MINISTRY OF HEALTH
MALAYSIA

EARLY WARNING DISEASE SURVEILLANCE

INSTITUTE FOR MEDICAL RESEARCH MALAYSIA

DISEASE MODELLING WORKSHOP

Faculty of Computer Science & Information Technology
UNIMAS
22 April 2019

DR BALVINDER SINGH GILL, ***MBBS, MPH, M.Inf Dis, PhD***
Institute for Medical Research
Ministry of Health Malaysia

THE DEFINITION

PUBLIC HEALTH SURVEILLANCE

"The ongoing systematic **collection, analysis, interpretation and dissemination** of health data for the **planning, implementation and evaluation** of public health action"

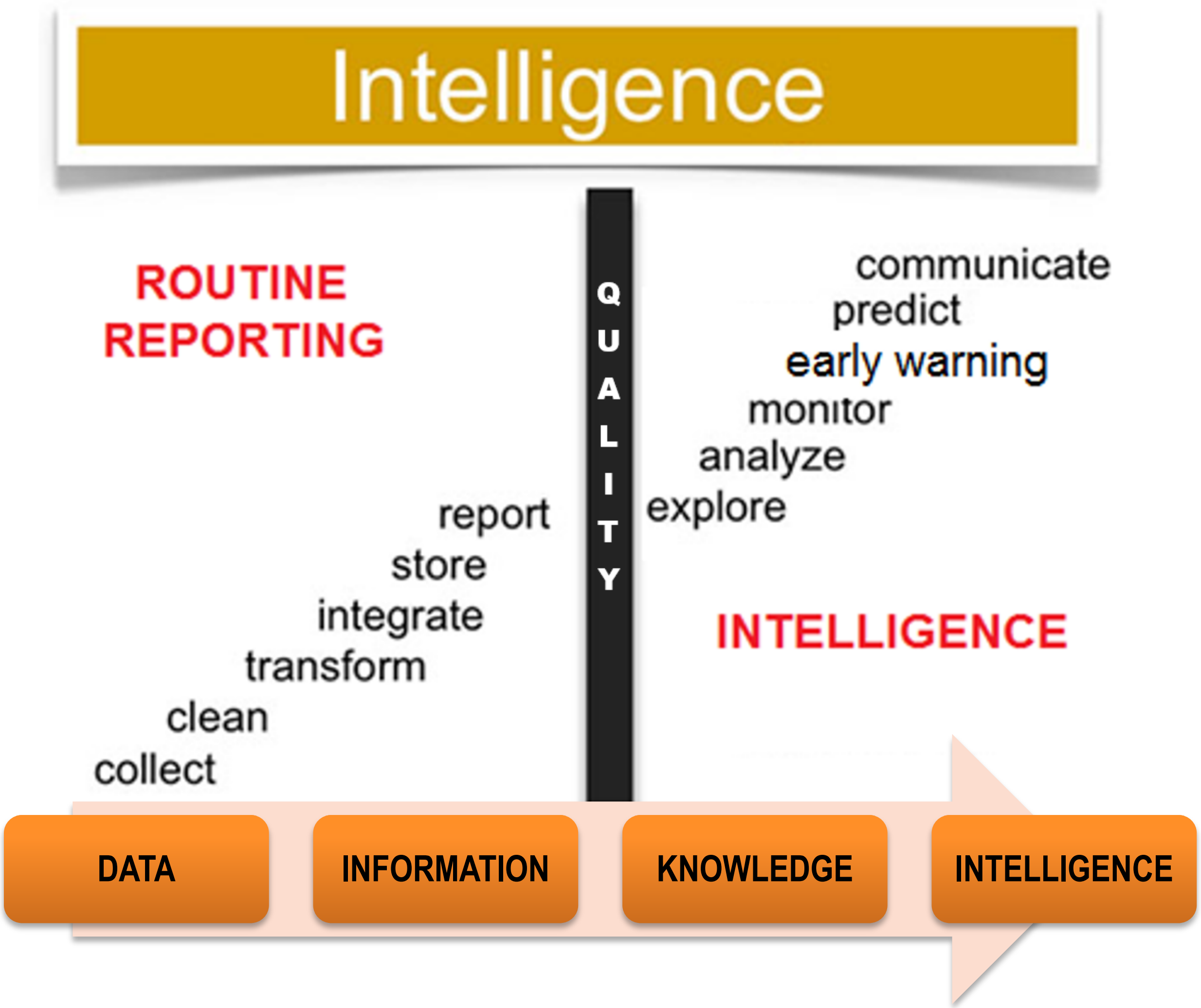
INFORMATION FOR ACTION

THE DEFINITION

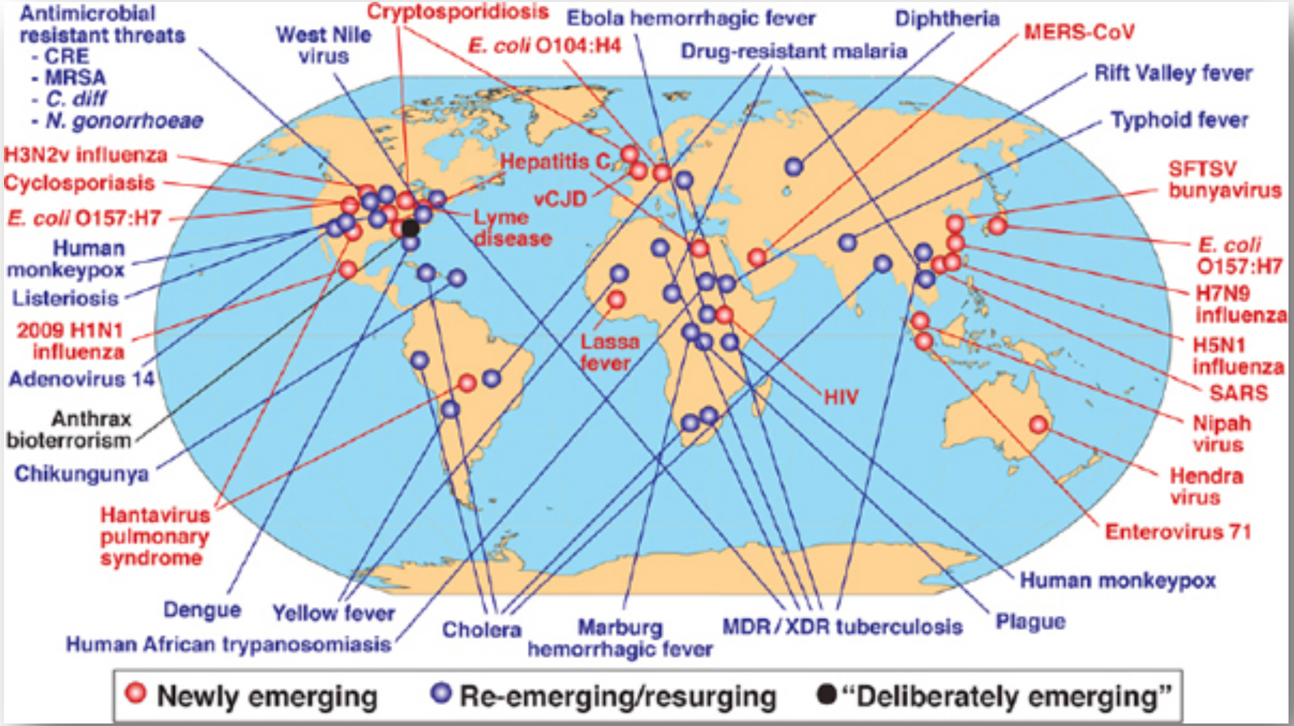
DISEASE EARLY WARNING SYSTEMS (WHO)

Early warning systems are Timely surveillance systems that Collect and analyse information/data on Epidemic-prone diseases in order to Trigger prompt public health interventions

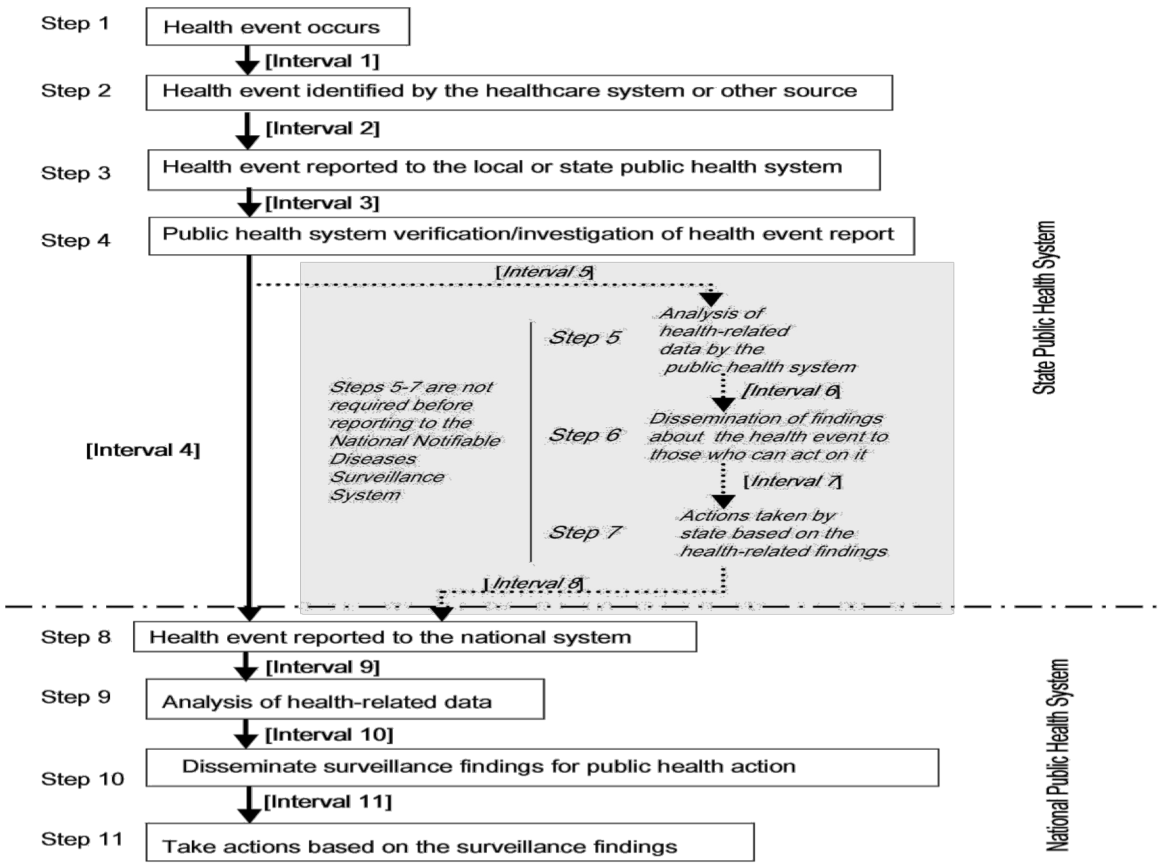
INFORMATION FOR ACTION


Intelligence
ROUTINE REPORTING
collect
clean
transform
integrate
store
report
QUALITY
explore
analyze
monitor
early warning
predict
communicate
INTELLIGENCE
DATA
INFORMATION
KNOWLEDGE
INTELLIGENCE

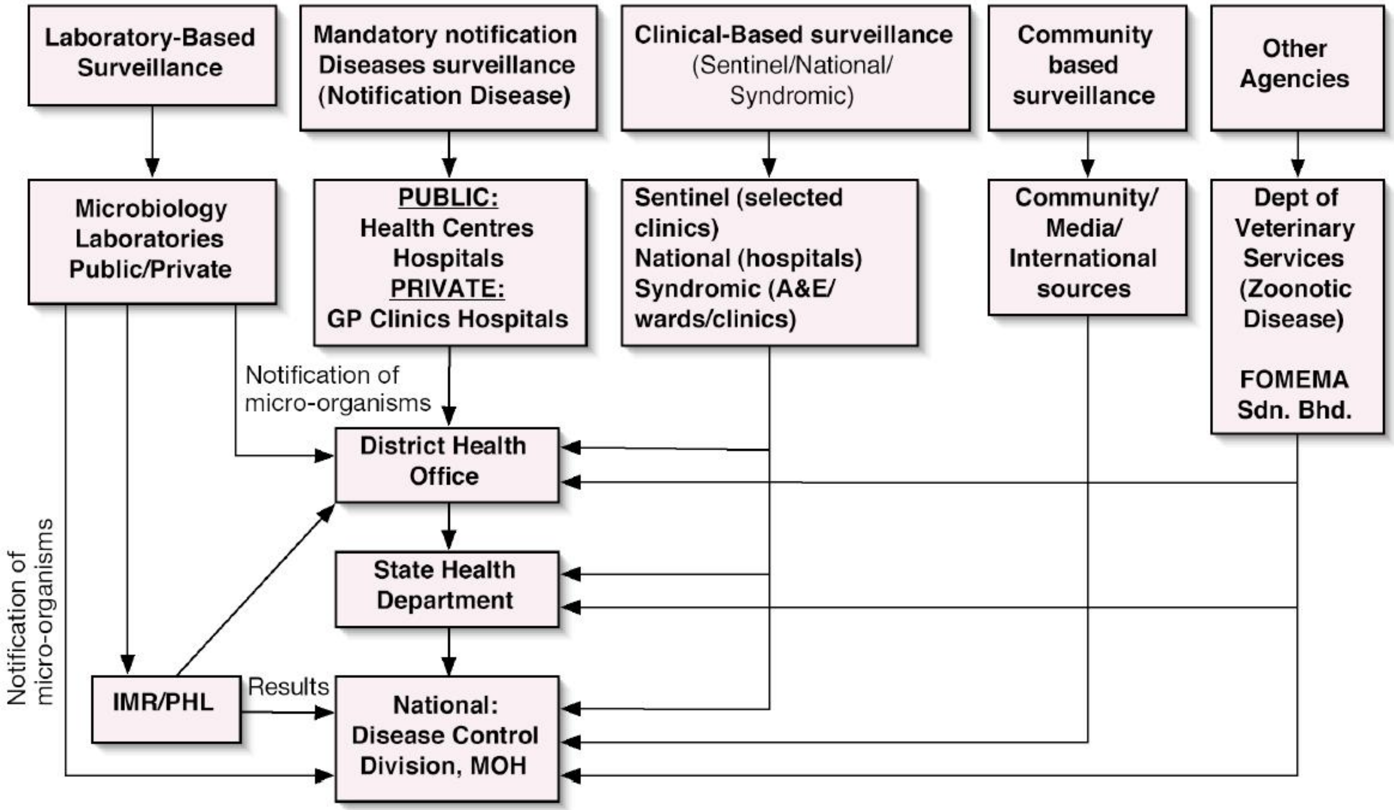
EMERGING & RE-EMERGING DISEASES



WHY EARLY WARNING - SURVEILLANCE TIMELINESS

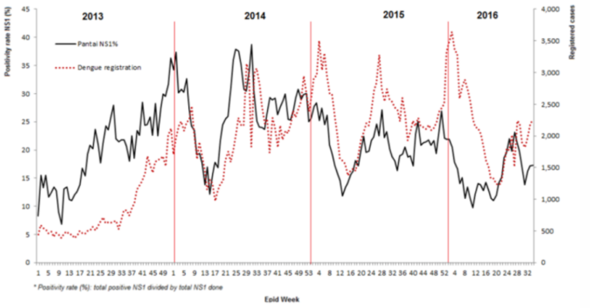


SURVEILLANCE SYSTEMS IN MALAYSIA



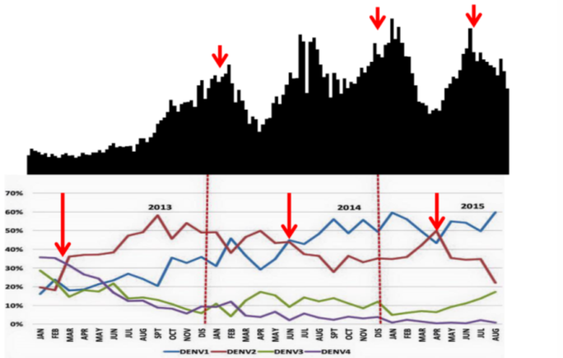
EARLY WARNING FOR DENGUE

LABORATORY CONFIRMATIONS – POSITIVITY RATE



Positivity rate NS1 tests (Pantai) with number of registered cases (MOH) by week, Wk 1/2013 – Wk 34/2016, Malaysia

DENGUE CASES AND SEROTYPES IN MALAYSIA



MECHANISTIC ENTOMOLOGY AND DISEASE MODEL

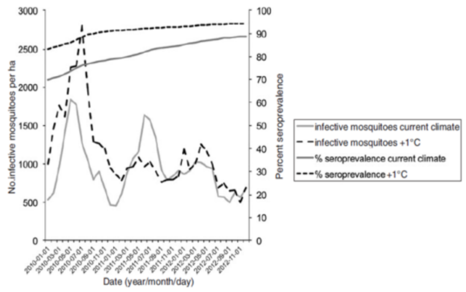
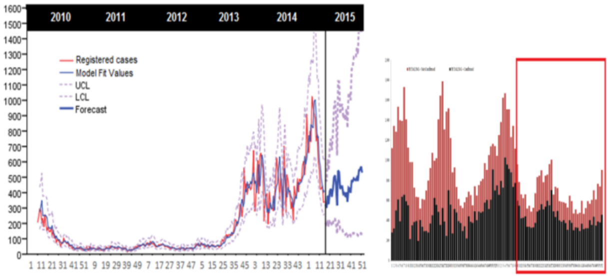
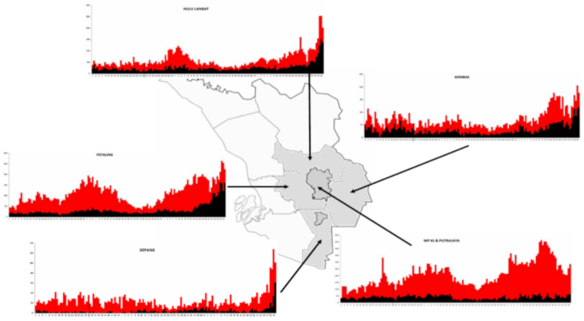


Fig. 5. Simulated dengue infective mosquitoes and human seroprevalence for dengue in Petaling district for 2010–2012 and with a 1 °C daily temperature increase (from simulation 3) to demonstrate the potential for the impact of climate change.

FORECASTS OF DENGUE USING ARIMA MODELS

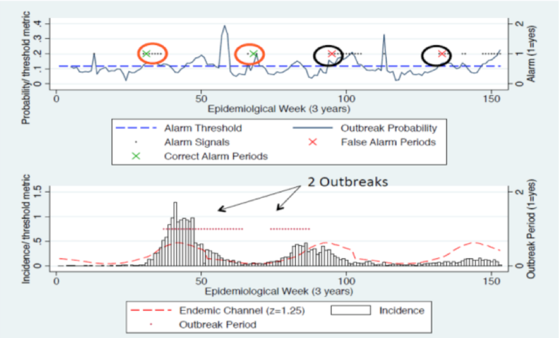


SPATIAL AND TEMPORAL DISEASE TRENDS



Number of dengue notification and registration by week, 2011-2013, Selangor and WPKL, Malaysia

ALERT INDICATORS



Notified and Registered dengue cases in States and selected Districts, Malaysia, Wk. 01/2015 – Wk. 11/2019

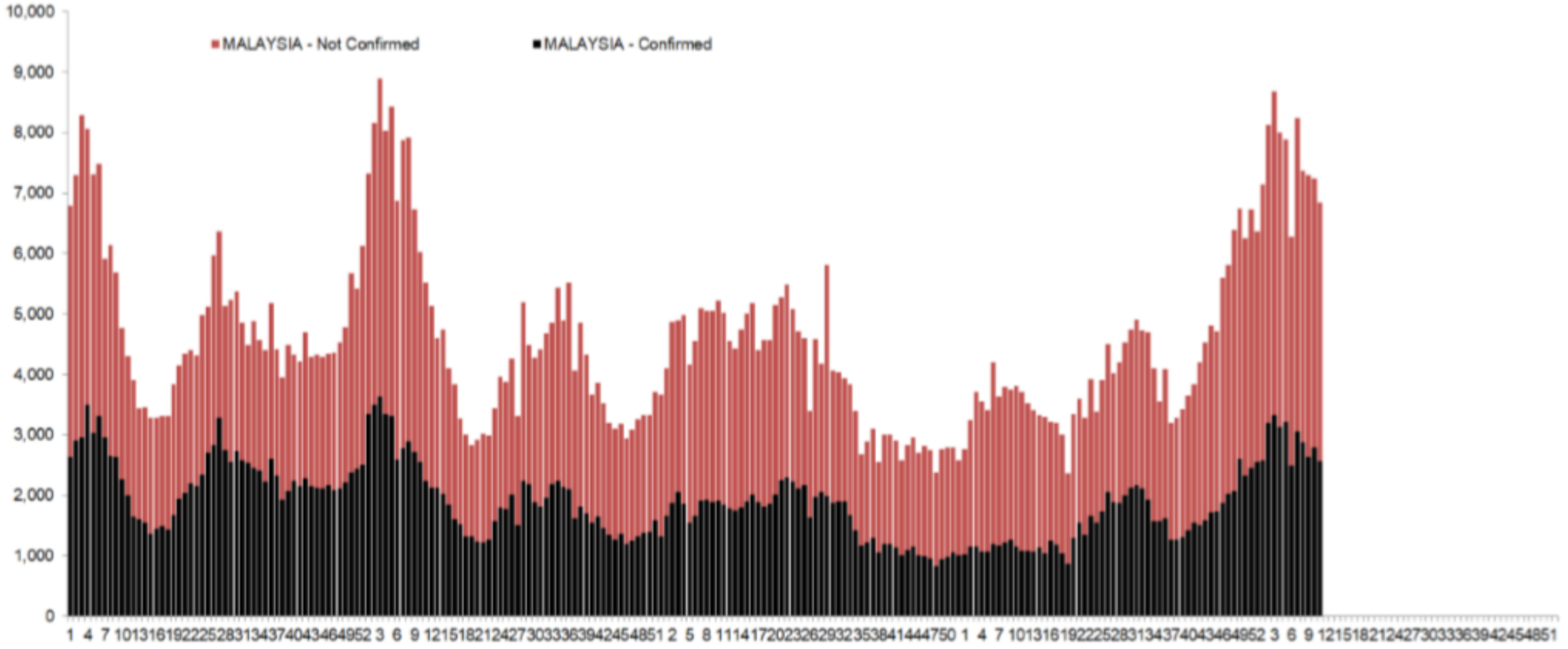


Figure 1: Notified and registered dengue cases by week, Wk. 01/2015 – Wk. 11/2019, Malaysia.

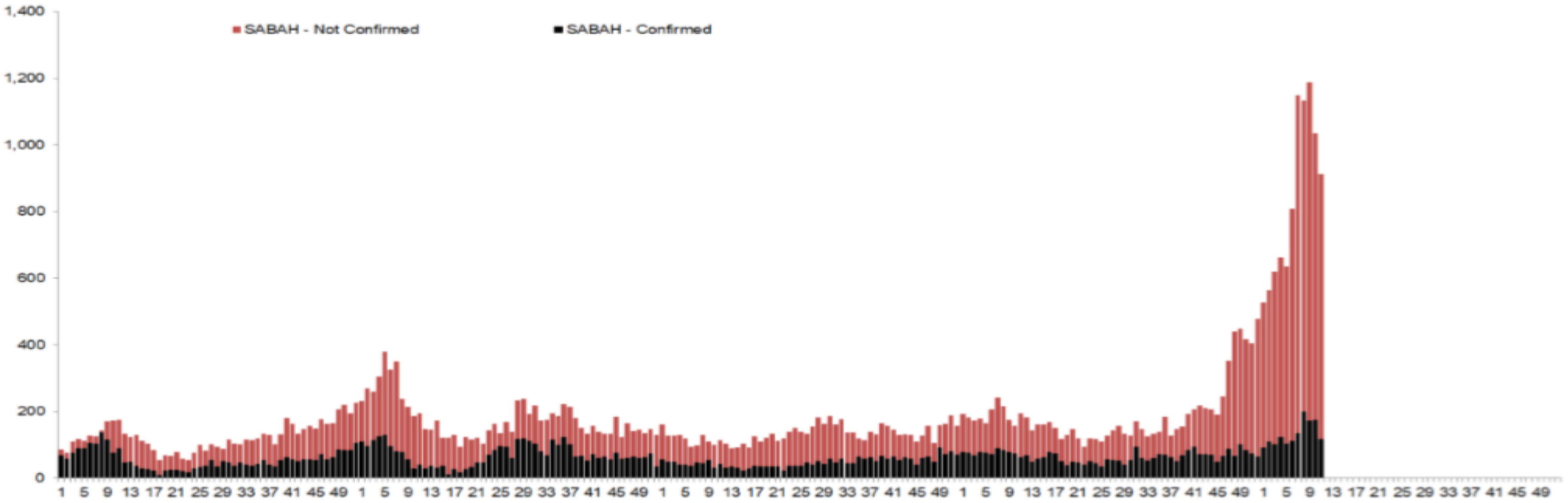


Figure 14: Notified and registered dengue cases by week, Wk. 01/2015 – Wk. 11/2019, Sabah.

