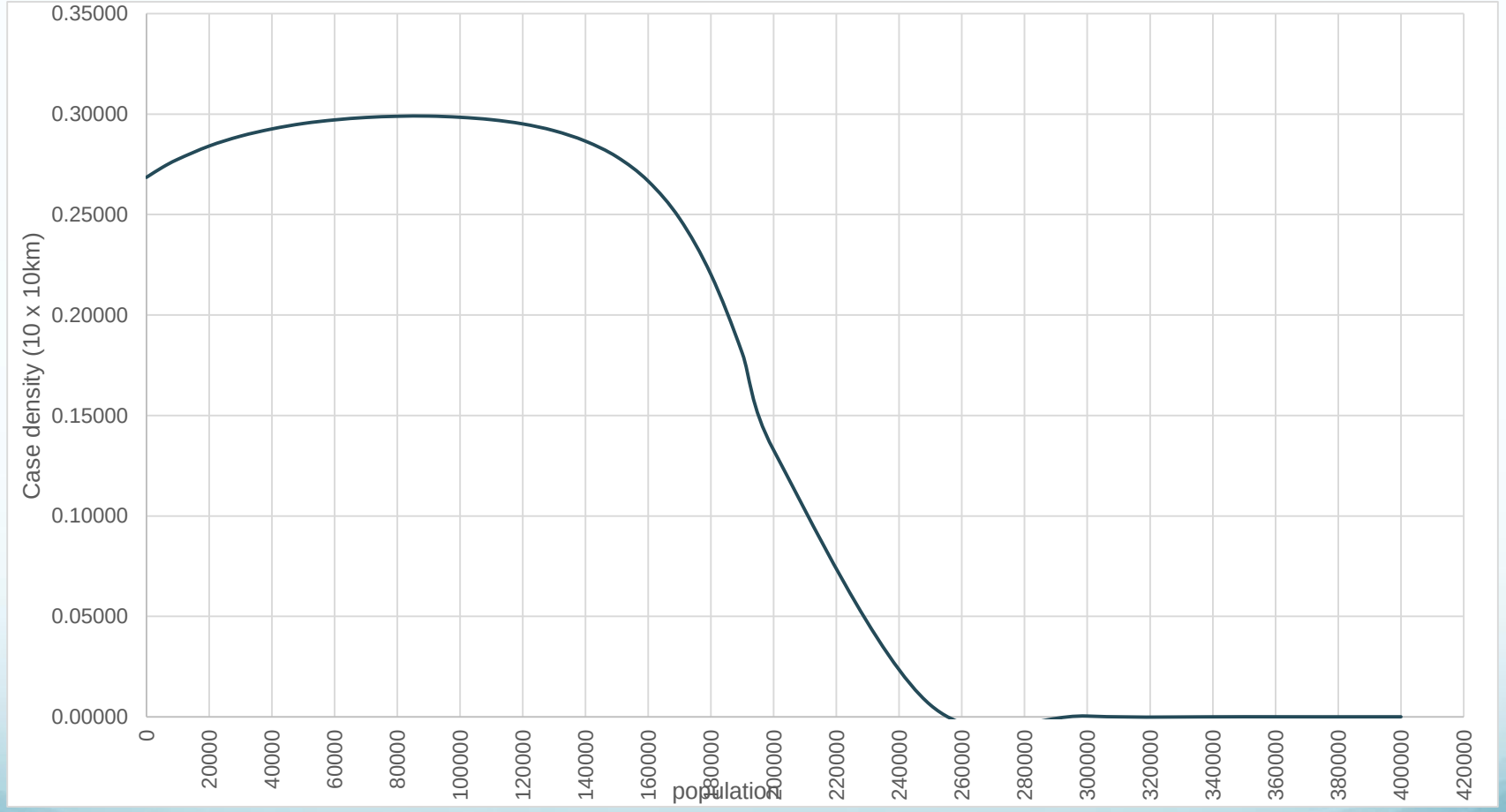
Elevation


0.35000
0.30000
0.25000
0.20000
0.15000
0.10000
0.05000
0.00000
Case density (10 x 10km)
0
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
elevation (m)

River density



Population


0.35000
0.30000
0.25000
0.20000
0.15000
0.10000
0.05000
0.00000
Case density (10 x 10km)
0
20000
40000
60000
80000
100000
120000
140000
160000
180000
200000
220000
240000
260000
280000
300000
320000
340000
360000
380000
400000
420000
population

DISCUSSION

- District located at Kudat division, West coast and some part of interior part of Sabah showing clustering of *P.knowlesi* infection, compare that other division.
- Subdistrict located at the west coast and interior part of Sabah such as in Ranau, Tambunan, Kota Marudu have slightly higher elevation as they located nearby the Sabah Range Croaker.
- A study was done in Kapit, Sarawak, found that An. Latens prefer to feed human and macaques at ground level however, they prefer to feed macaques at higher elevation (Tan CH. 2008). Human who lives at nearly mountain area are higher risk to get infected.

DISCUSSION

- Sabah is known for its preserved nature and tropical rainforest which provide a good natural habitats for both the vector as well as the macaques reservoir.
  - Close proximity to the forest could bring humans into contact with the macaques and vector (Collins WE.,2012, Barber BE.,2013).
  - Most of the traditional villages in Sabah are located near the forest edge and the source of income usually related to forest products. This will increase the chances of human-vector-animal contacts.

DISCUSSION

- There are various factors which play a role in *P. knowlesi* transmission particularly in Sabah, and management and control programme could be challenging for MOH.
  - Sabah have a combination of topographical regions, with the addition of climate suitability which makes its population susceptible to malaria.
  - *As the main vector for P. knowlesi is An. balabacensis* which breeds mostly in ground pool water, rainfall and temperature play an important role in *P. knowlesi* transmission. This study addresses the role of LST and rainfall, and a similar study done in Kudat, Sabah also showed strong correlations between these two factors and the incidence of *P. knowlesi* in Sabah. (Barber B.E 2012).
  - However, excess rainfall also can flush the breeding site of the Anopheles (Gbenga J.,2016).

CONCLUSION AND RECOMMENDATIONS

- *P. knowlesi* infection in Malaysia differs from *P. knowlesi* infection in other regions such as Thailand and Laos as in Malaysia, *P. knowlesi* infection do cause fatal outcome (WHO,2017).
  - Active case detection is one of the major strategies for the identification and early treatment of malaria, as it causes rapid parasetemia.
  - However, topographical area in Sabah, would be a major challenge for MOH.
  - It is important to identify high risk areas in Sabah, and ACD and entomological survey could be done effectively in monitoring this infection.
  - The accessibility to health region is also one of the major challenges in Sabah. Therefore high risk areas should be given priorities for treatment of *P. knowlesi*, as early treatment can prevent mortality.

ACKNOWLEDGEMENT

- HUKM for funding this project (FF-2015-367)
- Ministry of Health for approval to conduct this project.
- Main supervisor, Prof Jamal Hisham Hashim, and Associate Prof. Dr Rozita Hod
- To all our team members and co-researchers.
  - Dr Farrah Melissa Muharam from the Department of Agriculture Technology, Faculty of Agriculture, UPM
  - Dr Ummi Kalthom Shamsudin, Disease Control Division, MOH
- Special thanks to
  - Dr Nor Azura Husin, Faculty of Computer Science, UPM
  - Associate Prof Dr. Mohd Bakri Adam, Institute for Mathematical Research, UPM
  - Mr. Kathiresan Gopal, Institute for Mathematical Research, UPM
  - Malaysian Remote Sensing Agency
  - JUPEM
  - ESRI, Malaysia

Thank you