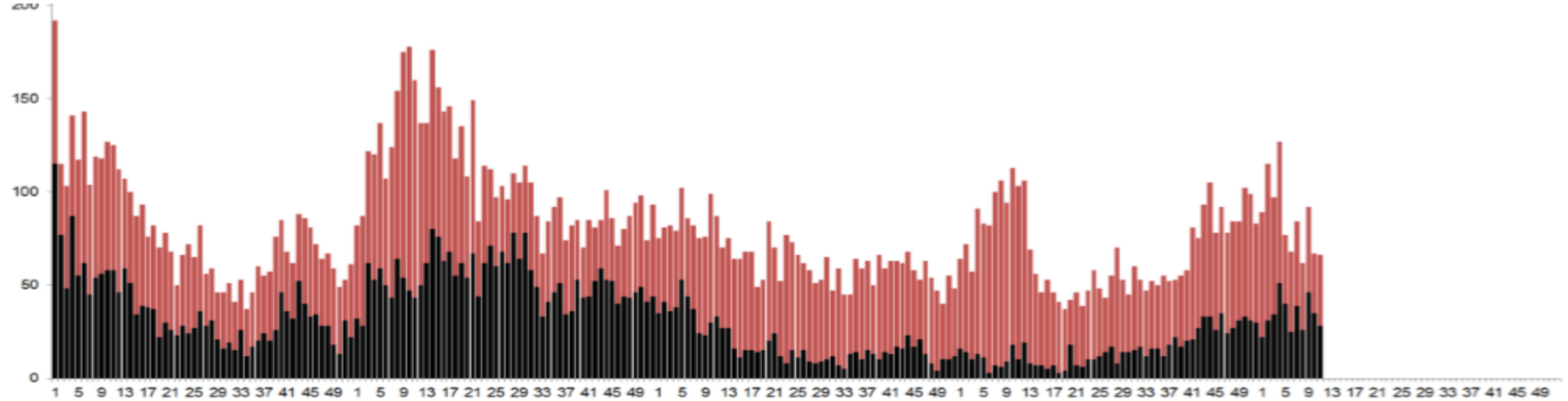
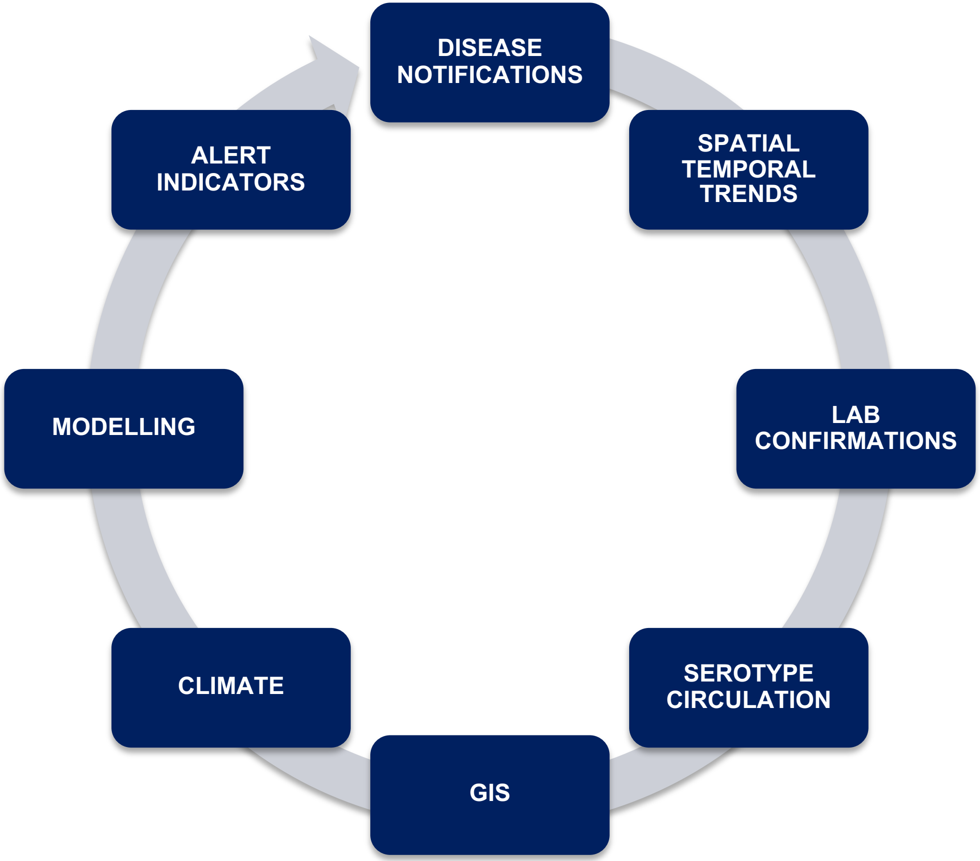
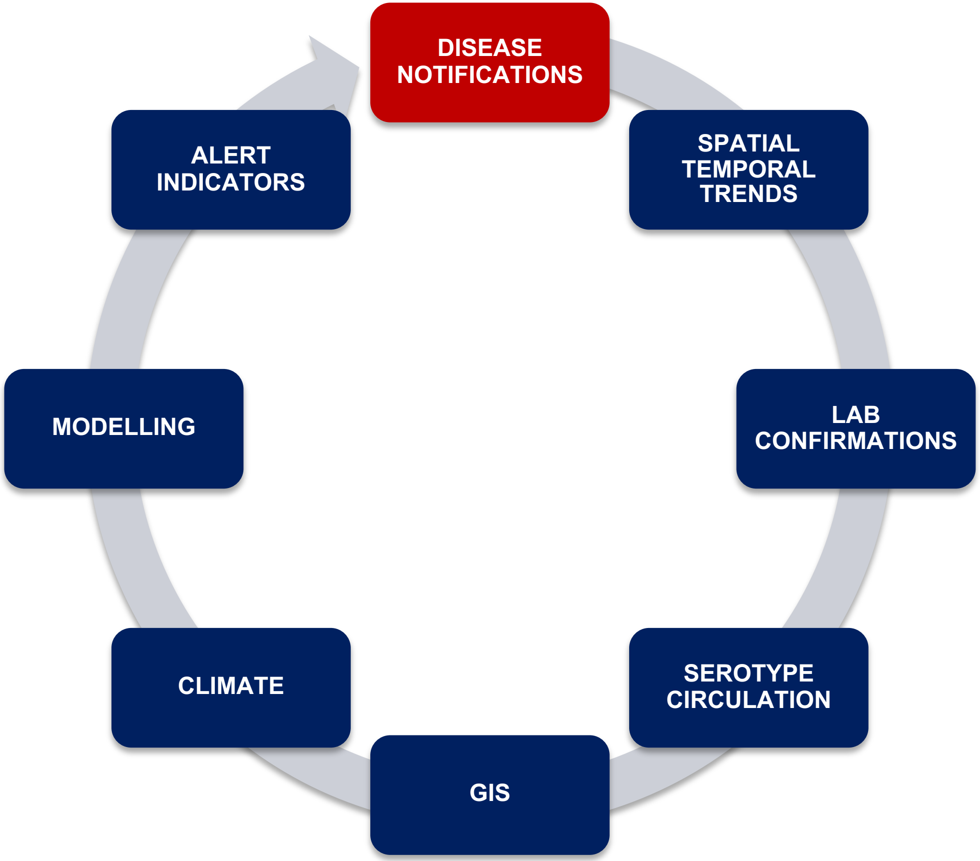


Figure 15: Notified and registered dengue cases by week, Wk. 01/2015 – Wk. 11/2019, Sarawak.

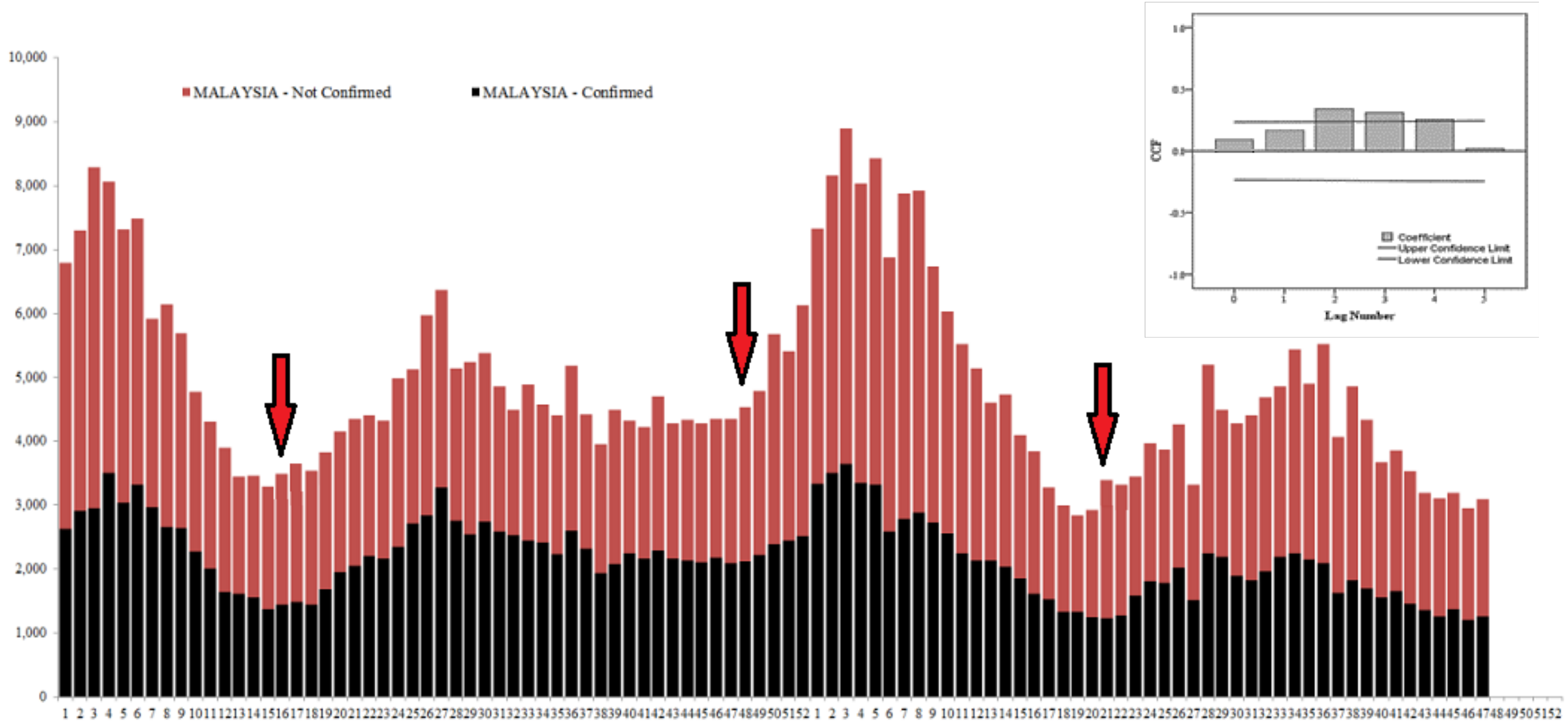
EARLY WARNING IN DISEASE SURVEILLANCE



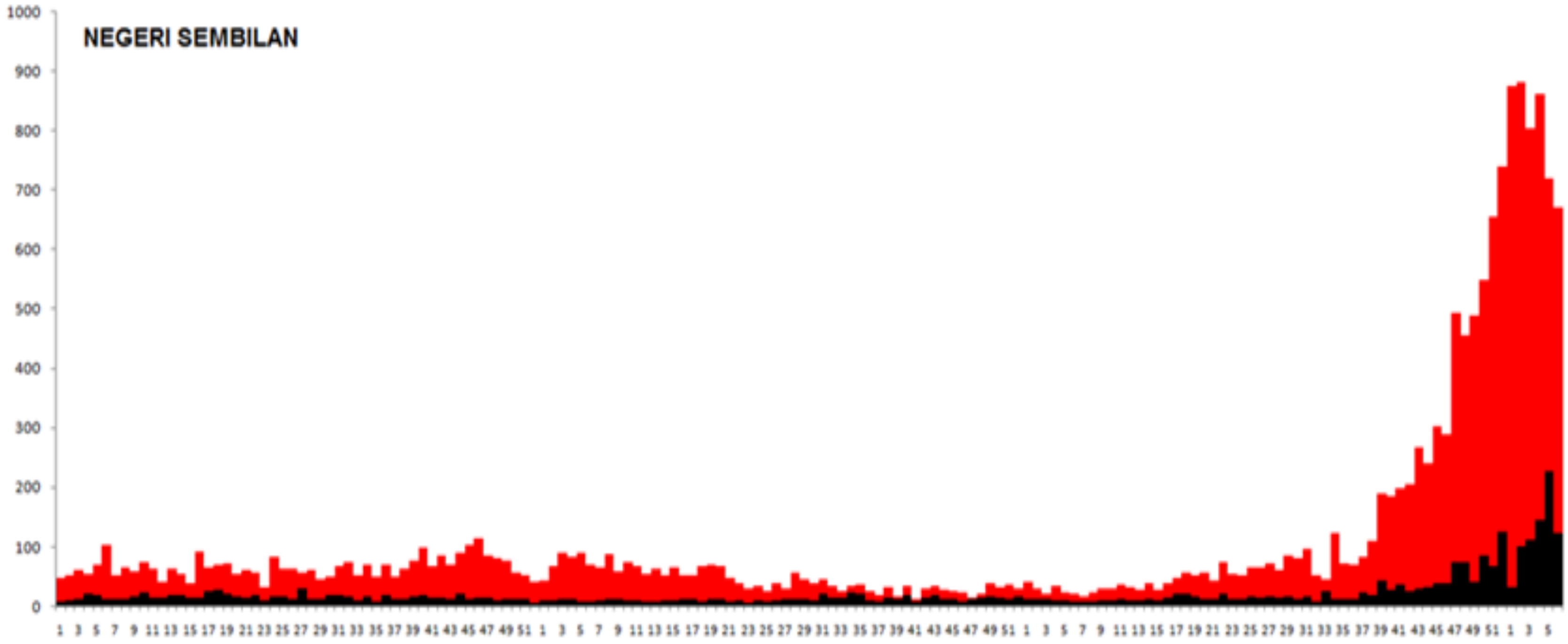
EARLY WARNING IN DISEASE SURVEILLANCE



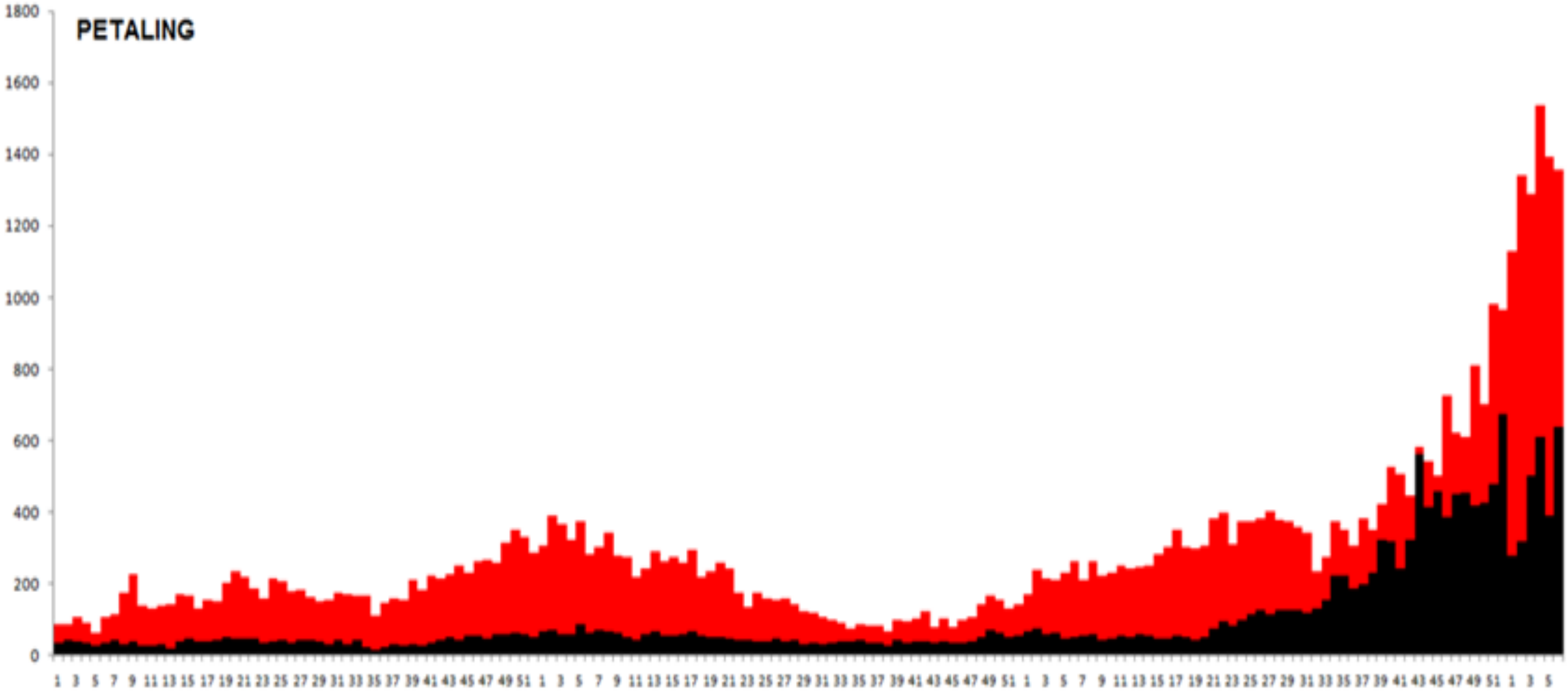
TEMPORAL TRENDS OF DISEASE NOTIFICATIONS



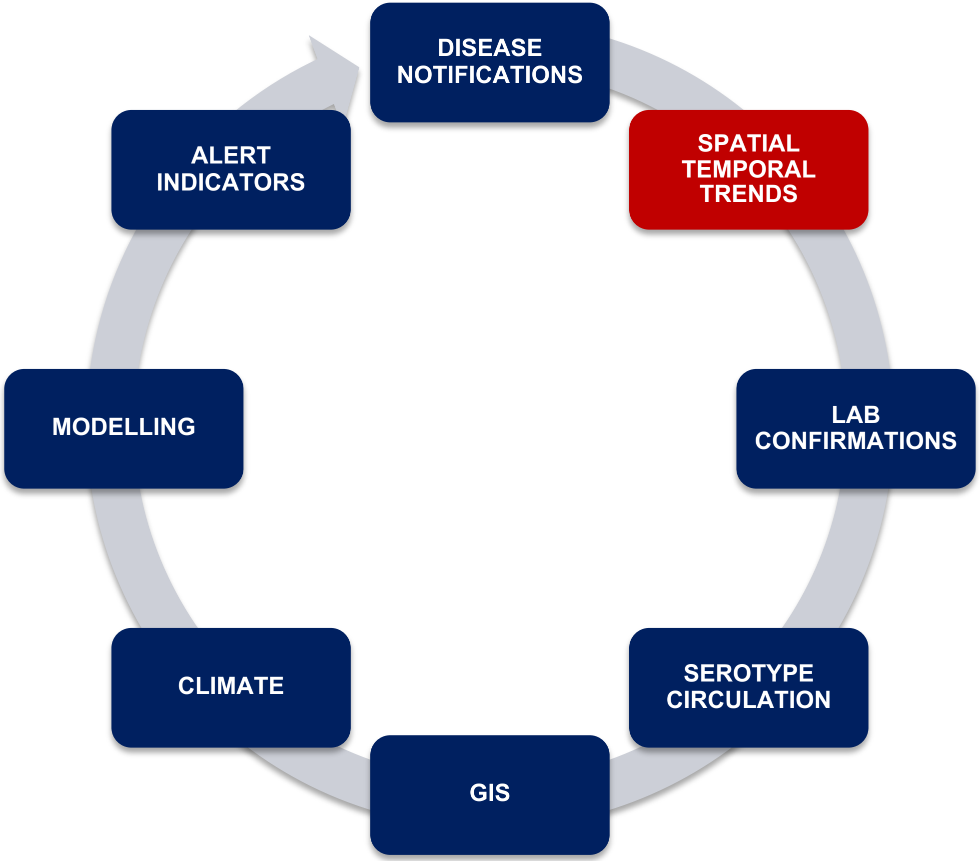
EARLY WARNING AT STATE



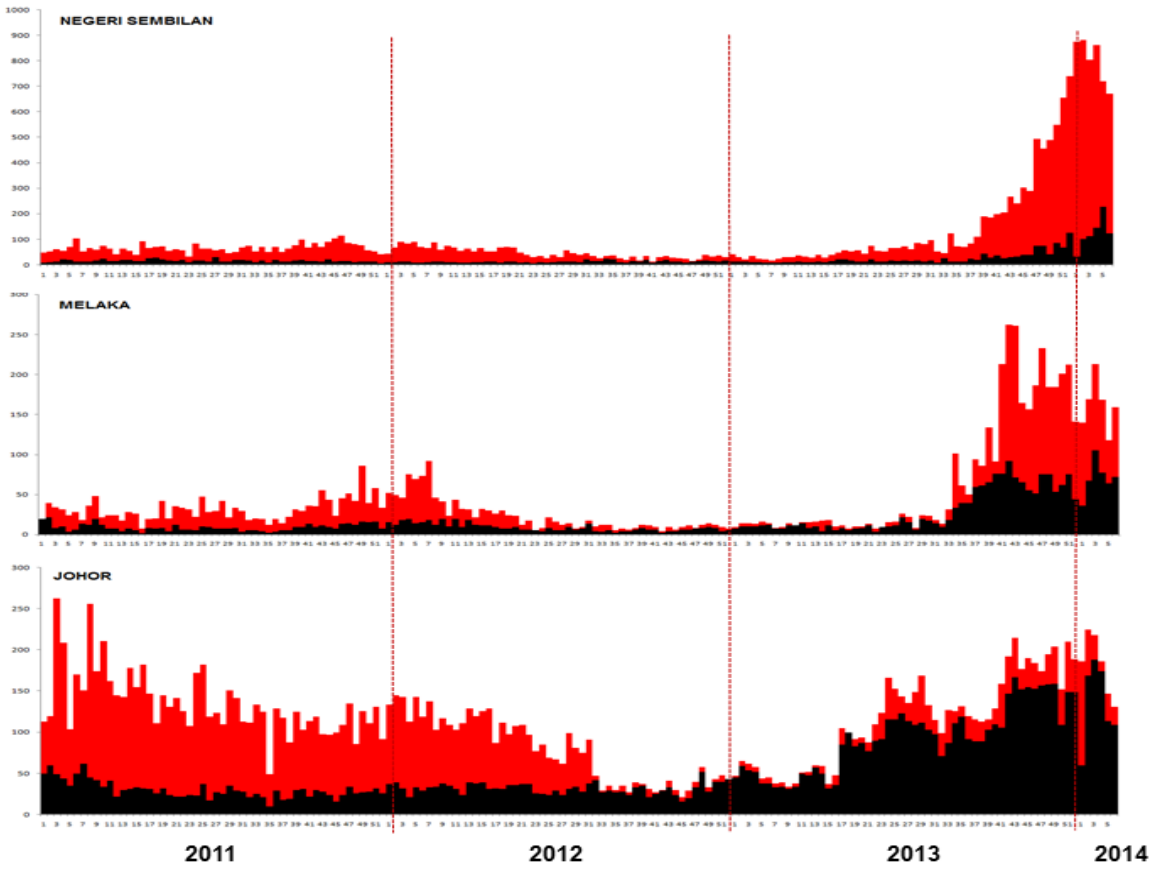
EARLY WARNING AT DISTRICT



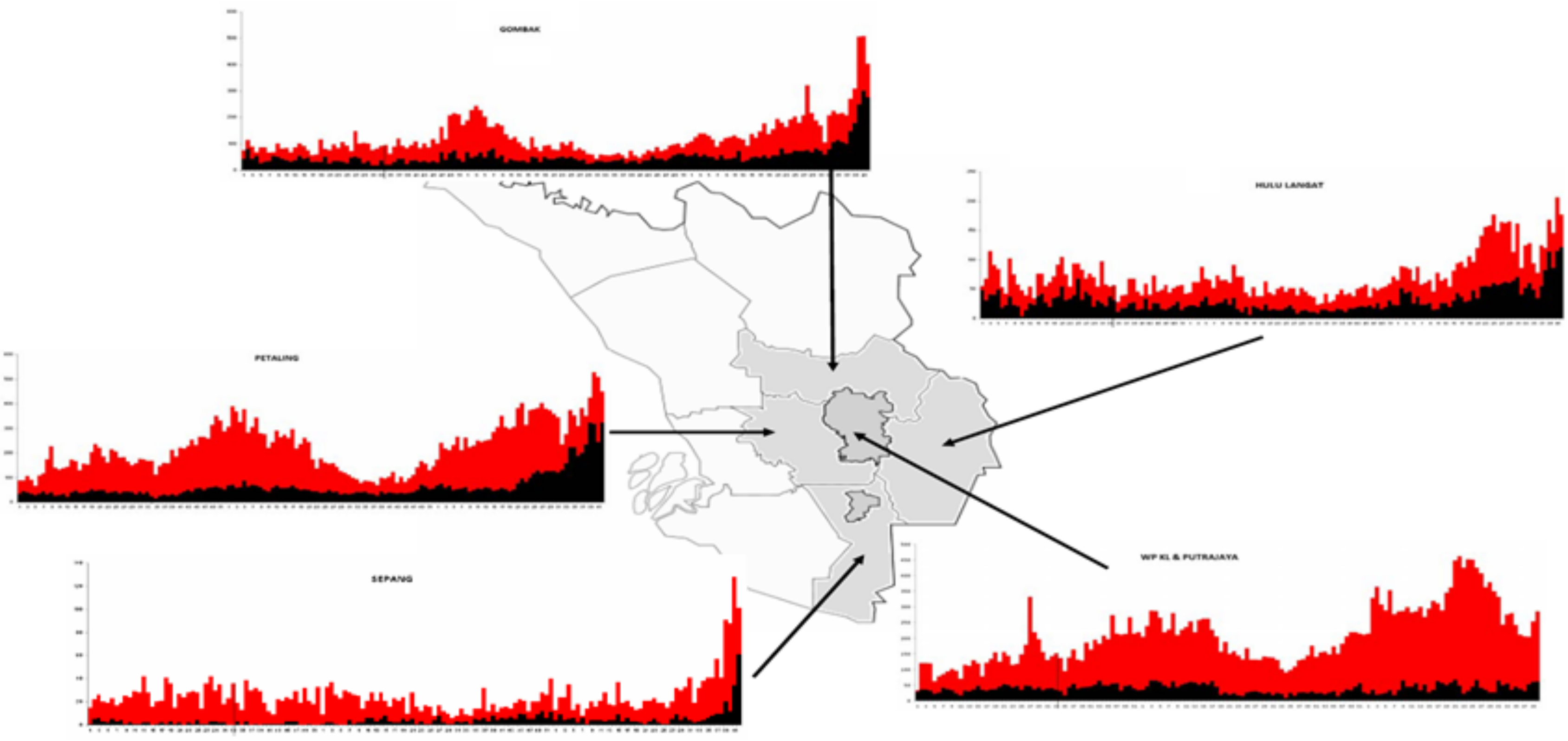
EARLY WARNING IN DISEASE SURVEILLANCE



SPATIAL AND TEMPORAL DISEASE TRENDS

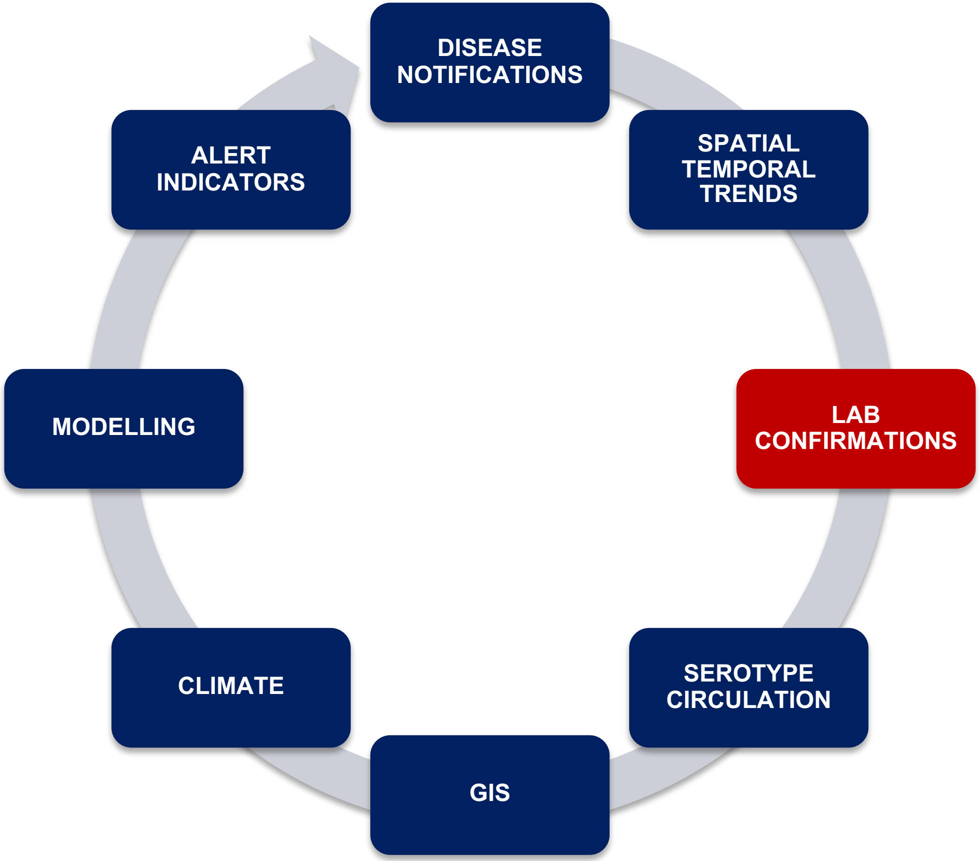


SPATIAL AND TEMPORAL DISEASE TRENDS

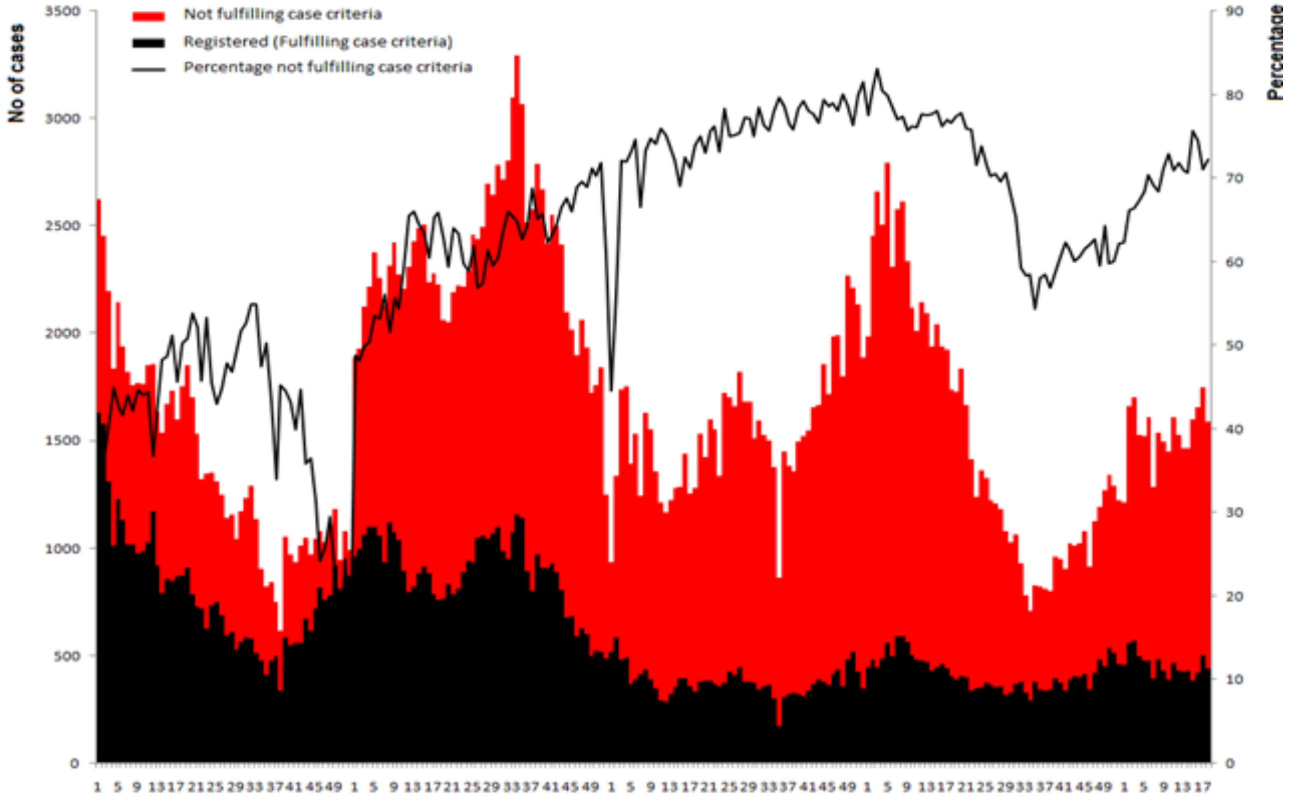


Number of dengue notification and registration by week, 2011-2013, Selangor and WPKL, Malaysia

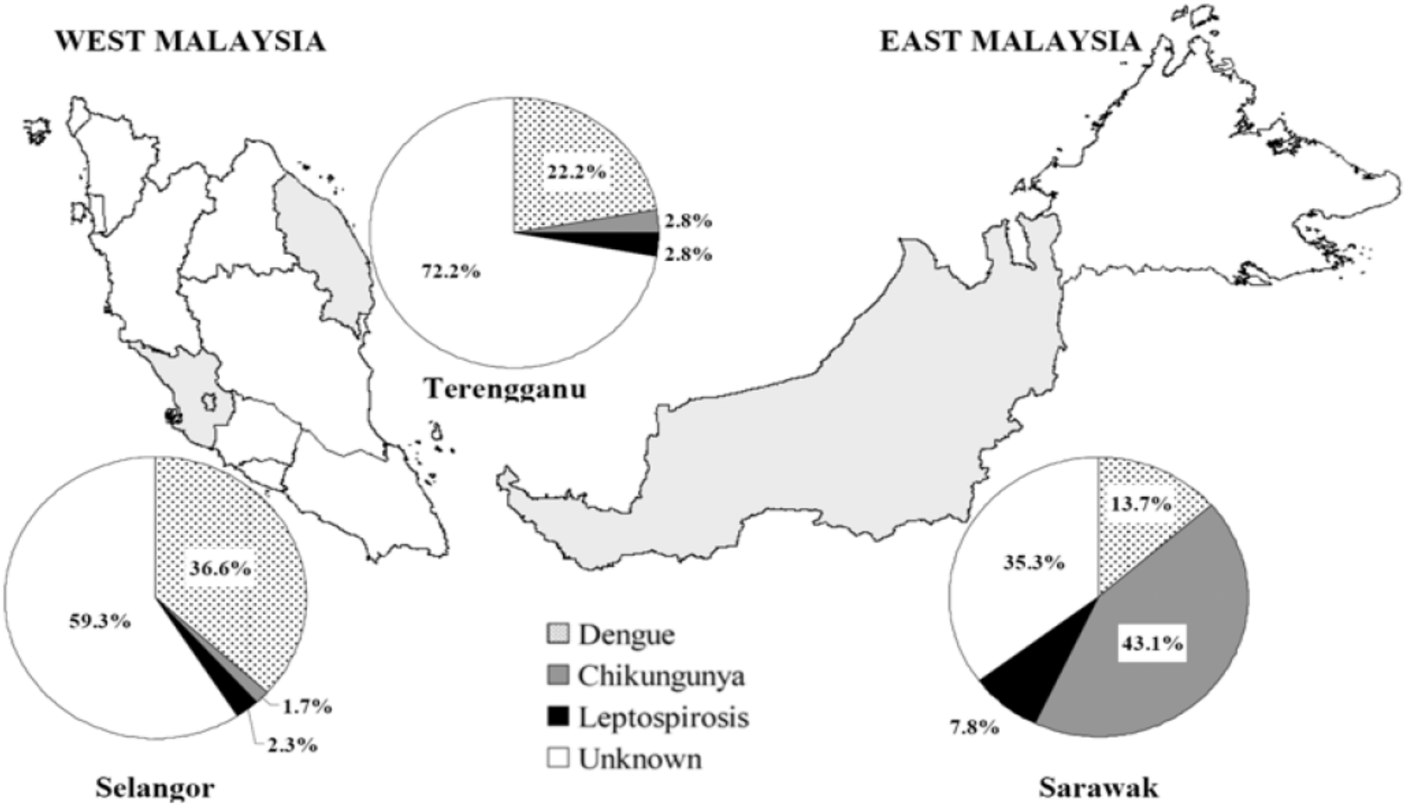
EARLY WARNING IN DISEASE SURVEILLANCE



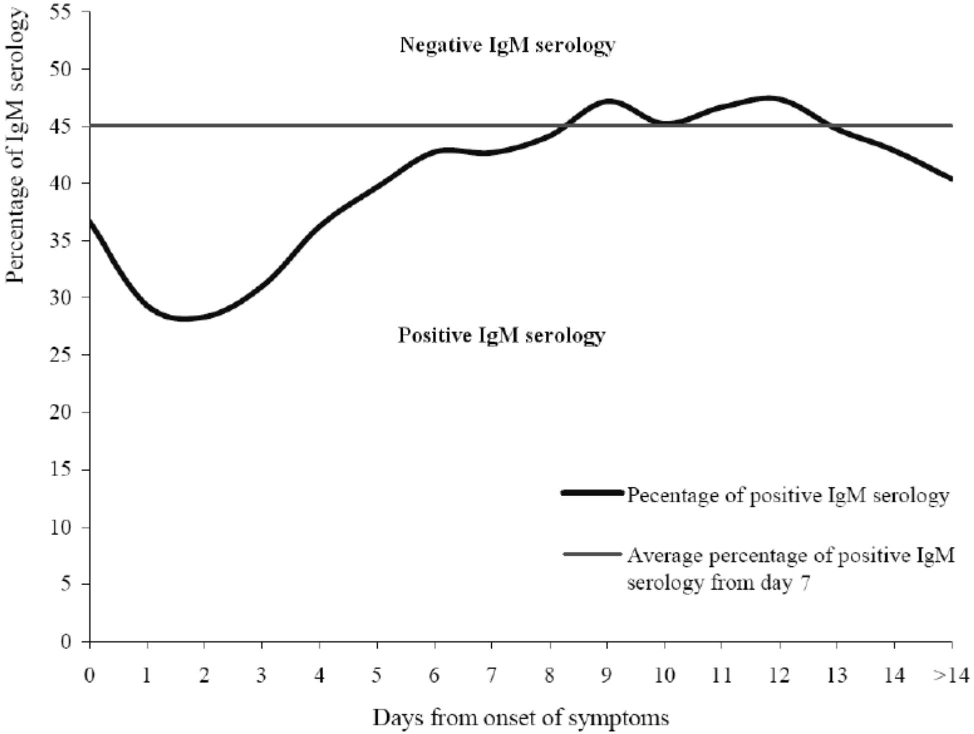
NOTIFICATIONS AND LAB CONFIRMATIONS FOR DENGUE



LAB CONFIRMATIONS FOR DENGUE

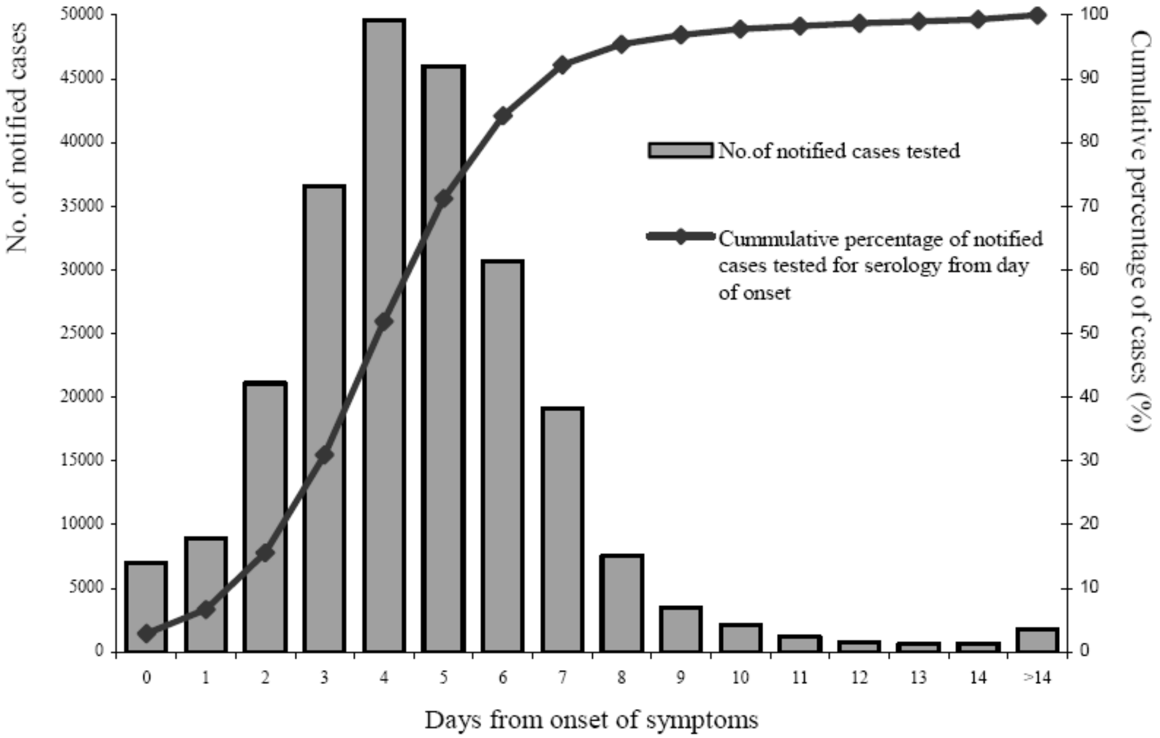


DENGUE NOTIFICATIONS - IgM POSITIVE FROM DATE OF ONSET



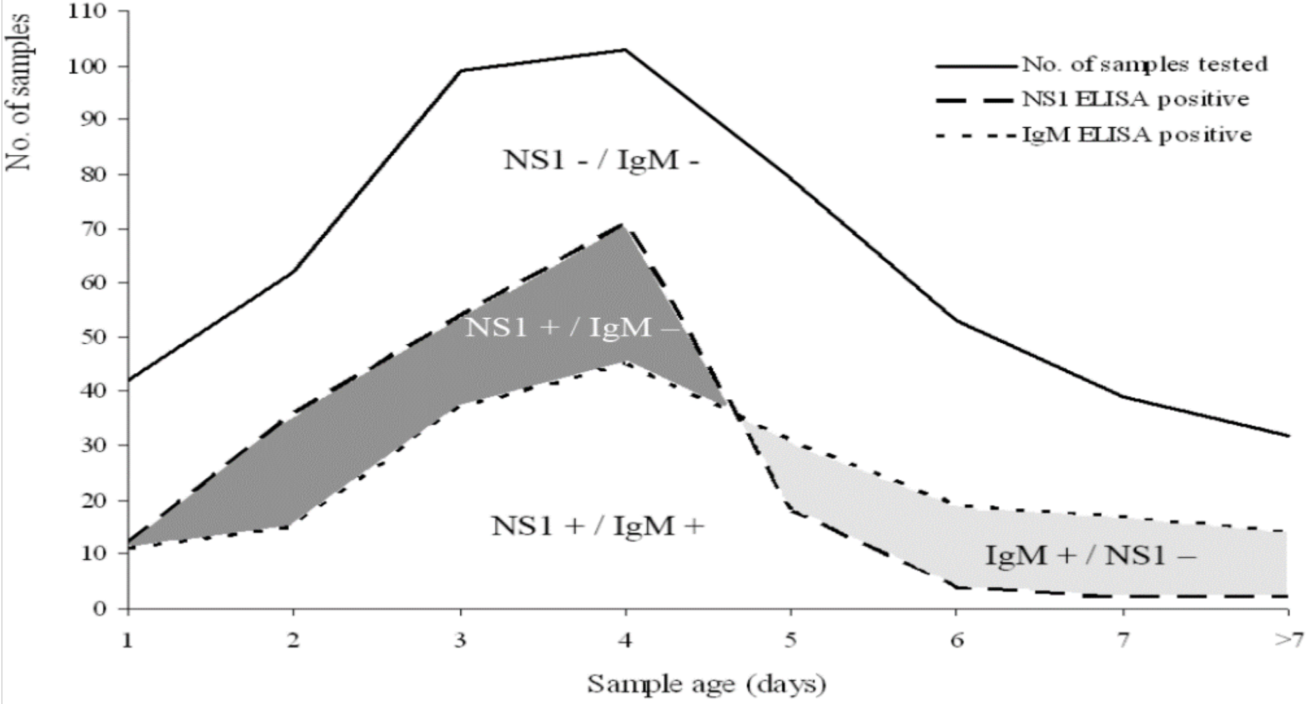
Proportion of IgM positive cases by day of onset gradually increased from day 1 of onset of illness of approximately 28.3% to a peak in day 9 with 47.2%, with an average for the total duration of 36.3%.

DENGUE NOTIFICATIONS - IgM POSITIVE FROM DATE OF ONSET



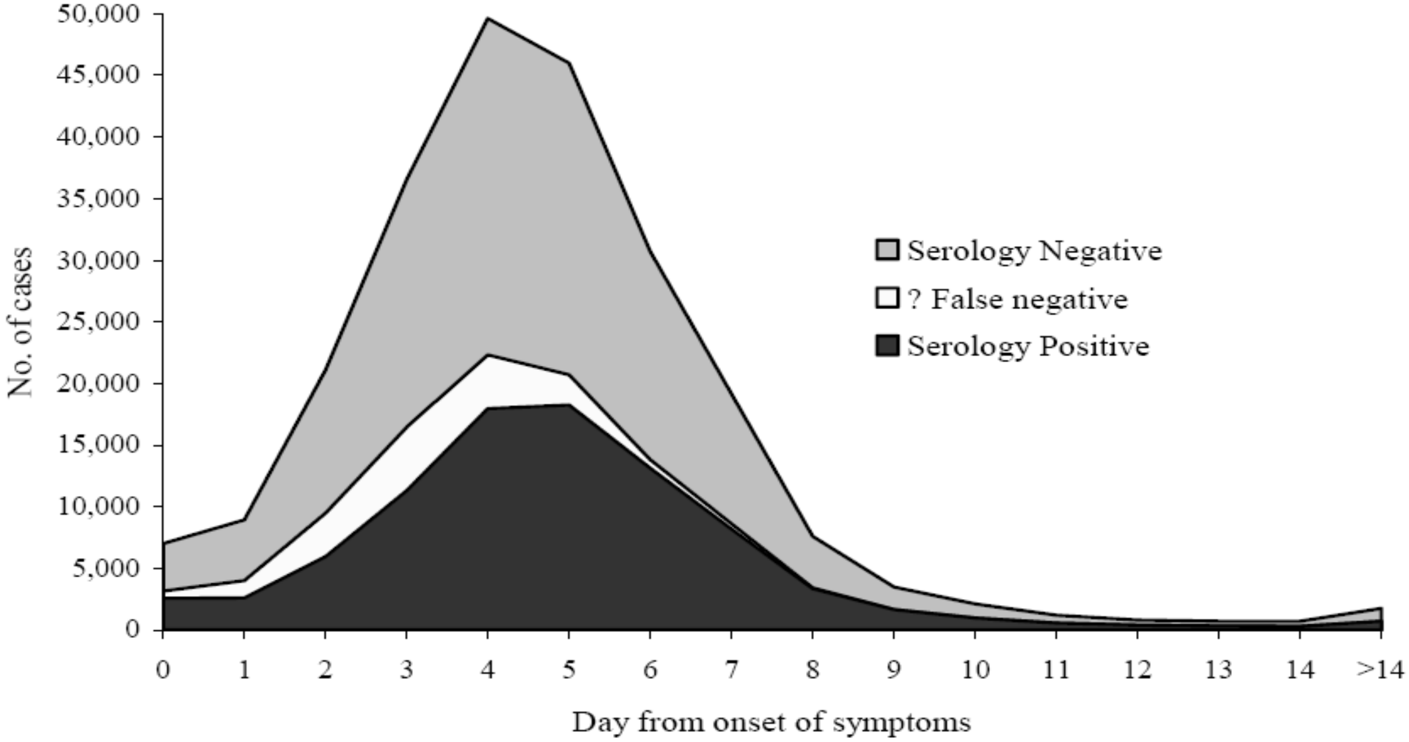
Highest tested on Day 4 from the onset of clinical symptoms, 20.3%. 71.2% of the cases were found to have been tested for IgM serology within the first five days from the onset of symptoms.

LAB CONFIRMATION TESTS FOR DENGUE



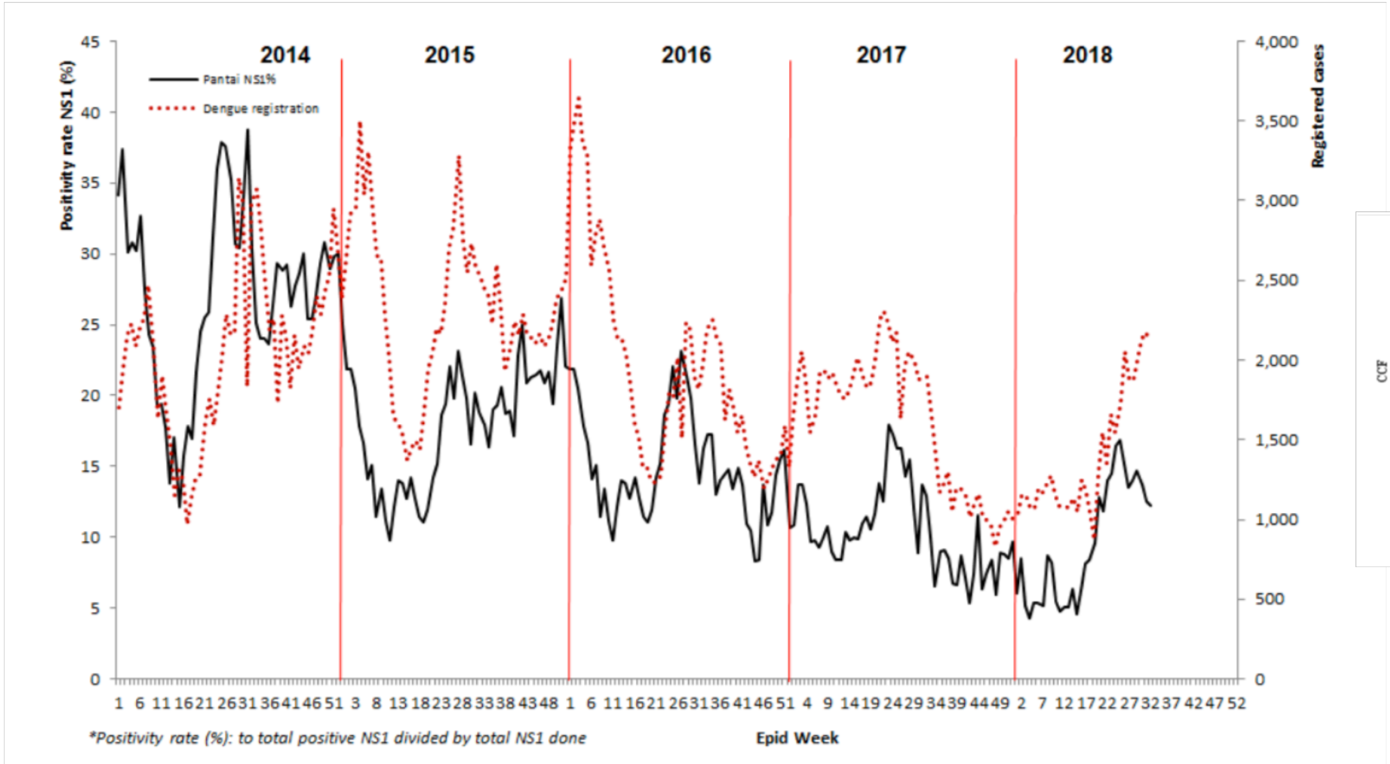
Number of samples tested positive for dengue by NS1-ELISA and IgM-ELISA
from days of onset of symptoms

DENGUE NOTIFICATIONS - IgM POSITIVE FROM DATE OF ONSET



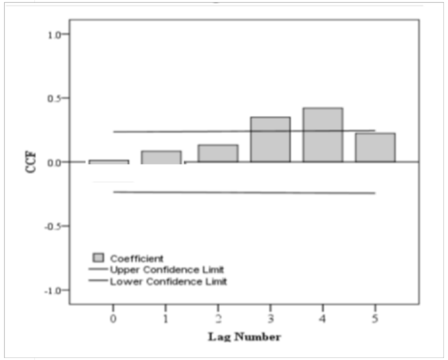
Model showed a 21% increase of the total confirmed cases seen in this analysis.

DENGUE - LAB CONFIRMATIONS AT PANTAI LABORATORIES

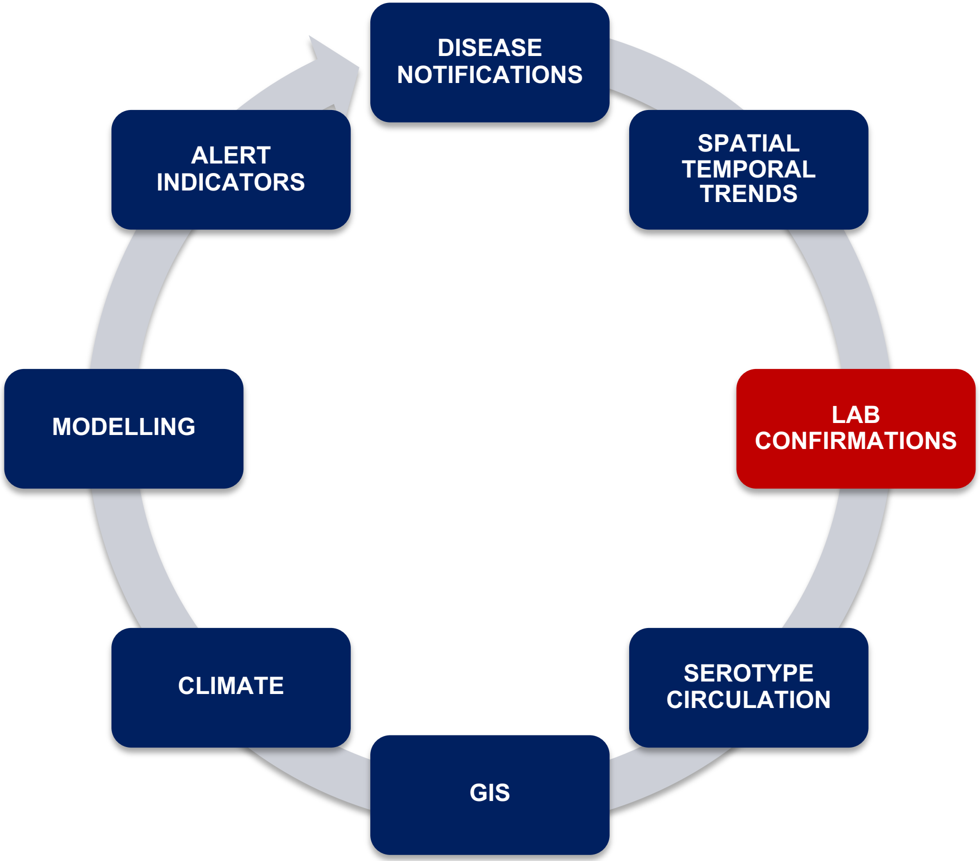


Positivity rate NS1 tests (Pantai) with number of registered cases (MOH) by week, Wk 01/2014 – Wk 32/2018, Malaysia

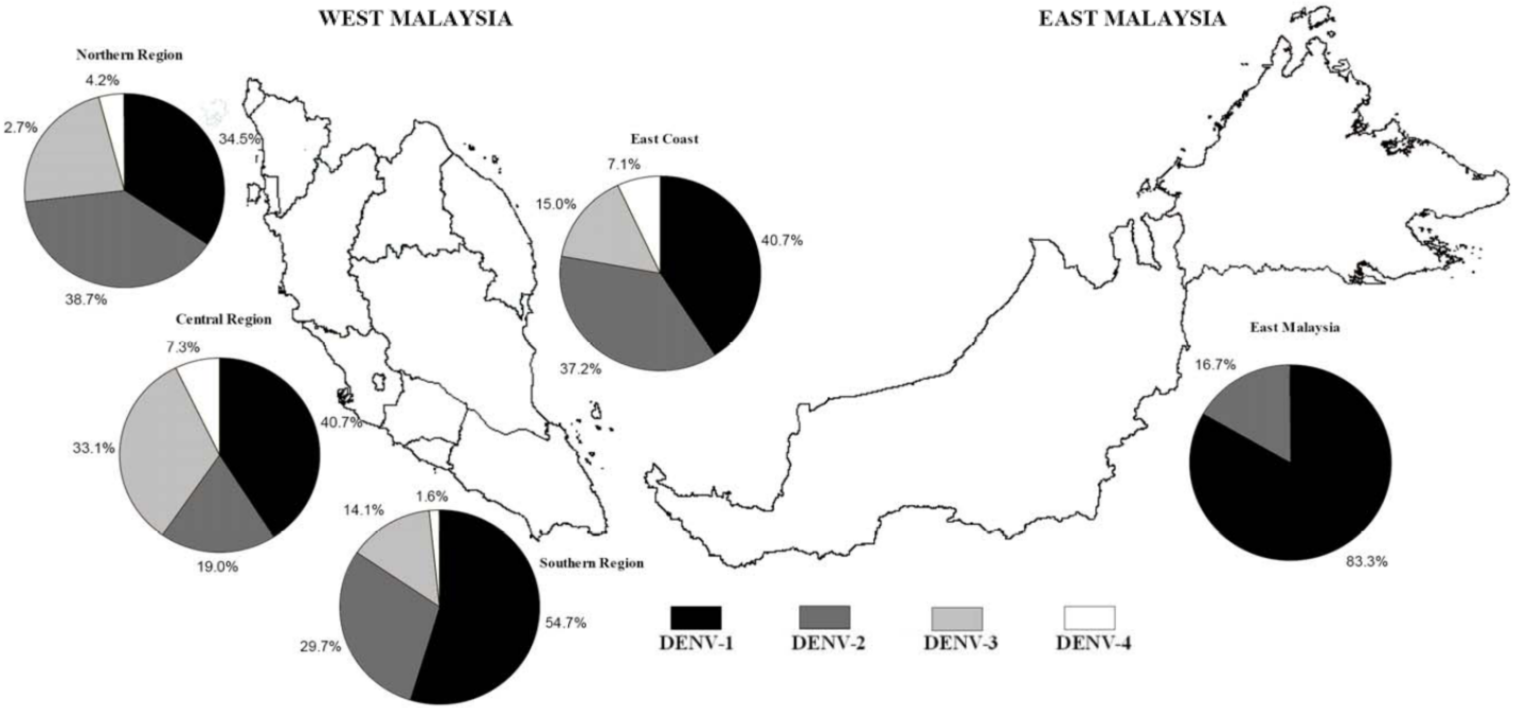
Pearson's correlation
$r = 0.94$ ($n = 161$, $p < 0.01$)



EARLY WARNING IN DISEASE SURVEILLANCE

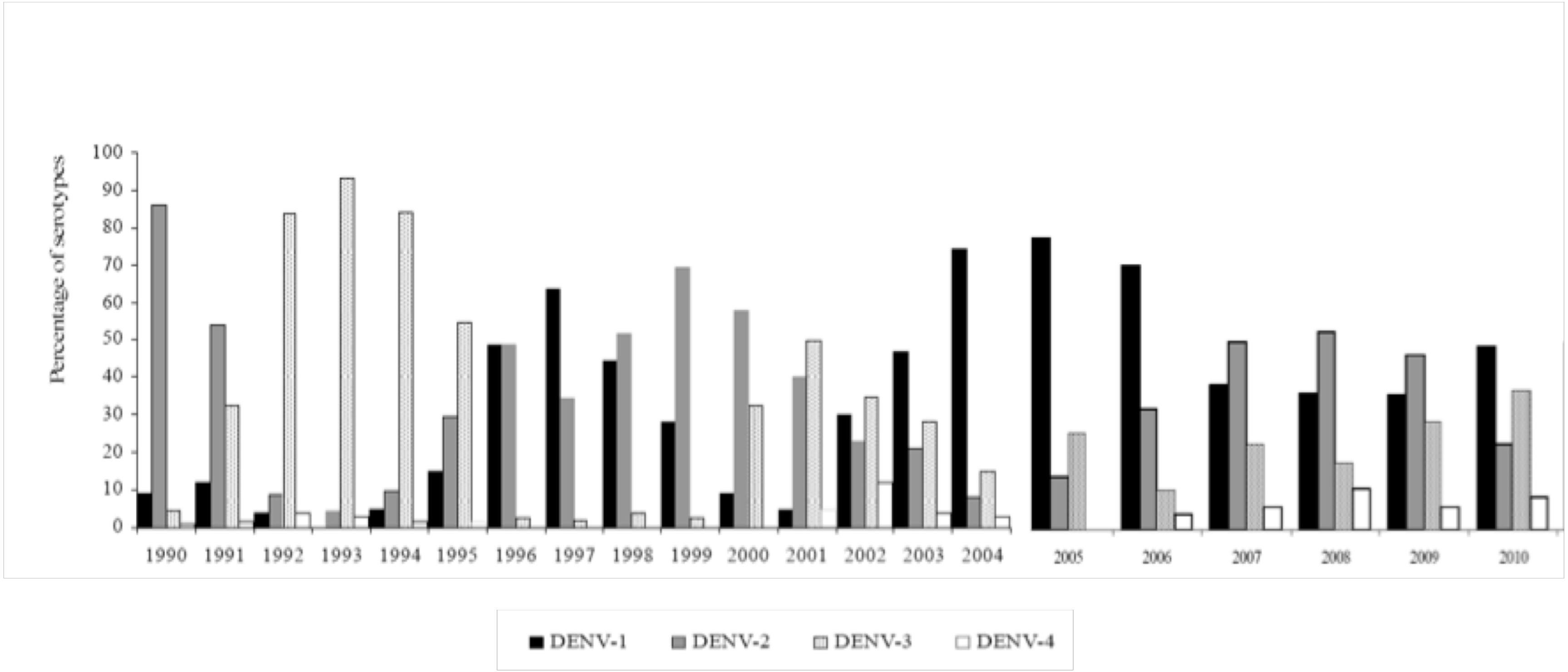


DISTRIBUTION OF DENGUE SEROTYPES IN MALAYSIA, 2005 - 2010

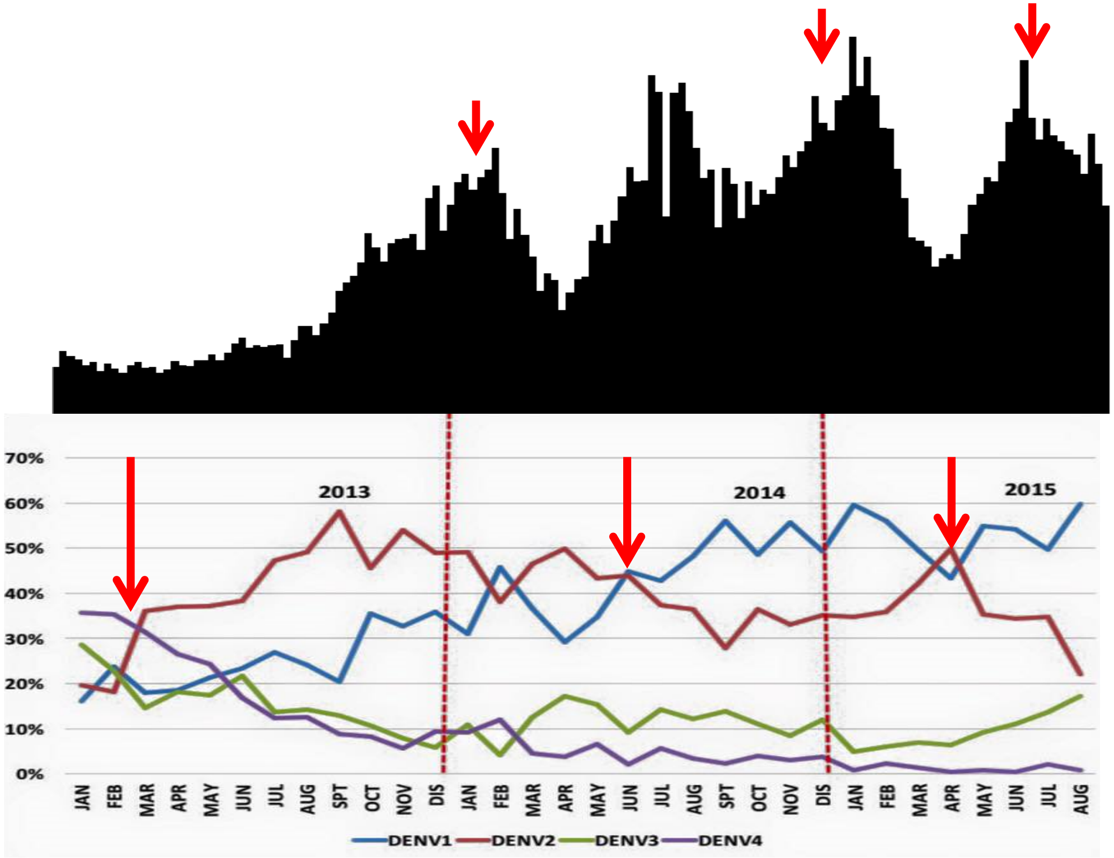


Distribution of DENV serotypes in Malaysia by regions, 2005 to 2010

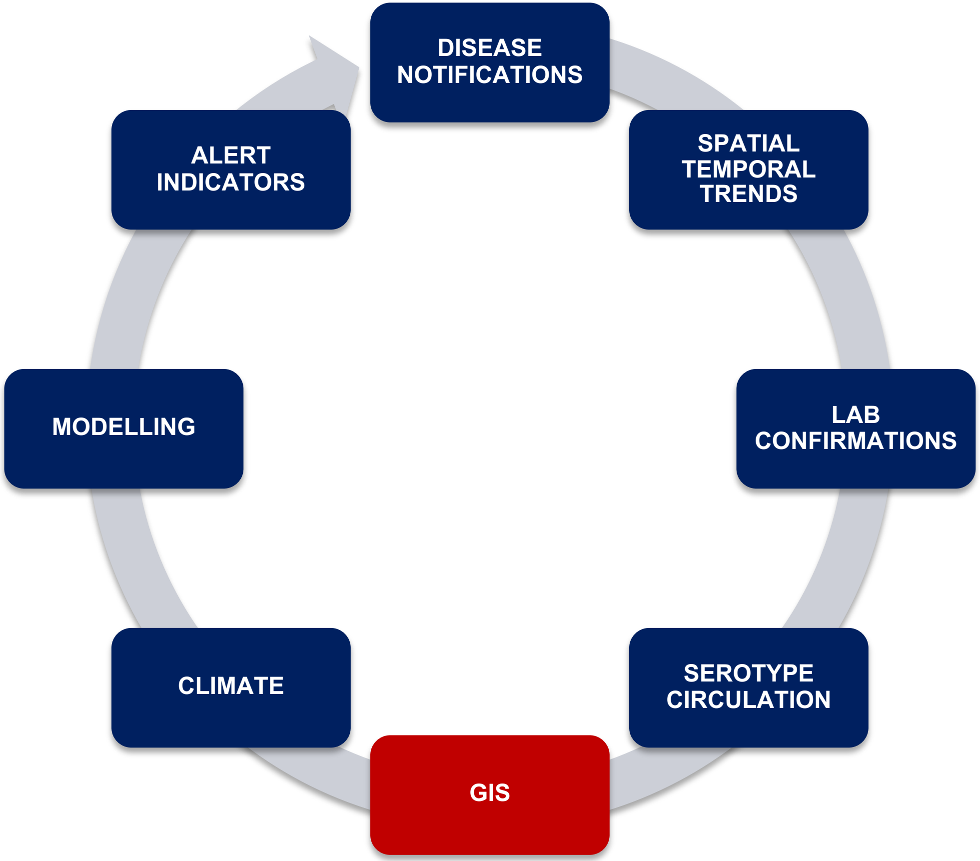
CIRCULATING DENGUE SEROTYPES IN MALAYSIA, 1990 – 2010



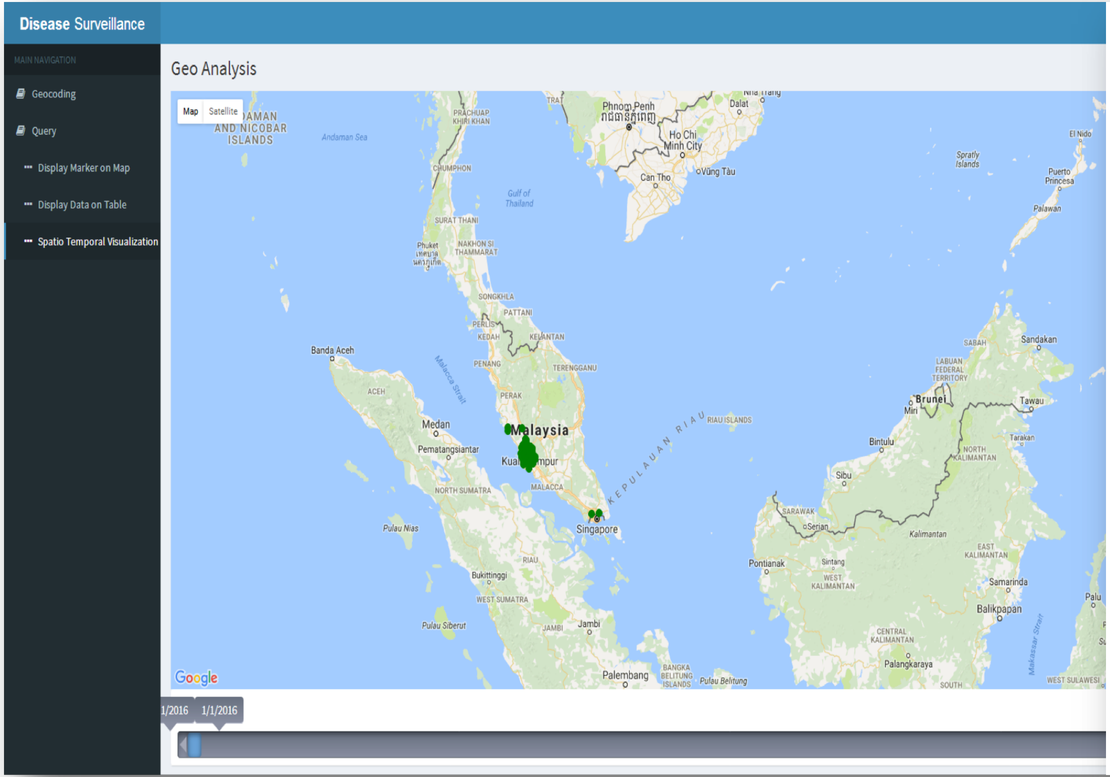
DENGUE CASES AND SEROTYPES IN MALAYSIA, 2013 - 2015



EARLY WARNING IN DISEASE SURVEILLANCE



EARLY WARNING USING GIS



DenMap: A Dengue Surveillance System for Malaysia

Muhammad Rizwan[1], Sarat C Dass[1], Vijanth S Asirvadam[2], Balvinder S Gill[3] and Lokman H Sulaiman[4]

[1]Department of Fundamental and Applied Sciences, Universiti Teknologi PETRONAS, Seri Iskandar, 32610 Tronoh, Perak, Malaysia.
[2]Department of Electrical and Electronic Engineering, Universiti Teknologi PETRONAS, Seri Iskandar, 32610 Tronoh, Perak, Malaysia.
[3]Disease Control Division (Surveillance), Ministry of Health Malaysia, Complex E, Federal Government Administrative Centre, 62590 Putrajaya, Malaysia.
[4]School of Medicine, International Medical University Malaysia, Bukit Jalil, 57000 Bukit Jalil, Wilayah Persekutuan Kuala Lumpur, Malaysia.

E-mail: muhammadrizwan312@gmail.com, sarat.dass@utp.edu.my, vijanth_sagayan@utp.edu.my, drbsgill@moh.gov.my, LokmanHakim@imu.edu.my.

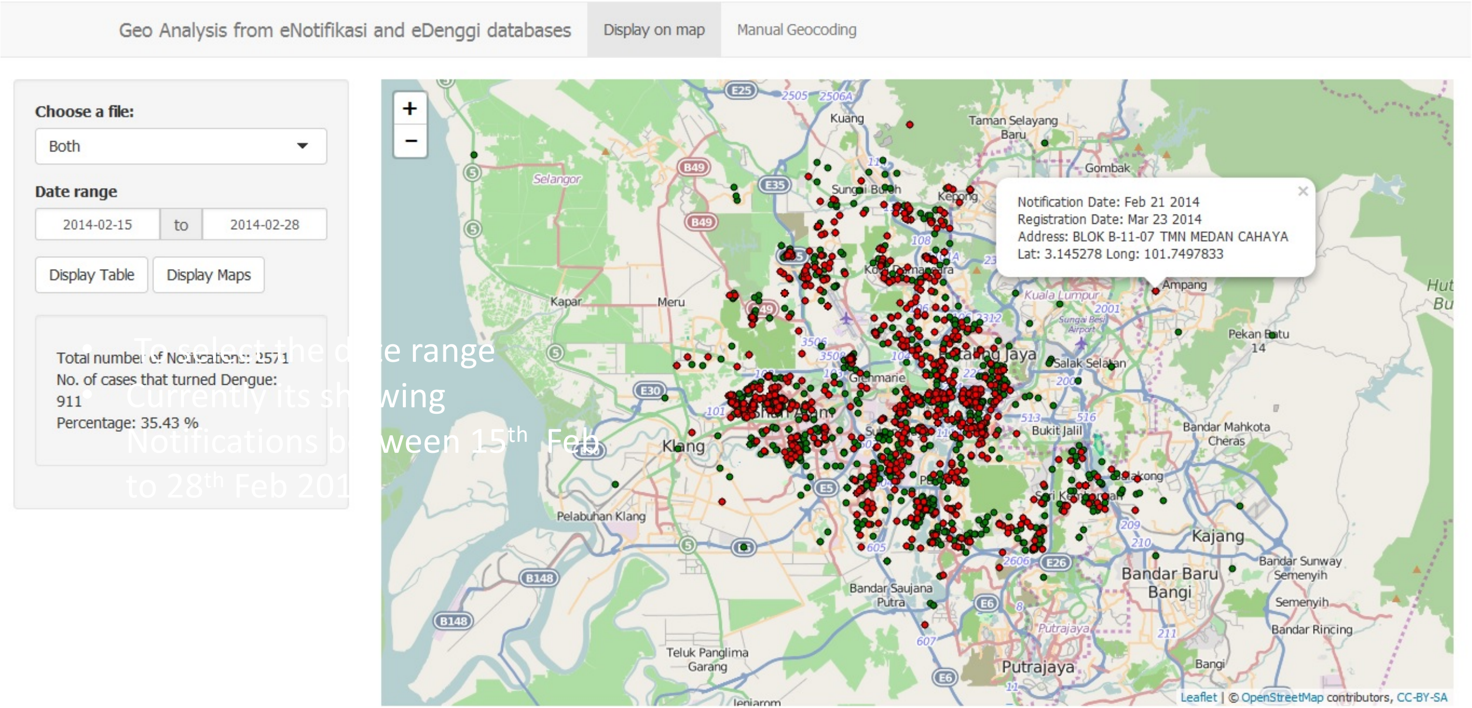
Abstract. Dengue is the world's most rapidly spreading and geographically widespread arthropod-borne disease which needs proper surveillance and control strategies. Effective detection and containment of dengue has proven to be challenging due to the complex nature of interactions among the governing epidemiological factors as well as a number of environmental, climactic and societal attributes. An interactive approach of visualization and mapping of dengue cases on Google Maps is proposed here for the purpose of disease monitoring and surveillance. Our dengue visualization system is a web based application. It is developed using the Shiny package of R software along with HTML and JavaScript interfaces.

Malaysia has the two types of databases for dengue: the e-Dengue database for registered cases and the e-Notifikasi database for notified cases. The e-Dengue database has latitude and longitude information, obtained manually, for each registered dengue case. The visualization system uses those latitudes and longitudes to plot the registered cases on Google Maps. Notified cases do not have any latitude and longitude information but have a case location address for each case. Automatic batch geocoding of addresses is developed for notified cases. Subsequently, notified cases are rendered on Google Maps separately or together with registered cases to gain an understanding of the statistics of disease spread. Filtering options are developed according to either the notification or registration dates.

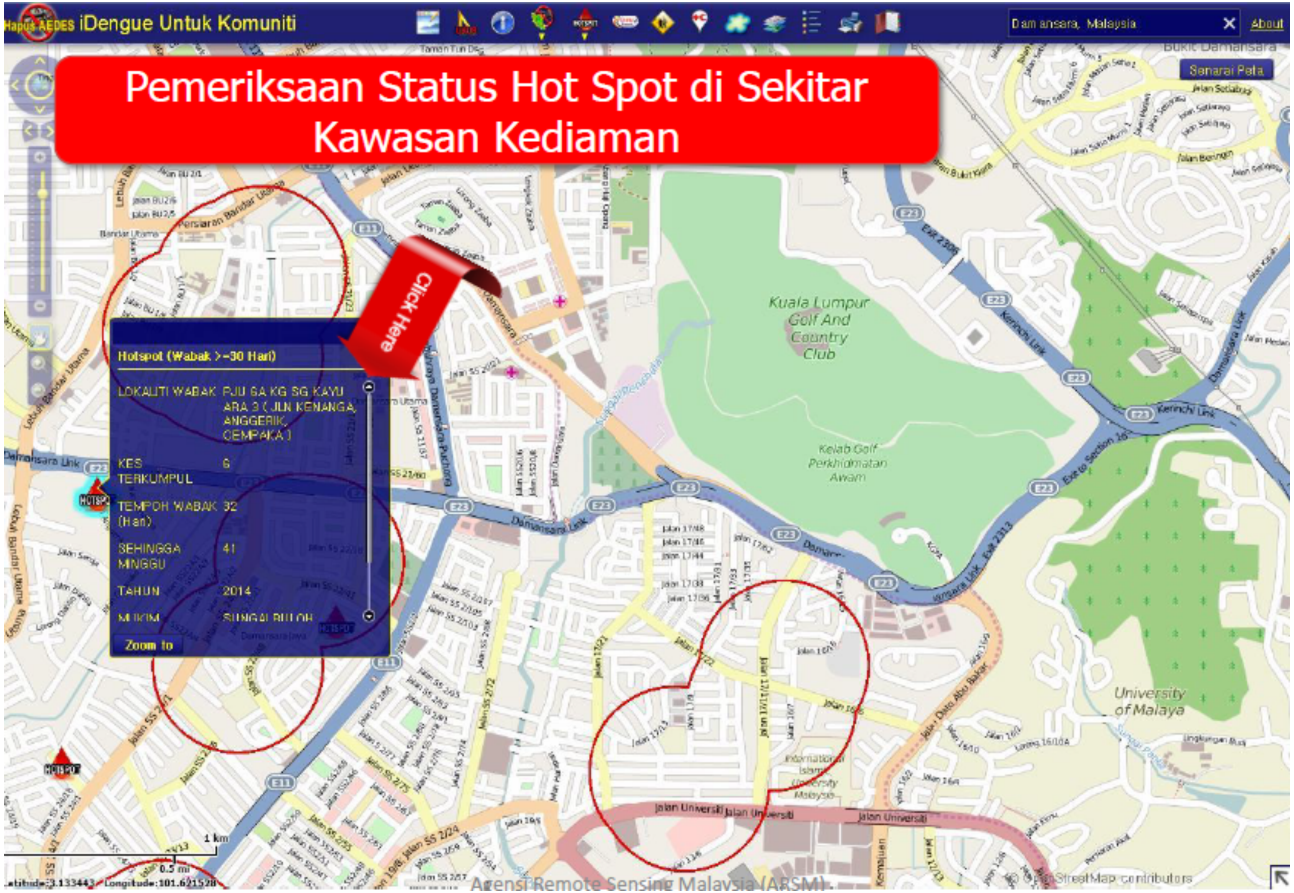
The dengue geocoding and visualization system, DenMap, is an interactive and easy-to-use application for producing maps of notified and registered cases rapidly. The maps display accurate locations of dengue cases and can be made to render other information of each case using map markers. This visualization and analysis system will not require any technical expertise for its usage.

EARLY WARNING USING GIS

- Ability to visualise and determined the spatial and temporal patterns of the cases



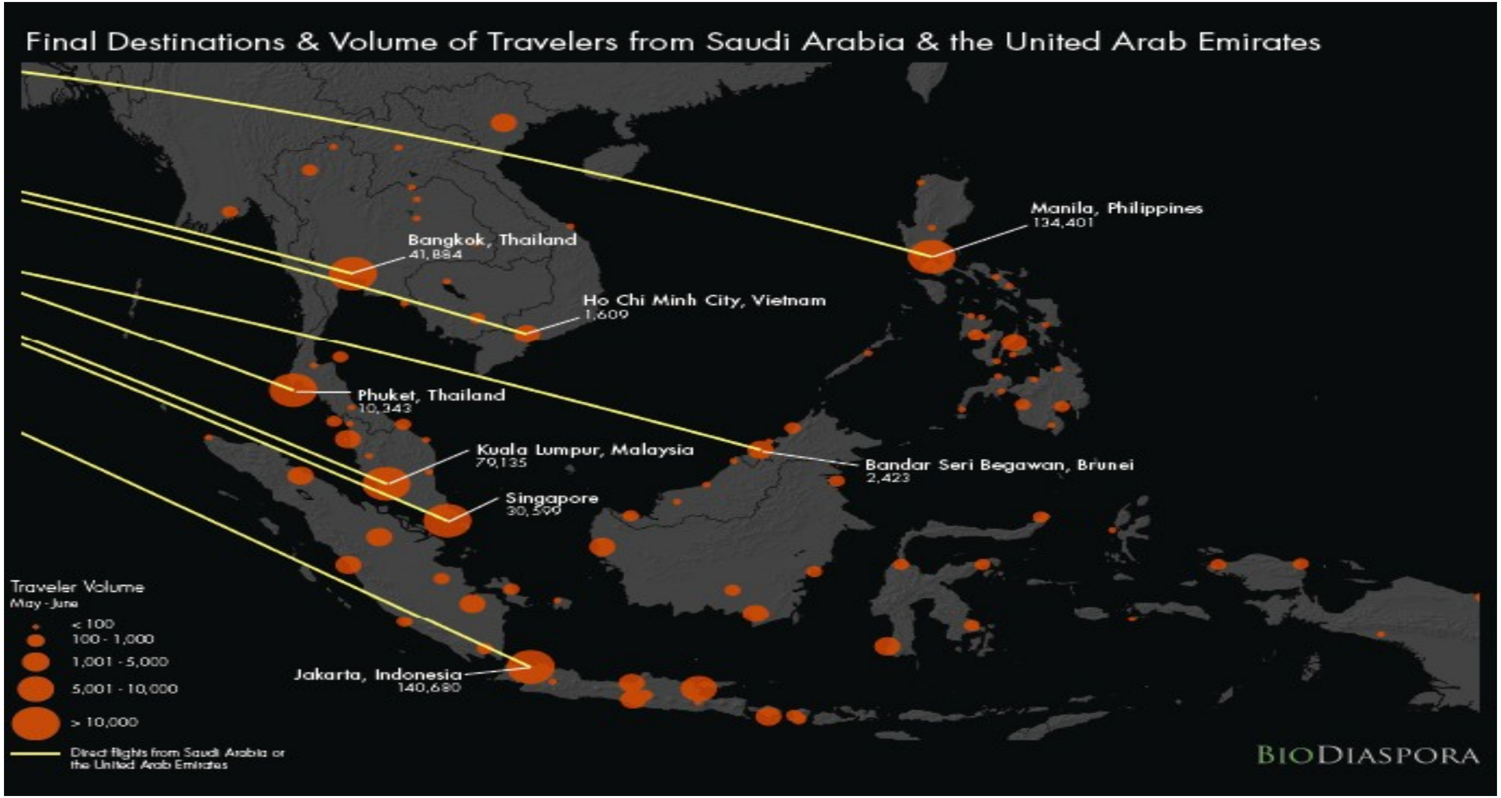
EARLY WARNING USING GIS – I DENGUE



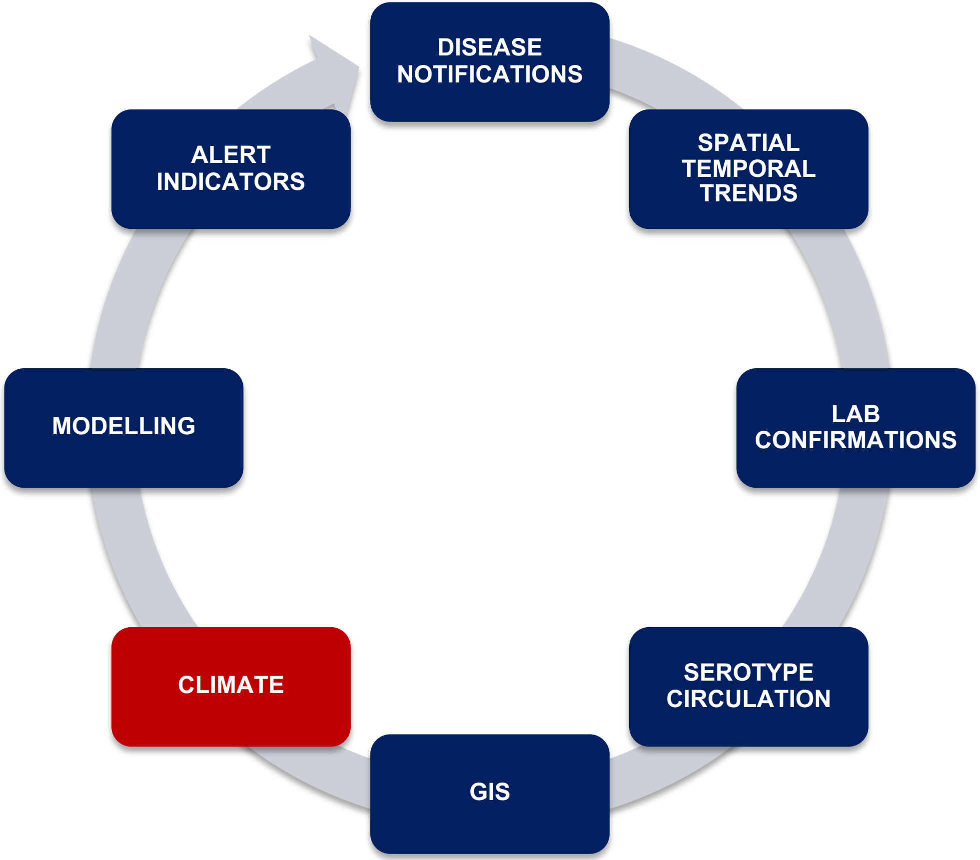
EARLY WARNING USING GIS – SPWD

EARLY WARNING USING GIS - BIODIASPORA

- Risk assessment for Mers-CoV – final destination of travellers



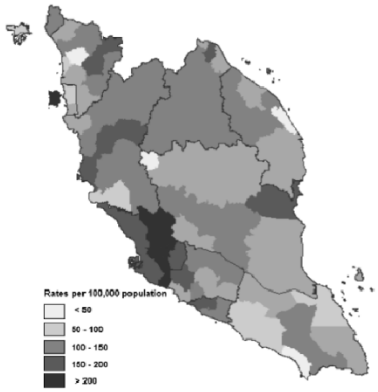
EARLY WARNING IN DISEASE SURVEILLANCE



CLIMATE FACTORS

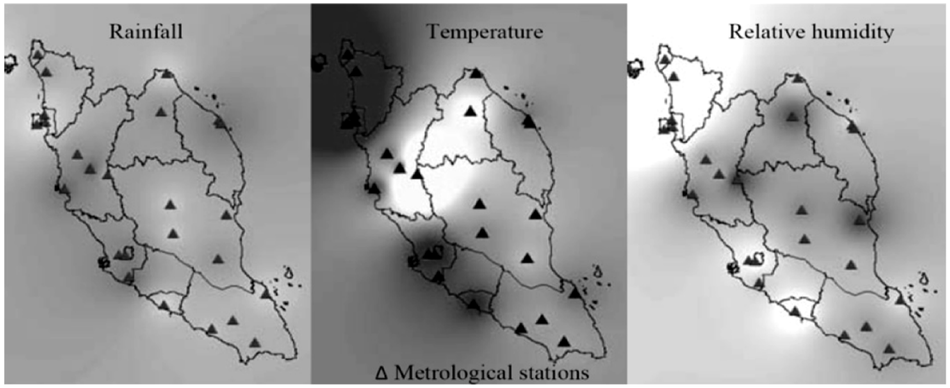
- Monthly climate readings *(rainfall (mm), mean temperature (°C), and average relative humidity (%))* converted from points into surfaces that matched notification rates within the boundaries.
- The inverse distance weighted (IDW) method used to interpolate metrological data to obtain estimate values of these climate variables.
- The raster surface was layered on the geospatial shape files with the state boundaries and the average value for all raster cells within the state boundary was calculated for each climate variable.

WEST / PENINSULAR MALAYSIA



Dengue notification rates in Malaysia from 2005 to 2010

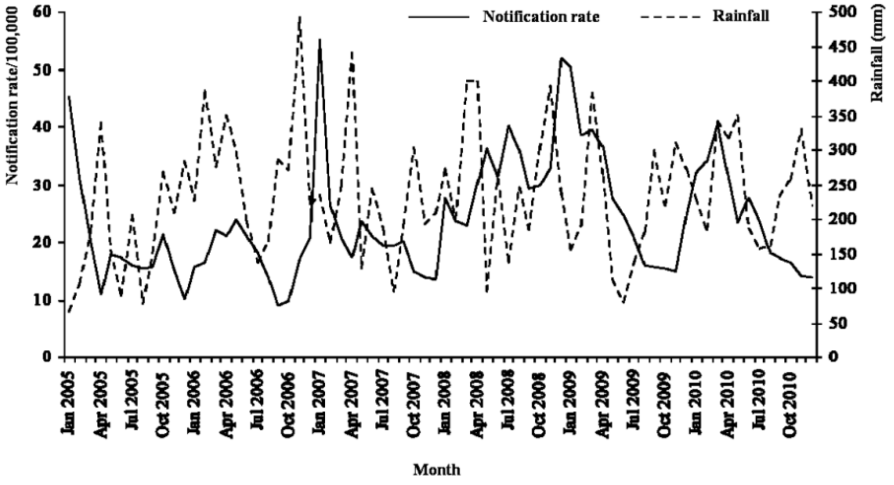
Names and locations of meteorological stations in Peninsular Malaysia

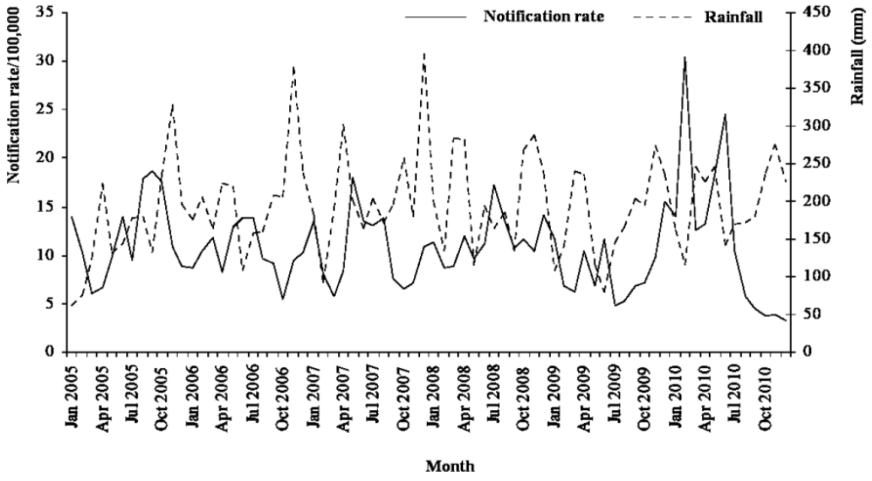


Raster surface for climate variables for January 2005, Peninsular Malaysia

CLIMATE FACTORS - RAINFALL

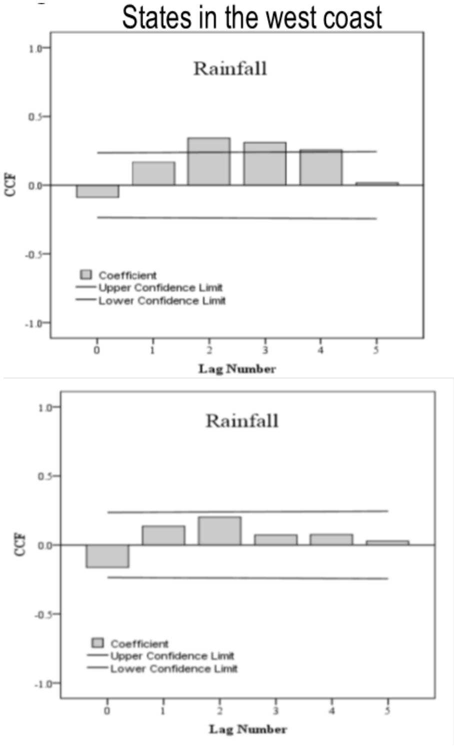
- In states of the west coast, peaks of dengue notification rates were generally seen in the months of January and February which coincides with the NEM from November to March, while secondary peaks were also seen during July to August, which in turn coincides with the SWM from May to September.

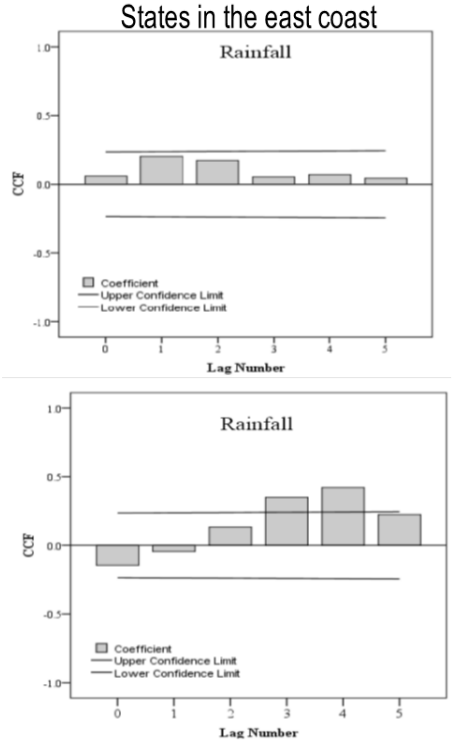




CLIMATE FACTORS - RAINFALL

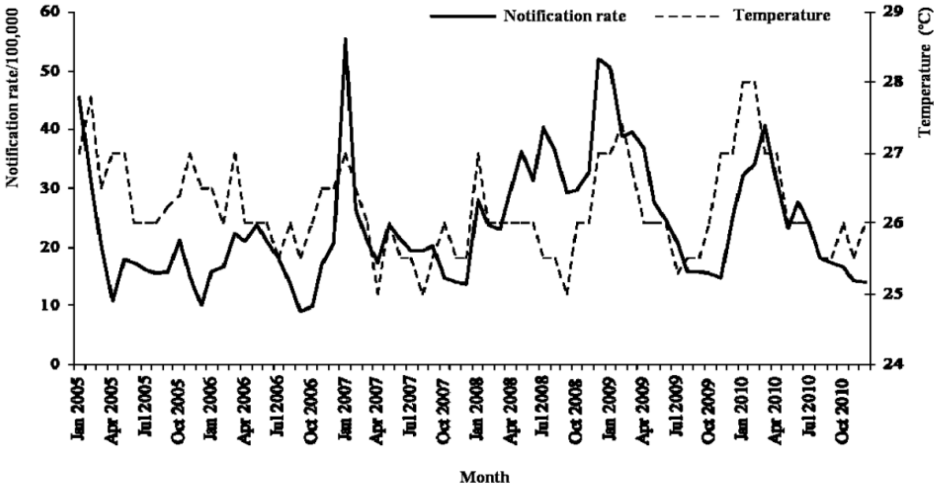
- Results of cross-correlations shows a negative relation between rainfall and dengue rates during the current month and a positive cross-correlation was observed after a months lag for most states.

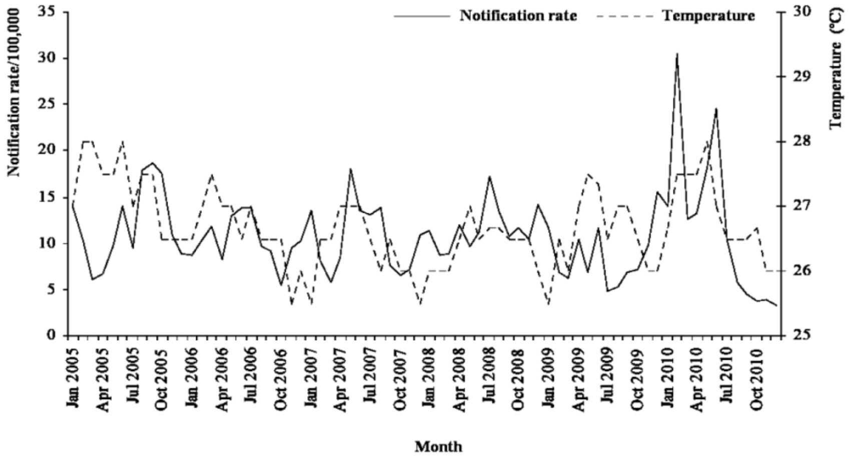




CLIMATE FACTORS - TEMPERATURE

- A positive association between temperature peaks and dengue notification rates were seen at several periods in the west coast states of Selangor and Negeri Sembilan.

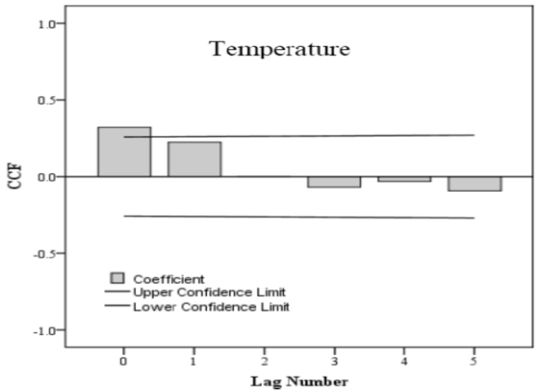


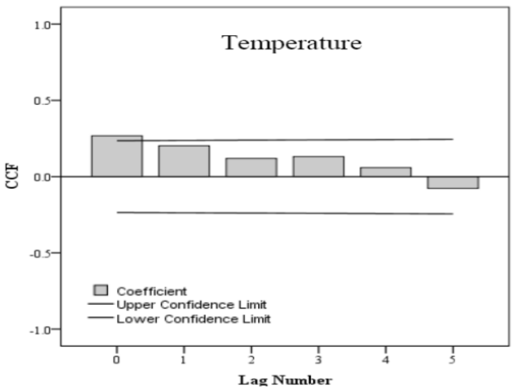


DENGUE – CLIMATE FACTORS - TEMPERATURE

- These associations were strengthened by results of cross-correlations that demonstrated a positive correlation between dengue notification rates and temperature at the current month for states in the west coast.

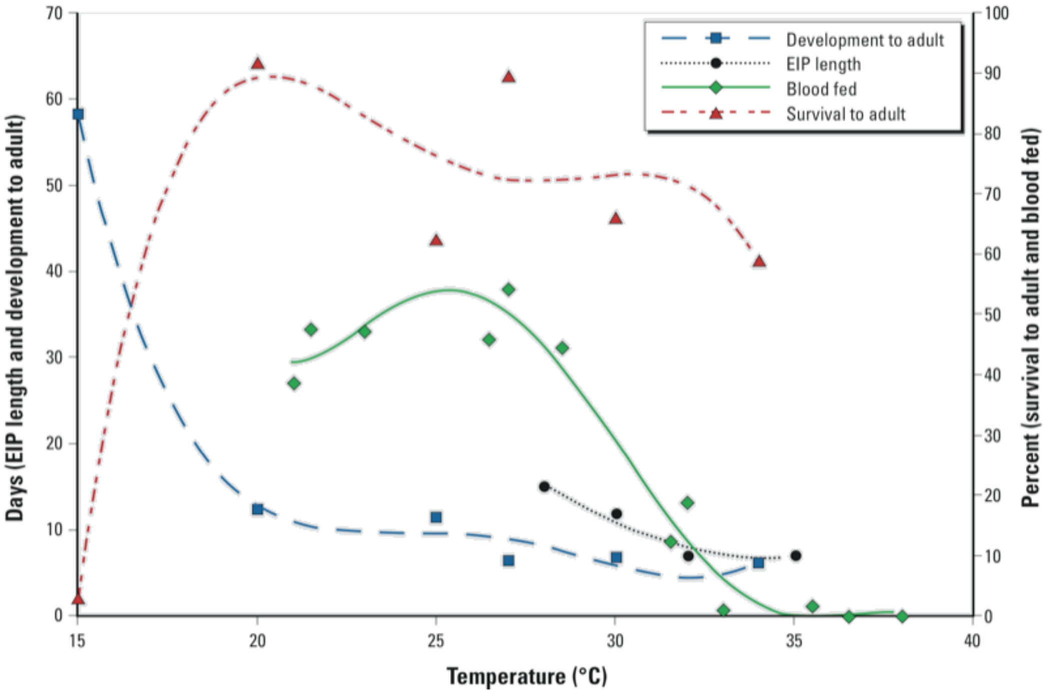
States in the west coast





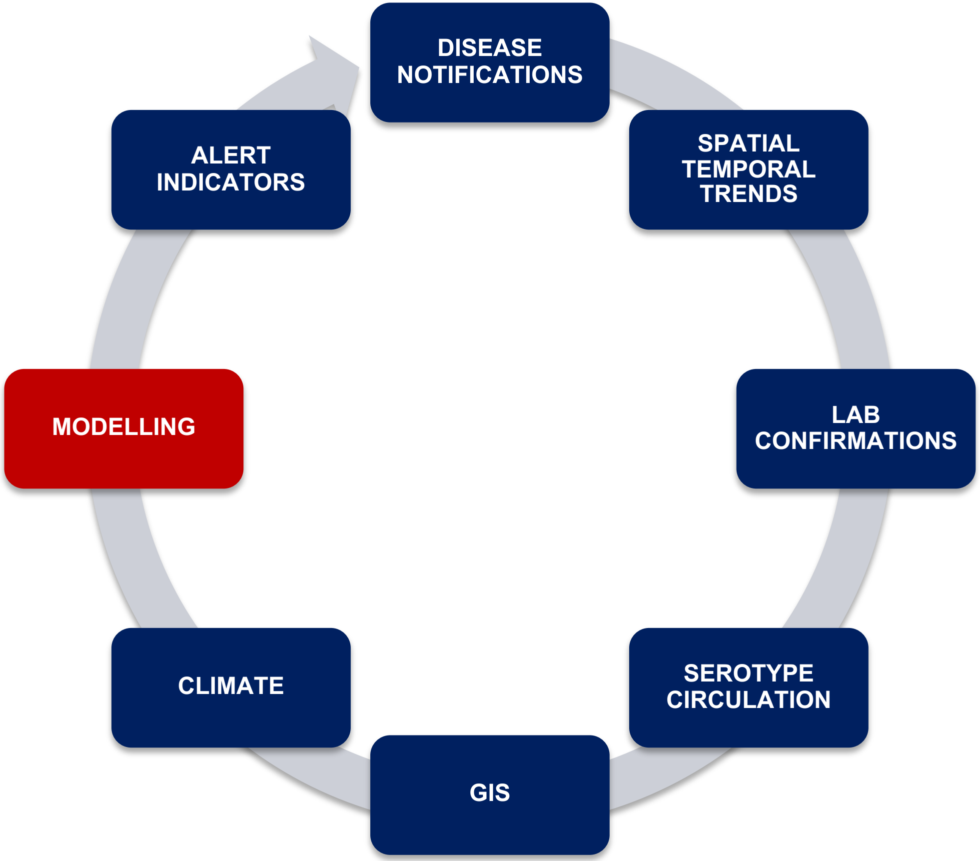
DENGUE – CLIMATE FACTORS - TEMPERATURE

- Warmer temperatures contribute to increased adult mosquito survival



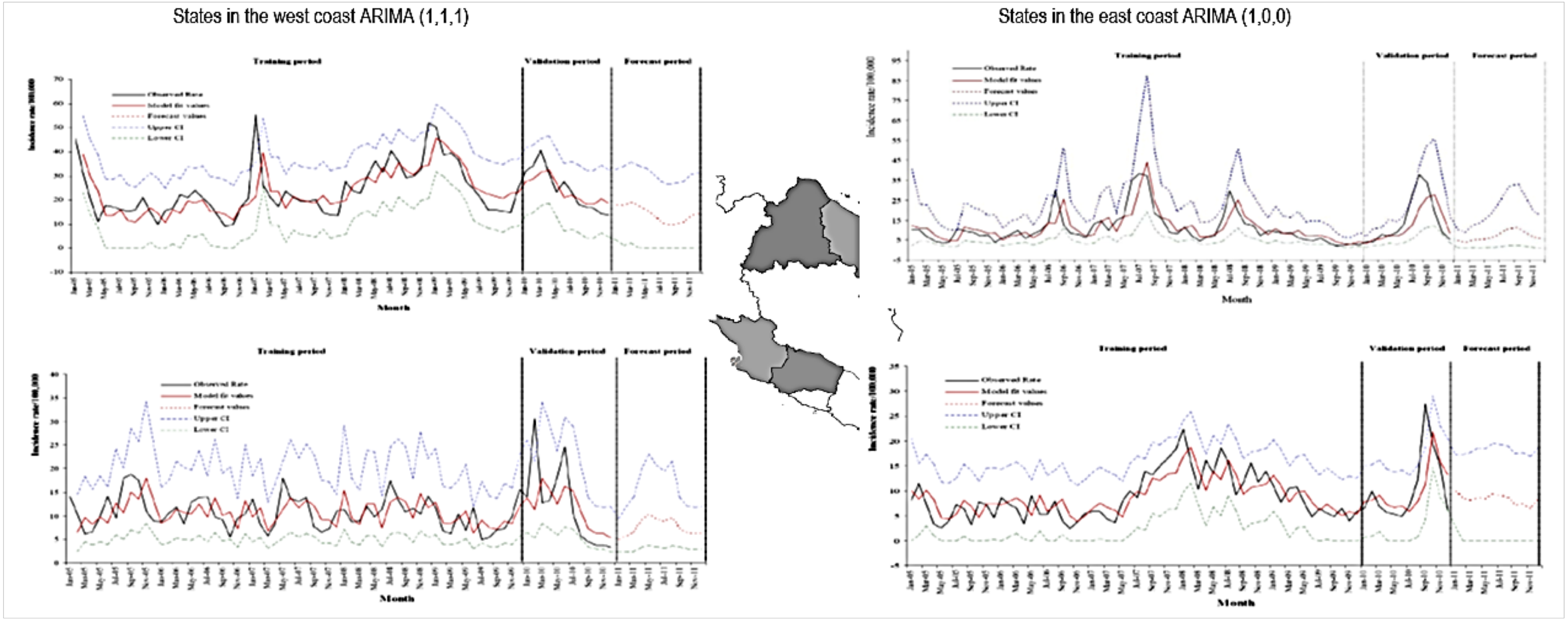
Focks DA, Haile DG, Daniels E, Mount GA. Dynamic life table model for Aedes aegypti (Diptera: Culicidae): simulation results and validation. Journal of Medical Entomology. 1993;30(6):1018-28.

EARLY WARNING IN DISEASE SURVEILLANCE



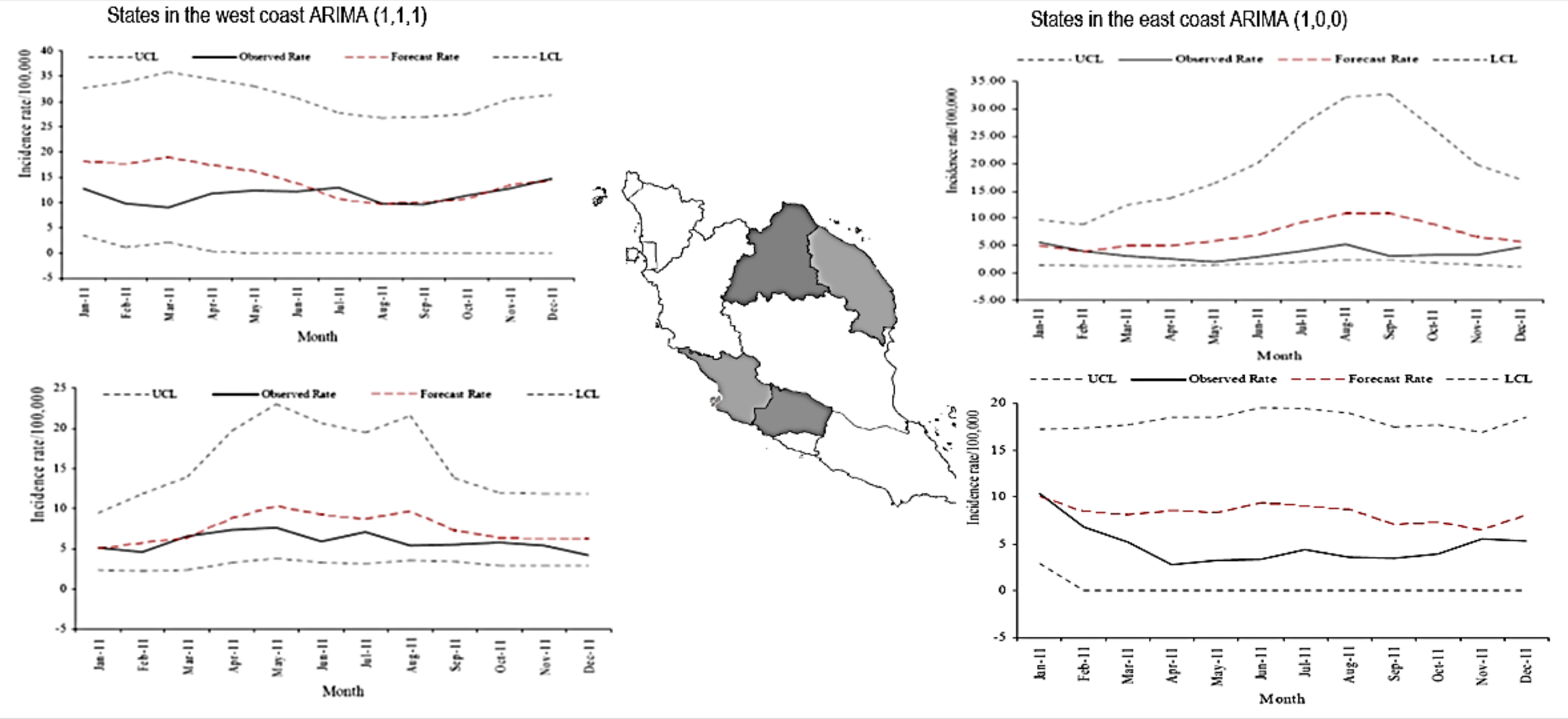
FORECASTS OF DENGUE USING ARIMA MODELS

- While both states in the east and west coast had non-seasonal ARIMA models, climate variables were found to improve the model fit for all states analysed with some climate parameters being apparent.



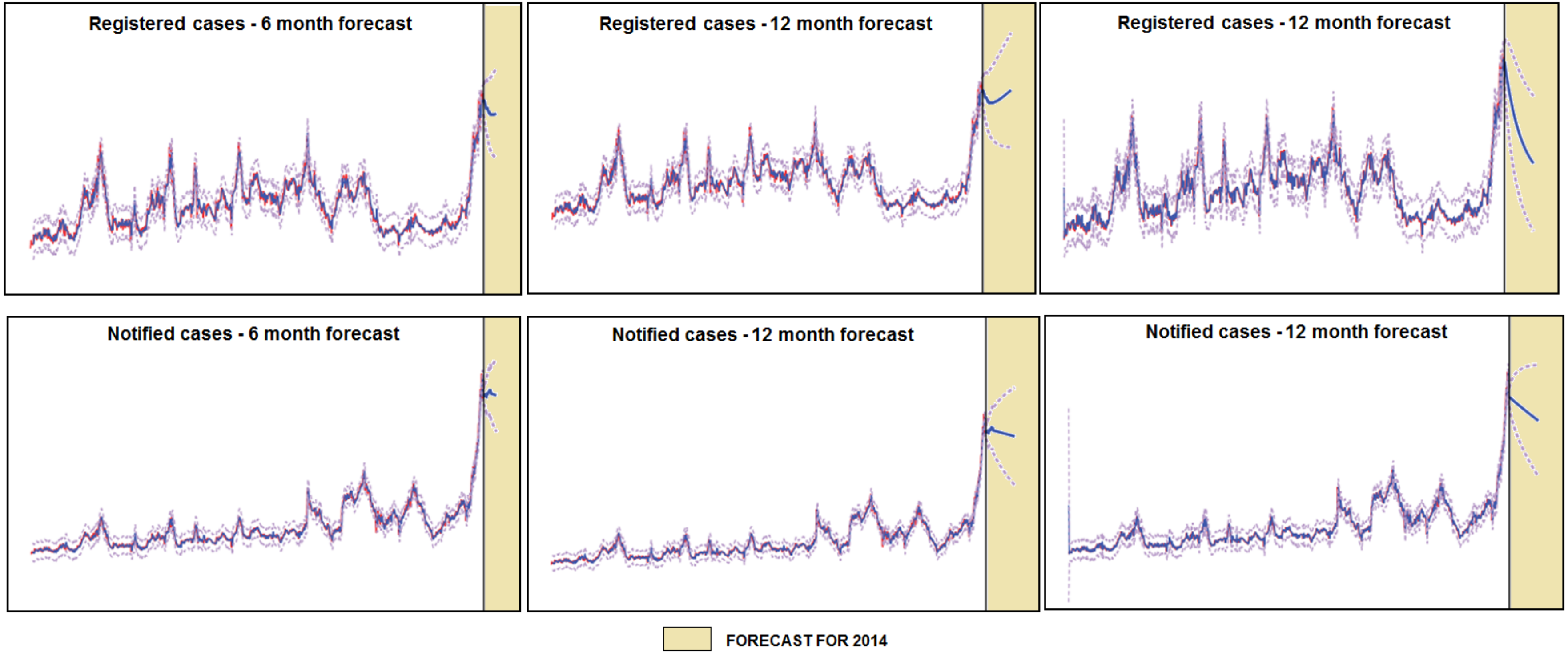
FORECASTS OF DENGUE USING ARIMA MODELS

❑ Models for all states were able to forecast the trends of dengue notification rates within its 95% CI.



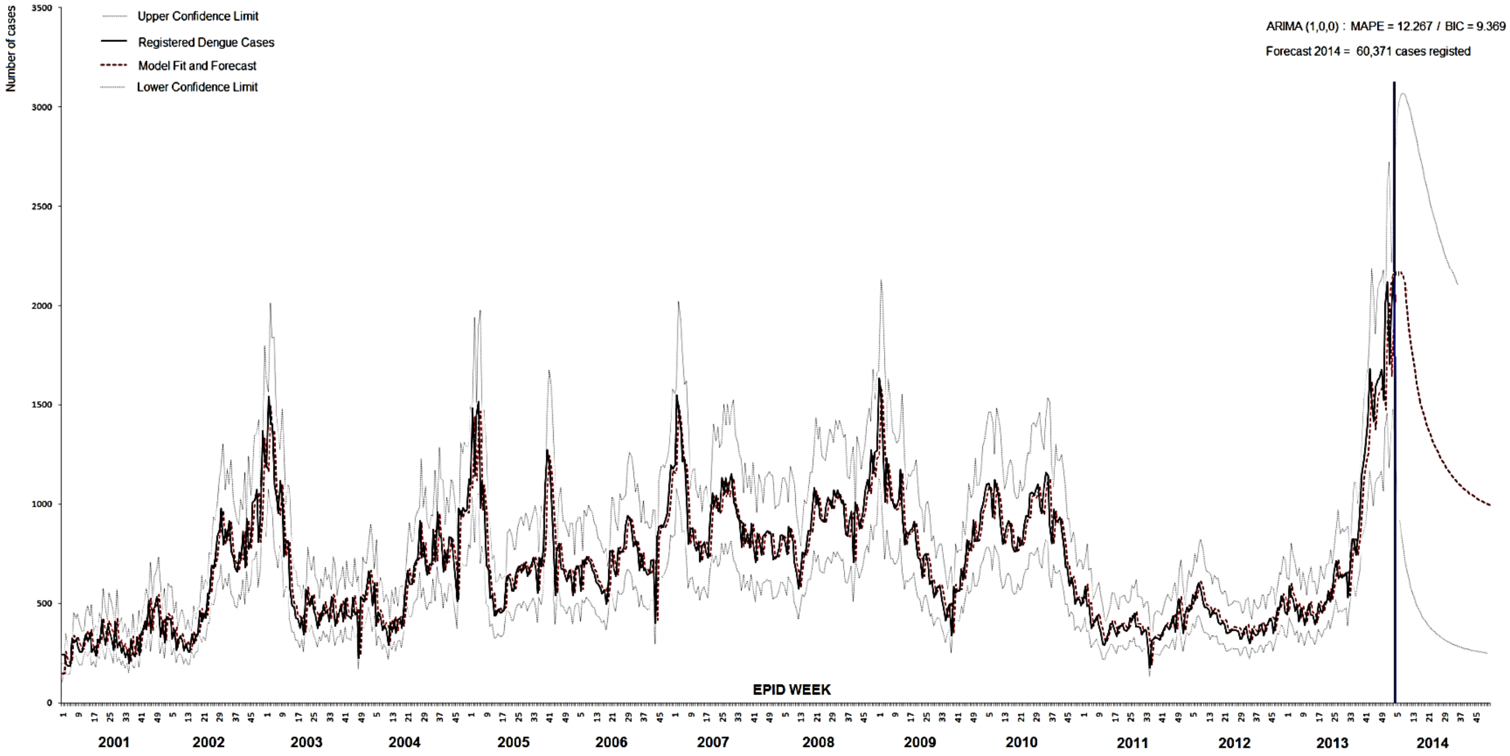
FORECASTS OF DENGUE USING ARIMA MODELS

- Models of 6 and 12 month forecasts using registered and notified cases consistently showed the peak of the epidemic in early part of the year followed by a decline of cases.



FORECASTS OF DENGUE USING ARIMA MODELS

- 12 month forecasts using registered cases (best case scenario)



Registered dengue cases by week from 2001 to 2013 and forecasted registered cases for 2014, Malaysia

FORECASTS OF DENGUE USING ARIMA MODELS

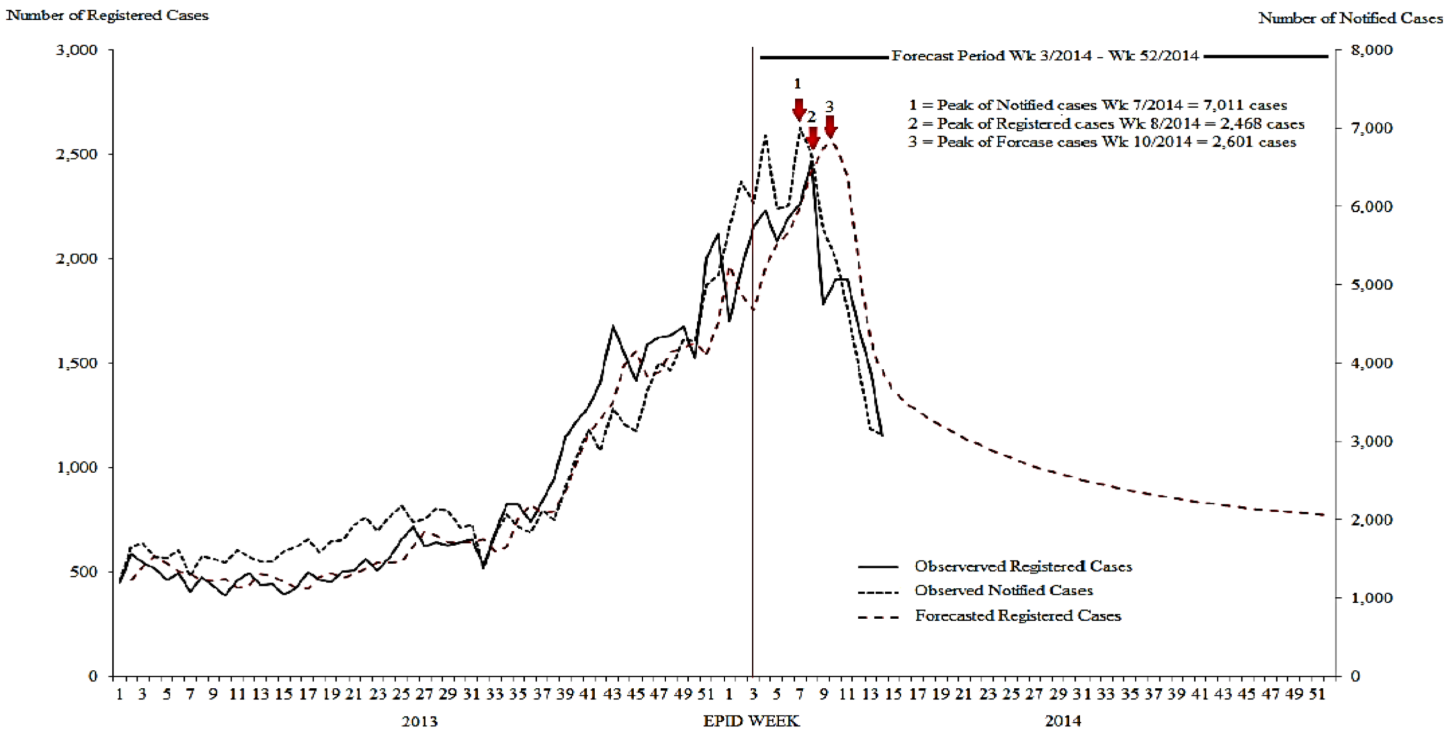
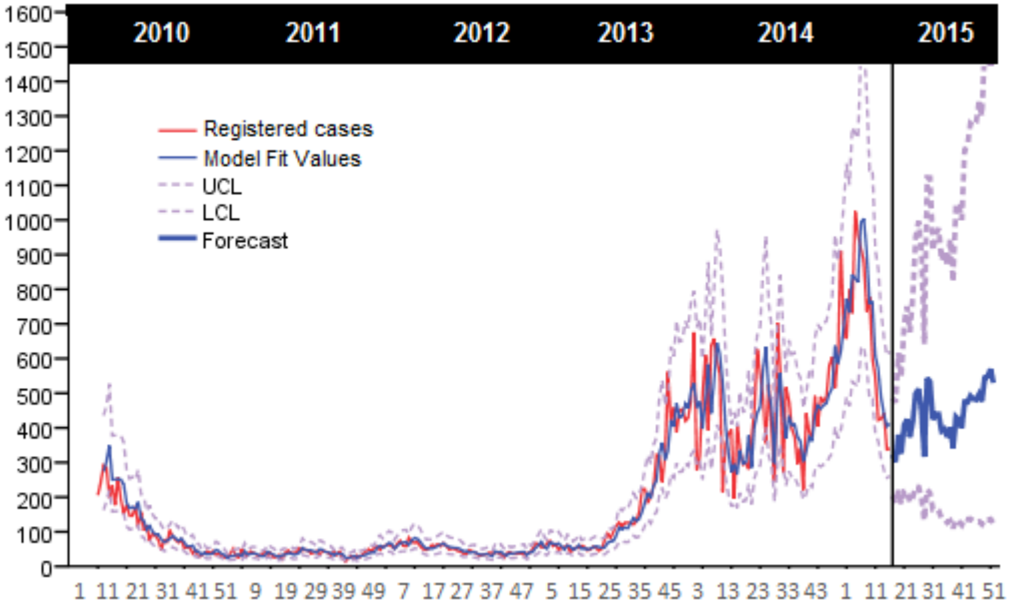
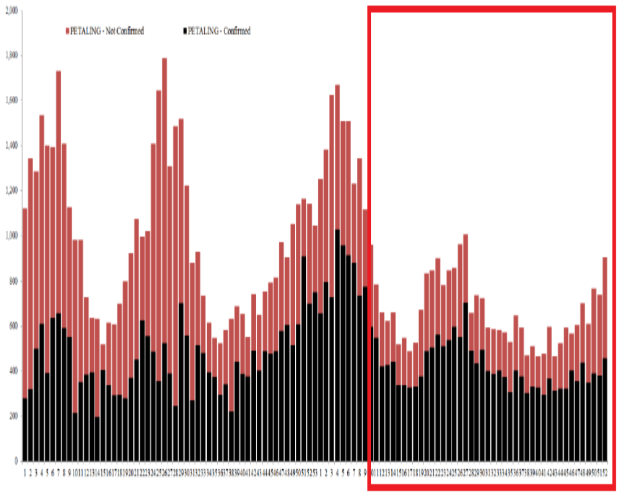


Figure 1: Observed notified and registered dengue cases by week from Wk 1/2013 to Wk 14/2014 and forecasted registered cases from Wk 3/2014 to Wk 52/2014, Malaysia

FORECASTS OF DENGUE USING ARIMA MODELS

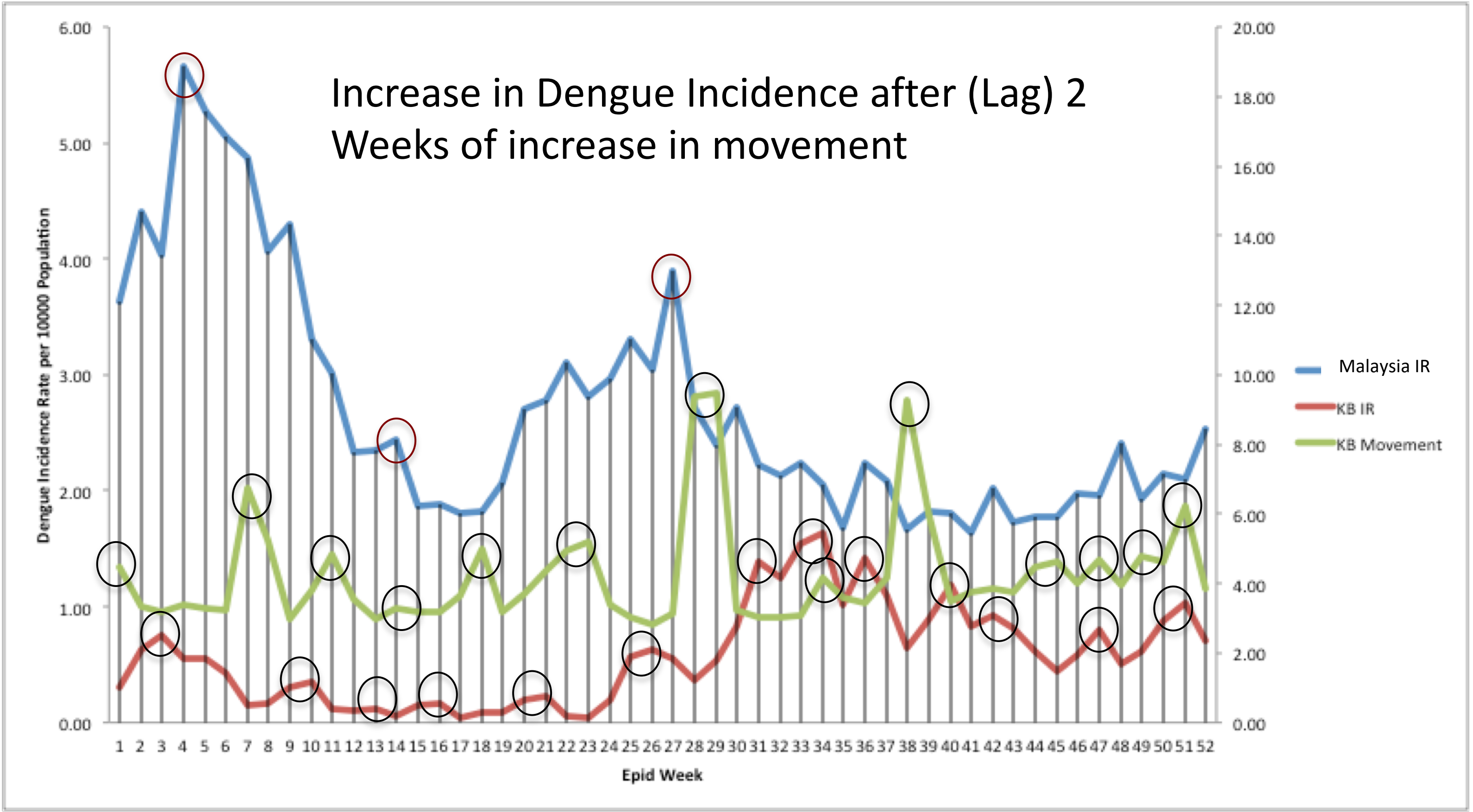




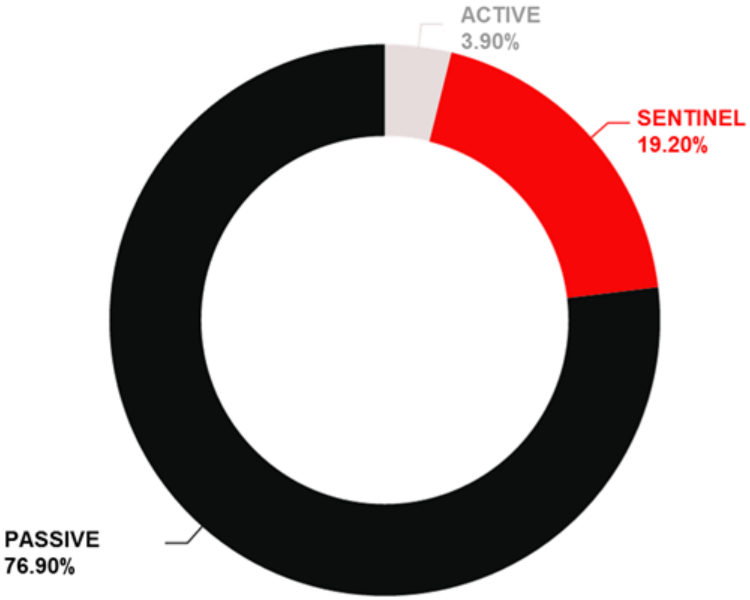
CORRELATION BETWEEN HUMAN MOVEMENT WITH DENGUE INCIDENCE IN MALAYSIA

Study Area	Lags	Dengue Incidence and Human Movement from Petaling
Kota Bharu	Lag r (sig) Sig Lag period	2 (0.2975, 0.0379) Nil
Penang Island	Lag r (sig) Sig Lag period	1 (0.2923, 0.0394) Nil
Johor Bharu	Lag r (sig) Sig Lag period	3 (0.2963, 0.0409) Nil

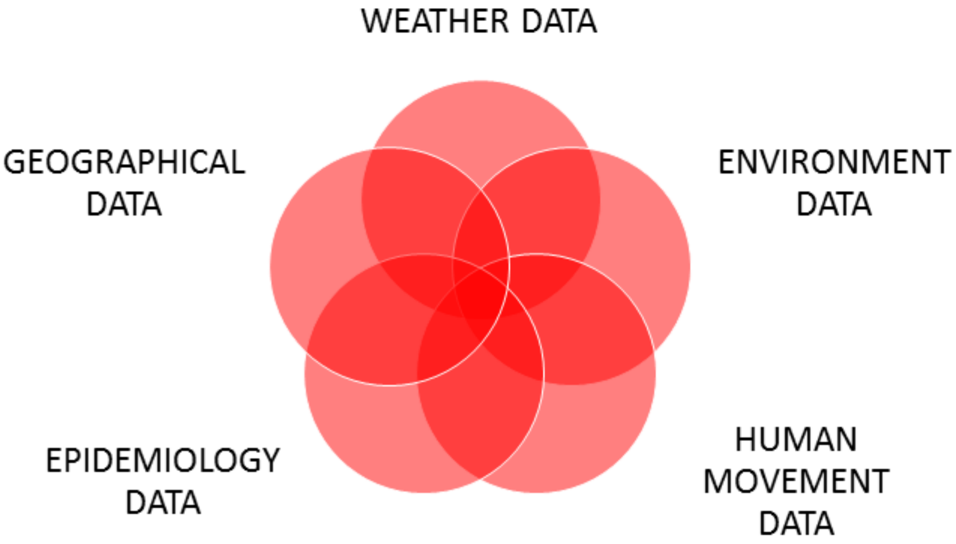
HUMAN MOVEMENT AND DENGUE INCIDENCE IN KOTA BHARU, MALAYSIA, 2015



ARTIFICIAL INTELLIGENCE



CURRENT RESPONSE



EPIDEMIOLOGICAL + AI RESEARCH

SOURCE: ASIA-PACIFIC DENGUE PREVENTION BOARD AND THE AMERICAS DENGUE PREVENTION BOARD

MECHANISTIC ENTOMOLOGY AND DISEASE MODEL

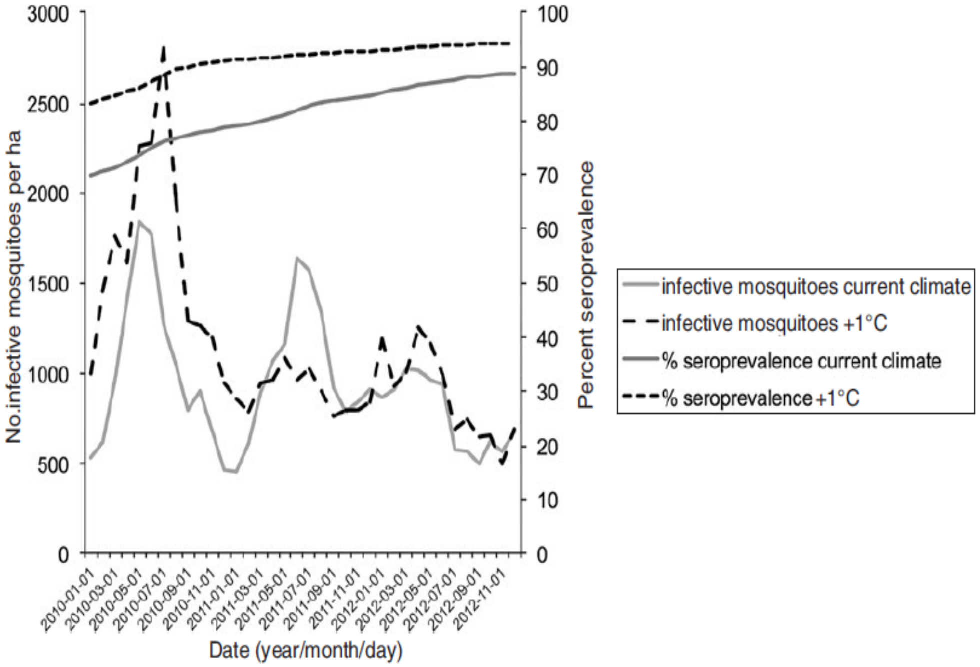


Fig. 5. Simulated dengue infective mosquitoes and human seroprevalence for dengue in Petaling district for 2010–2012 and with a 1 °C daily temperature increase (from simulation 3) to demonstrate the potential for the impact of climate change.

Epidemiol. Infect., Page 1 of 9. © Cambridge University Press 2015
doi:10.1017/S095026881400380X

Testing the impact of virus importation rates and future climate change on dengue activity in Malaysia using a mechanistic entomology and disease model

C. R. WILLIAMS[1]*, B. S. GILL[2], G. MINCHAM[1], A. H. MOHD ZAKI[2], N. ABDULLAH[3], W. R. W. MAHIYUDDIN[3], R. AHMAD[4], M. K. SHAHAR[4], D. HARLEY[5], E. VIENNET[5], A. AZIL[6] AND A. KAMALUDDIN[7]

[1] *Sansom Institute for Health Research, University of South Australia, Adelaide, Australia*
[2] *Disease Control Division, Ministry of Health Malaysia*
[3] *Epidemiology and Biostatistics Unit, Institute for Medical Research, Malaysia*
[4] *Medical Entomology Unit & WHO Collaborating Centre, Institute for Medical Research, Malaysia*
[5] *National Centre for Epidemiology and Population Health, Australian National University, Canberra, Australia*
[6] *Department of Parasitology and Medical Entomology, Universiti Kebangsaan Malaysia, Malaysia*
[7] *Environmental Health Research Centre, Institute for Medical Research, Malaysia*

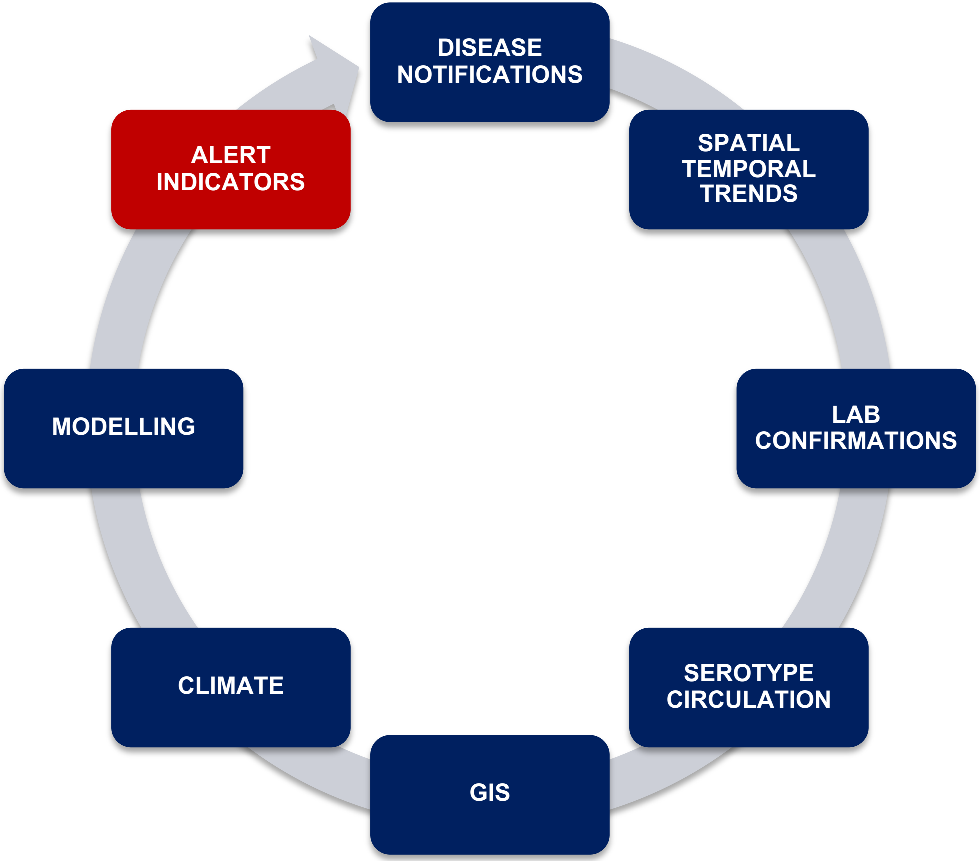
Received 12 September 2014; Final revision 19 November 2014; Accepted 12 December 2014

SUMMARY

We aimed to reparameterize and validate an existing dengue model, comprising an entomological component (CIMSiM) and a disease component (DENSiM) for application in Malaysia. With the model we aimed to measure the effect of importation rate on dengue incidence, and to determine the potential impact of moderate climate change (a 1 °C temperature increase) on dengue activity. Dengue models (comprising CIMSiM and DENSiM) were reparameterized for a simulated Malaysian village of 10 000 people, and validated against monthly dengue case data from the district of Petaling Jaya in the state of Selangor. Simulations were also performed for 2008-2012 for variable virus importation rates (ranging from 1 to 25 per week) and dengue incidence determined. Dengue incidence in the period 2010–2012 was modelled, twice, with observed daily weather and with a 1 °C increase, the latter to simulate moderate climate change. Strong concordance between simulated and observed monthly dengue cases was observed (up to $r = 0{\cdot}72$). There was a linear relationship between importation and incidence. However, a doubling of dengue importation did not equate to a doubling of dengue activity. The largest individual dengue outbreak was observed with the lowest dengue importation rate. Moderate climate change resulted in an overall decrease in dengue activity over a 3-year period, linked to high human seroprevalence early on in the simulation. Our results suggest that moderate reductions in importation with control programmes may not reduce the frequency of large outbreaks. Moderate increases in temperature do not necessarily lead to greater dengue incidence.

Key words: Arboviruses, dengue fever, epidemiology, estimating, modelling, prevalence of disease.

EARLY WARNING IN DISEASE SURVEILLANCE



ALERT INDICATORS

Objective

- Using retrospective country datasets, the aim was to define and detect dengue outbreaks using probable cases as the outbreak variable, and successfully predict these outbreaks using earlier changes in various entomological, meteorological and epidemiological alarm variables.

Method

- This study considered the Shewhart method and Endemic Channel to build a simple model based on logistic regression that can predict forthcoming outbreaks, with high sensitivity (↑number of true positive outbreak detections) and a low number of false alarms (↑PPV).

Sample

- Study conducted at five participating countries (Brazil, Dominican Republic, Malaysia, Mexico and Vietnam)

Indicators

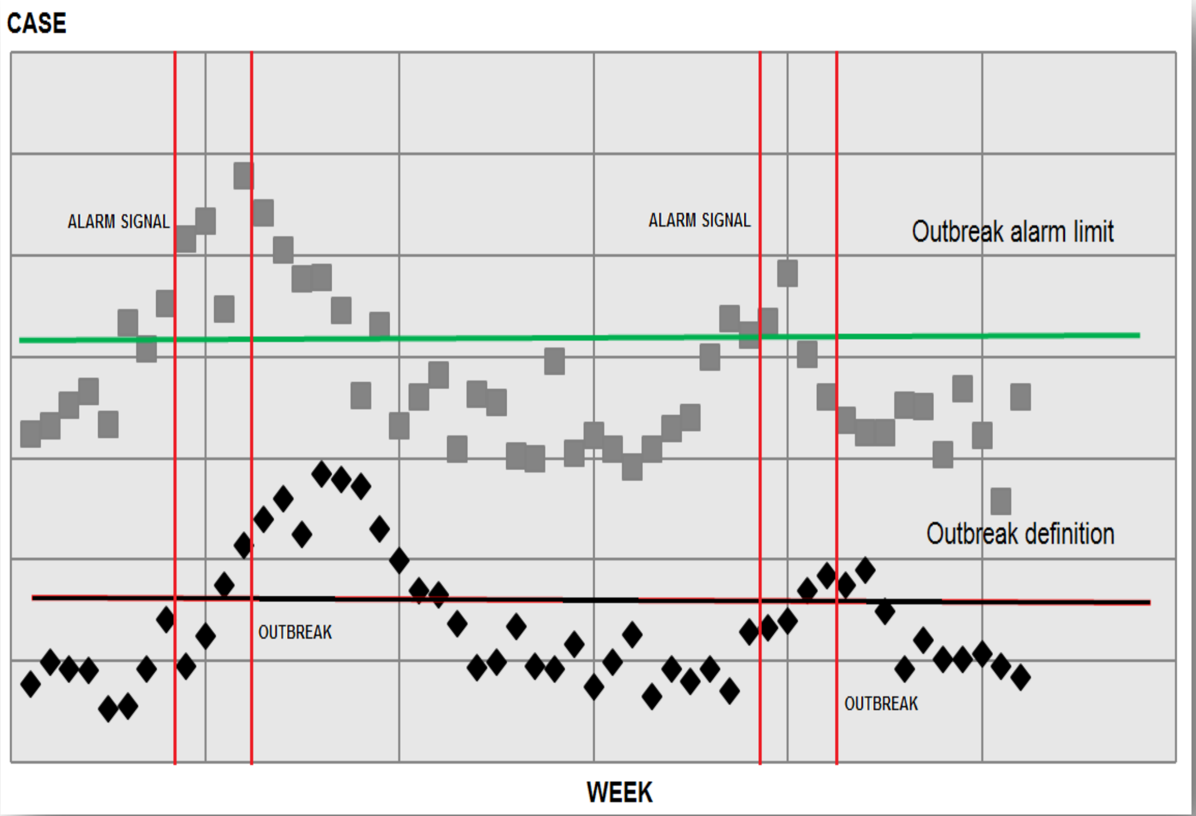
- Meteorological (outdoor mean air temperature, rainfall, outdoor relative humidity);
- Epidemiological (mean age, circulating serotype, probable dengue cases, hospitalized dengue cases);
- Entomological (Breteau Index, House Index, Ovitrap Index (Mexico only)).

ALERT INDICATORS

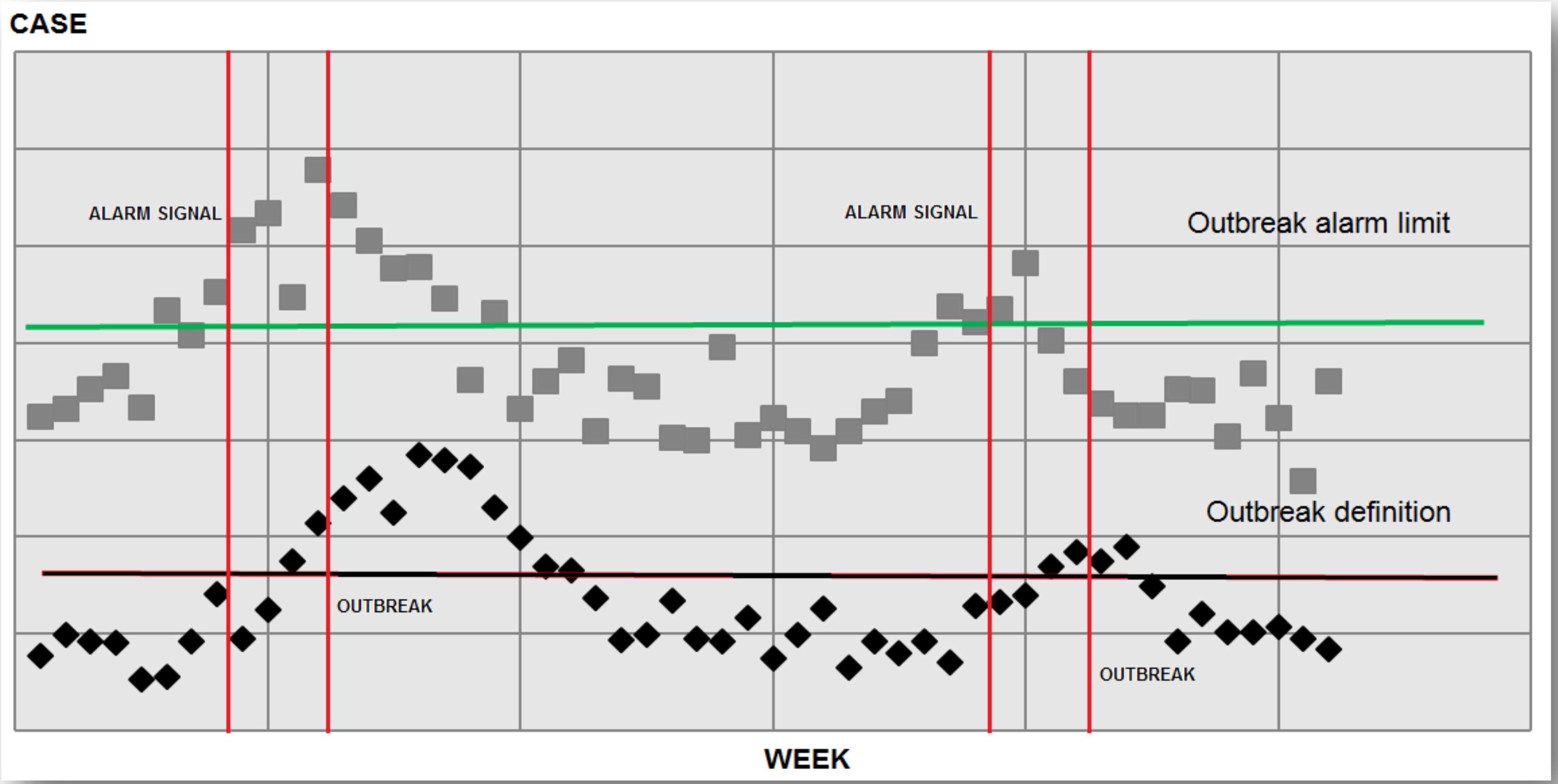
The Shewhart method

- This method involves the use of control charts to define ‘in-control’ and ‘out-of-control’ states, using the historic mean and standard deviation of the outcome variable.

- the Endemic Channel represents the number of cases within the expected normal range, or the ‘in control’ state, while anything above this moving threshold would be considered representative of an ‘out of control’ state i.e. an outbreak.



ALERT INDICATORS

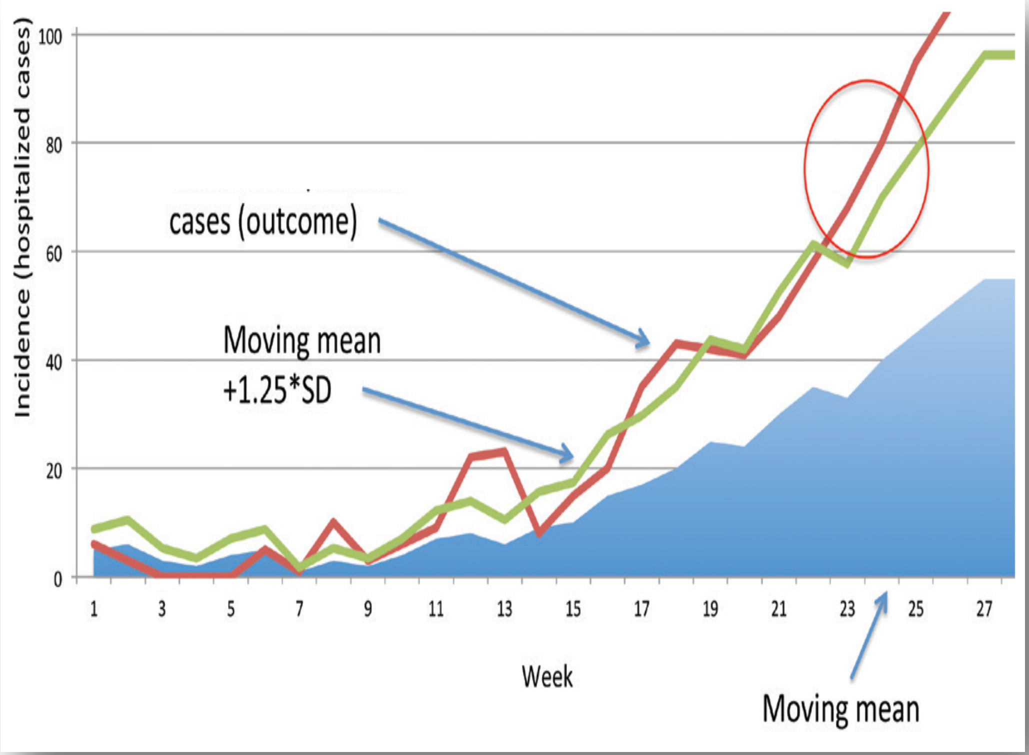


THE ENDEMIC CHANNEL

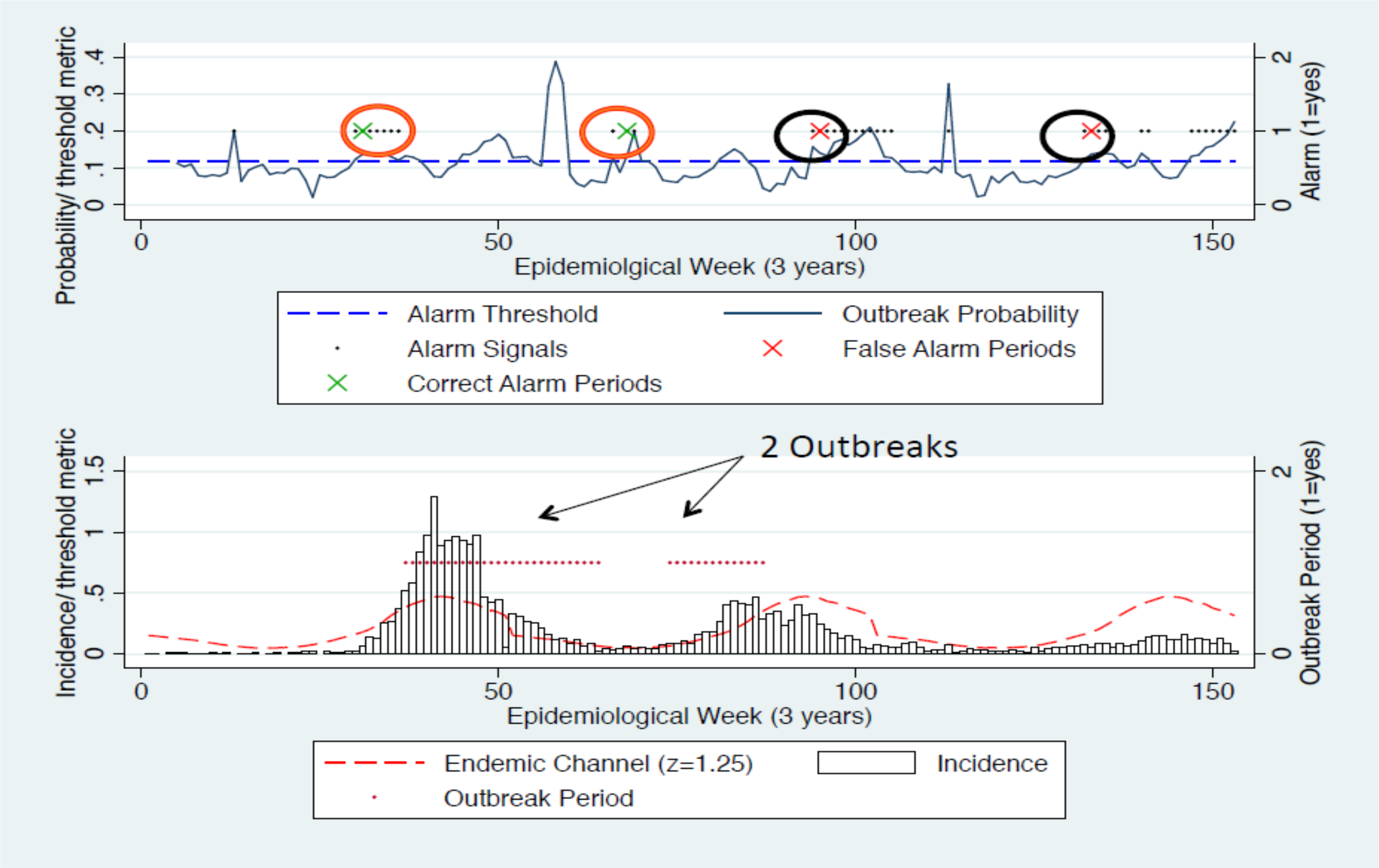
The Endemic Channel

- The Endemic Channel was calculated for each district using a smoothed moving mean and standard deviation, with a multiplier of the standard deviation known as ‘z, to vary the Endemic Channel within the evaluation period.

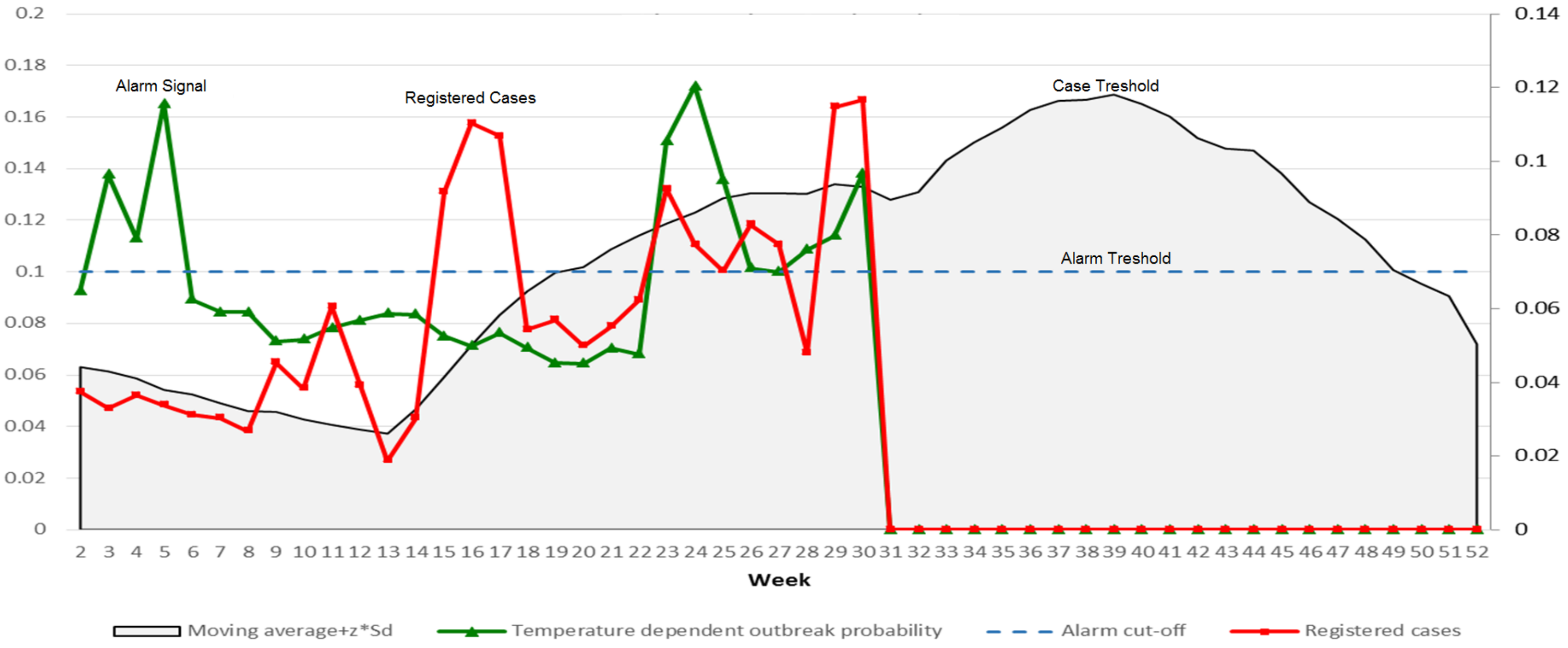
- Incident cases with a value above the Endemic Channel triggered outbreak signals.



ALERT INDICATORS



ALERT INDICATORS



ALERT INDICATORS

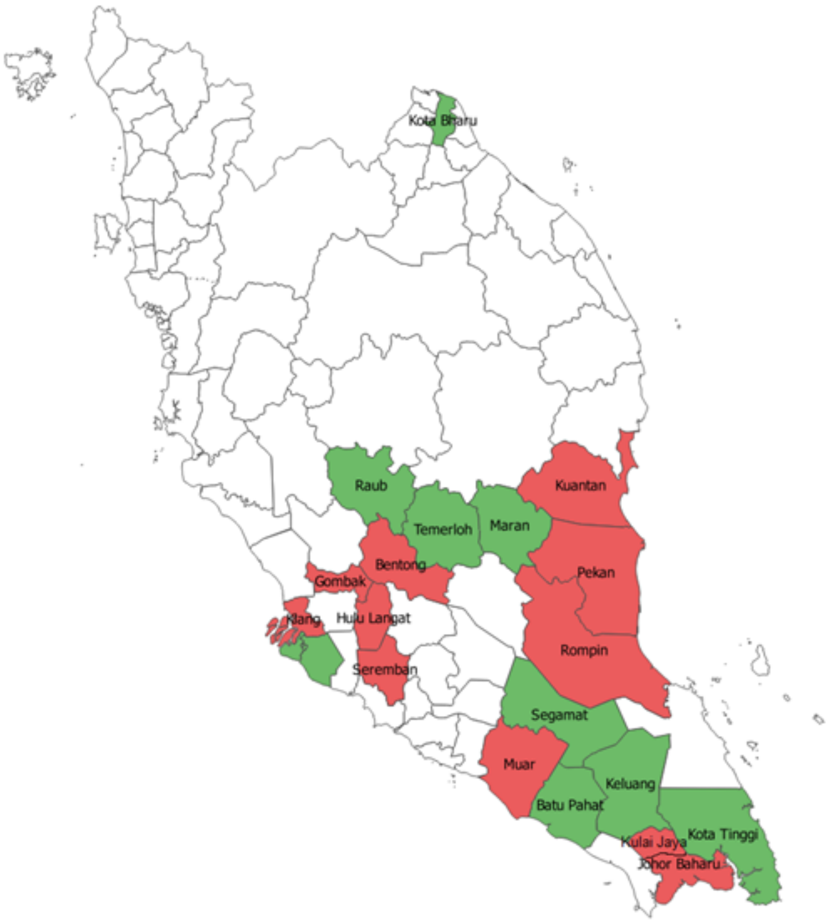
Country	Alarm Variable	Outbreak variable	Lag Period (weeks)	Sensitivity (%)	Positive Predictive Value (%)
Mexico	Mean Temperature	Hospitalised Cases	1–12	79	73
Mexico	Rainfall	Hospitalised Cases	3–12	59	63
Mexico	Mean Age	Hospitalised Cases	4–16	72	74
Mexico	Probable Cases	Hospitalised Cases	1–12	93	83
Brazil	Mean Temperature	Hospitalised Cases	1–12	81	46
Brazil	Probable Cases	Hospitalised Cases	1–12	97	43
Brazil	Rainfall	Hospitalised Cases	3–12	70	33
Brazil	Mean Humidity	Hospitalised Cases	2–12	79	46
Brazil	Mean Temperature	Probable Cases	1–12	49	50
Brazil	Mean Age	Hospitalised Cases	4–16	86	41
Malaysia	Mean Age	Probable Cases	4–16	96	45
Malaysia	Mean Temperature	Probable Cases	1–12	14	35
Malaysia	Mean Humidity	Probable Cases	2–12	9	32
Dominican Republic	Rainfall	Hospitalised Cases	3–12	17	76
Dominican Republic	Mean Temperature	Hospitalised Cases	1–12	24	82
Dominican Republic	Mean Humidity	Hospitalised Cases	2–12	6	80
Dominican Republic	Probable Cases	Hospitalised Cases	1–12	97	86
Dominican Republic	Mean Humidity	Probable Cases	2–12	5	71
Dominican Republic	Mean Temperature	Probable Cases	1–12	23	81
Dominican Republic	Rainfall	Probable Cases	3–12	16	70
Vietnam	Mean Age	Probable Cases	4–16	57	45
Vietnam	Probable Cases	Hospitalised Cases	1–12	93	43

INTERVENTION DISTRICTS

District	State
Johor Bahru	Johor
Muar	Johor
Kulai Jaya	Johor
Seramban	Negeri Sembilan
Kuantan	Pahang
Pekan	Pahang
Bentong	Pahang
Rompin	Pahang
Gombak	Selangor
Hulu Langat	Selangor

CONTROL DISTRICTS

District	State
Batu Pahat	Johor
Kluang	Johor
Kota Tinggi	Johor
Segamat	Johor
Kota Bahru	Kelantan
Maran	Pahang
Raub	Pahang
Temerloh	Pahang
Klang	Selangor
Kuala Langat	Selangor



PLOS | ONE

RESEARCH ARTICLE

Alarm Variables for Dengue Outbreaks: A Multi-Centre Study in Asia and Latin America

Leigh R. Bowman[1,5]*, Gustavo S. Tejeda[2], Giovanini E. Coelho[3], Lokman H. Sulaiman[4], Balvinder S. Gill[4], Philip J. McCall[1], Piero L. Olliaro[5], Silvia R. Ranzinger[5,6], Luong C. Quang[7], Ronald S. Ramm[8], Axel Kroeger[1,5], Max G. Petzold[6,9]

1 Department of Vector Biology, Liverpool School of Tropical Medicine, Liverpool, United Kingdom, **2** Ministry of Health, Mexico City, Mexico, **3** Ministry of Health, Brasilia, Brazil, **4** Ministry of Health, Kuala Lumpur, Malaysia, **5** UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR), Geneva, Switzerland, **6** Institute of Public Health, University of Heidelberg, Heidelberg, Germany, **7** Pasteur Institute, Ho Chi Minh City, Vietnam, **8** Ministry of Health, Santo Domingo, Dominican Republic, **9** University of Gothenburg, Gothenburg, Sweden

* leigh.bowman@gmail.com

CrossMark

OPEN ACCESS

Citation: Bowman LR, Tejeda GS, Coelho GE, Sulaiman LH, Gill BS, McCall PJ, et al. (2016) Alarm Variables for Dengue Outbreaks: A Multi-Centre Study in Asia and Latin America. PLoS ONE 11(6): e0157971. doi:10.1371/journal.pone.0157971

Editor: Ying-Hen Hsieh, China Medical University, TAIWAN

Received: January 29, 2016

Accepted: June 8, 2016

Published: June 27, 2016

Copyright: © 2016 Bowman et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All raw data files are available from the Open Science Framework database (DOI 10.17605/OSF.IO/RTC5A | ARK c7605/osf.io/rtc5a).

Funding: The project was financially supported by a grant from the European Commission (grant number m281803) to the IDAMS network (www.idams.eu) within the 7th Framework Programme and by the Special Programme for Research and Training in Tropical Diseases (TDR-WHO). The contents of this publication are the sole responsibility of the authors and do not necessarily reflect the views of the European Commission. The funders had no role in

Abstract

Background

Worldwide, dengue is an unrelenting economic and health burden. Dengue outbreaks have become increasingly common, which place great strain on health infrastructure and services. Early warning models could allow health systems and vector control programmes to respond more cost-effectively and efficiently.

Methodology/Principal Findings

The Shewhart method and Endemic Channel were used to identify alarm variables that may predict dengue outbreaks. Five country datasets were compiled by epidemiological week over the years 2007–2013. These data were split between the years 2007–2011 (historic period) and 2012–2013 (evaluation period). Associations between alarm/ outbreak variables were analysed using logistic regression during the historic period while alarm and outbreak signals were captured during the evaluation period. These signals were combined to form alarm/ outbreak periods, where 2 signals were equal to 1 period. Alarm periods were quantified and used to predict subsequent outbreak periods. Across Mexico and Dominican Republic, an increase in probable cases predicted outbreaks of hospitalised cases with sensitivities and positive predictive values (PPV) of 93%/ 83% and 97%/ 86% respectively, at a lag of 1–12 weeks. An increase in mean temperature ably predicted outbreaks of hospitalised cases in Mexico and Brazil, with sensitivities and PPVs of 79%/ 73% and 81%/ 46% respectively, also at a lag of 1–12 weeks. Mean age was predictive of hospitalised cases at sensitivities and PPVs of 72%/ 74% and 96%/ 45% in Mexico and Malaysia respectively, at a lag of 4–16 weeks.

Conclusions/Significance

An increase in probable cases was predictive of outbreaks, while meteorological variables, particularly mean temperature, demonstrated predictive potential in some countries, but not all. While it is difficult to define uniform variables applicable in every country context, the use

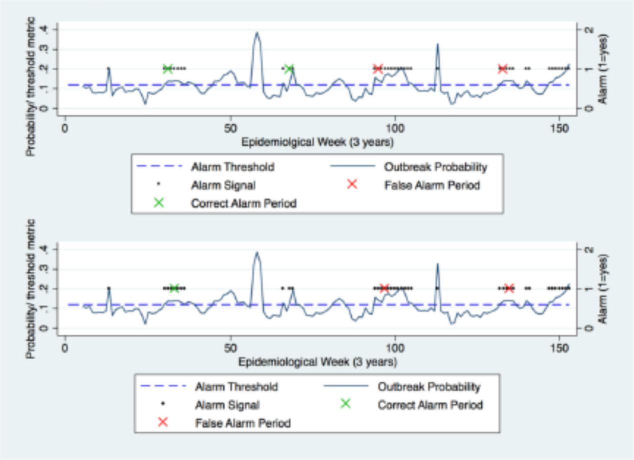


Fig 5. Test dataset: Alarm threshold = 0.12, z-value = 1.25. Top: alarm periods defined by 2 alarms signals (black dots). Bottom: alarm periods defined by 4 alarm signals.

doi:10.1371/journal.pone.0157971.g005

inconsistent across the years. This would not be surprising given that the length of historic periods was relatively low when compared to similar forecasting models [15,19,46].

There are almost certainly other factors at play here. The observed differences between PPV values could reflect the context-dependent nature of dengue transmission, which has long been argued as a feature of dengue [47–49]. Equally, country surveillance systems are often unique, resulting in heterogeneous case registration and reporting systems [10,30]. Indeed these differences could also be due to the presence of co-circulating infections with similar clinical presentations, such as Chikungunya or Zika viruses [50,51], which may be confounding probable dengue case diagnoses, or because case definitions are less specific (or likely a combination of both) [4,52].

Nonetheless, while suspected or probable cases are notifiable within many existing disease surveillance systems [10,30], these data suggest that probable case data can, in some cases, be predictive of dengue outbreaks and should be considered for use in early warning systems.

Alarm variable: mean age. Theoretically, since population-level serotype shifts are known to fluctuate inter-annually [53–56] thereby influencing the herd immunity of a population [55], it should be possible to detect such changes through a proxy increase or decrease in the mean age of infection [57]. Throughout these analyses the model performance metrics for

PLOS | ONE

RESEARCH ARTICLE

Early warning and response system (EWARS) for dengue outbreaks: Recent advancements towards widespread applications in critical settings

Laith Hussain-Alkhateeb[1*], Axel Kroeger[2,3], Piero Olliaro[2], Joacim Rocklöv[4,5], Maquins Odhiambo Sewe[4], Gustavo Tejeda[6], David Benitez[2], Balvinder Gill[7], S. Lokman Hakim[8,9], Roberta Gomes Carvalho[10], Leigh Bowman[11], Max Petzold[12]

1 Occupational and Environmental Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg Sweden, **2** Special Programme for Research and Training in Tropical Diseases (TDR), World Health Organization, Geneva, Switzerland, **3** Centre for Medicine and Society/ Anthropology, Uniklinikum Freiburg, Freiburg, Germany, **4** Department of Public Health and Clinical Medicine, Epidemiology and Global Health, Umeå University, Sweden, **5** Institute of Public Health, Heidelberg University, Heidelberg, Germany, **6** Ministry of Health, Mexico City, Mexico, **7** Information and Documentation Surveillance section, Disease Control Division, Ministry of Health, Putrajaya, Malaysia, **8** Office of the Deputy Director General of Health (Public Health), Ministry of Health, Level 12, Block E7, Federal Government Administrative Complex, Putrajaya, Malaysia, **9** School of Medicine, International Medical University, Bukit Jalil, Kuala Lumpur, Malaysia, **10** Secretaria de Vigilância em Saúde, Ministério da Saúde, Brasilia, DF, Brasil, **11** Umeå Centre for Global Health Research, Umeå University, Sweden, **12** Health Metrics Unit, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

* laith.hussain@gu.se

Check for updates

OPEN ACCESS

Citation: Hussain-Alkhateeb L, Kroeger A, Olliaro P, Rocklöv J, Sewe MO, Tejeda G, et al. (2018) Early warning and response system (EWARS) for dengue outbreaks: Recent advancements towards widespread applications in critical settings. PLoS ONE 13(5): e0196811. https://doi.org/10.1371/journal.pone.0196811

Editor: Jeffrey Shaman, Columbia University, UNITED STATES

Received: November 27, 2017

Accepted: April 22, 2018

Published: May 4, 2018

Copyright: © 2018 Hussain-Alkhateeb et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All three countries Data files are available from the https://osf.io/j5nyh database (accession number(s) http://dx.doi.org/10.17605/OSF.IO/J5NYH | ARK: c7605/osf.io/j5nyh.

Funding: This work was supported by a grant from the European Commission (grant number m281803) to the IDAMS network (www.idams.eu) within the 7th Framework Programme and by the Special Programme for Research and Training in

Abstract

Background

Dengue outbreaks are increasing in frequency over space and time, affecting people's health and burdening resource-constrained health systems. The ability to detect early emerging outbreaks is key to mounting an effective response. The early warning and response system (EWARS) is a toolkit that provides countries with early-warning systems for efficient and cost-effective local responses. EWARS uses outbreak and alarm indicators to derive prediction models that can be used prospectively to predict a forthcoming dengue outbreak at district level.

Methods

We report on the development of the EWARS tool, based on users' recommendations into a convenient, user-friendly and reliable software aided by a user's workbook and its field testing in 30 health districts in Brazil, Malaysia and Mexico.

Findings

34 Health officers from the 30 study districts who had used the original EWARS for 7 to 10 months responded to a questionnaire with mainly open-ended questions. Qualitative content analysis showed that participants were generally satisfied with the tool but preferred

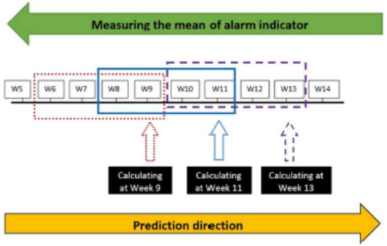


Fig 1. The mechanism of calculating the mean of alarms indicators. The mean of each alarm indicator was consecutively measured from the point of estimate (W = epidemiological week) and for a preceding number of weeks. The window size of the alarm indicator is objectively set to define the appropriate length of the preceding period when calculating the mean alarm indicator (e.g. choosing alarm window size of 4, this step will measure the mean of each alarm indicator during the last four consecutive weeks including the week we are measuring from). The calculated alarm mean then enters the logistic regression model as a predictor of an outbreak.

https://doi.org/10.1371/journal.pone.0196811.g001

- Implementation of an external interface to reduce human error and increase users' acceptability. The shift from STATA into EWARS-R facilitated the migration from the typical programming-based STATA do-file interface [15] to a more user-friendly interface designed to focus user's data inputs to specific 'boxes' of interest during the process of the program setting and data calibration, see Fig 3.

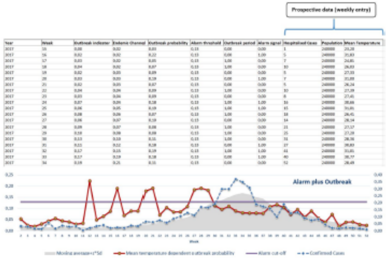


Fig 2. Prospective data entry and interpretations based on coefficients and outbreak probability from retrospective data. Columns with indications by blue arrows are locations for prospective data entry. Alarm signal column ("0" is no alarm signal and, "1" is alarm signal) would inform about a forthcoming outbreak.

https://doi.org/10.1371/journal.pone.0196811.g002

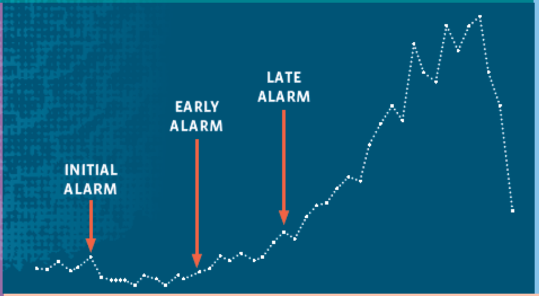
TECHNICAL HANDBOOK

Technical handbook for dengue surveillance, dengue outbreak prediction/detection and outbreak response ("model contingency plan")

World Health Organization

TDR For research on diseases of poverty
UNICEF • UNDP • World Bank • WHO

OPERATIONAL GUIDE



Early Warning and Response System (EWARS) for Dengue Outbreaks

World Health Organization

TDR For research on diseases of poverty
UNICEF • UNDP • World Bank • WHO

THANK YOU