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DENGUE EARLY WARNING MODEL USING DEVELOPMENT STAGES OF *Aedes aegypti* MOSQUITO AND CLIMATE INFORMATION

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ABSTRACT

This study aims at developing a dengue early warning model using climate information. The model was developed through three steps of analyses. The first step was to determine the length of periods used in prediction and optimal time for eradicating *Aedes aegypti* mosquito's breeding sites. The second step was to identify the best prediction model of dengue Incidence Rate (IR). The third step was to develop an early warning model using stochastic spreadsheet. It was found that the best predictor for predicting dengue incidence rate at week-n (IR_n) was (1) rainfall index with two weeks lead time (ICH_{n-2}). The rainfall index of week-nth is a function of three week moving averages rainfall (CH3), *i.e.* ($CH3_n$-1.155*$CH3_{n-1}$+0.702*CHn-2), and (2) IR with one week lead time (IR_{n-1}). The IR model prediction was $IR_n = 0.795*IR_{n-1}+0.067*ICH_{n-2}$ with R^2=76.6%. These models (models resulted from the first and third steps) can be used to provide early warning on optimum time for controlling the mosquito's breeding sites and the need for fogging action in order to prevent the dengue incidence rate beyond the critical limit as defined by the Ministry of Health.

Key words: *Aedes aegypti* , early warning model, breeding site, time control, climate variability, climate change

INTRODUCTION

Since mid 20th century (Christopher 1960), until the beginning of the 21st century, the disease of dengue haemorragic fever (DHF) has been given attention worldwide. Data of 2007 indicated that the number of cases and death rate of the

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patients, as well as the number of cities infected by this disease keeps on increasing. According to IPCC (2007), the attack will increase due to climate changes at high confidence level. The use of early warning system and epidemic prediction is one potential of adaptation options to reduce the impact of weather and climate in the field of health (Mc Michael *et al.* in Kovats *et al.* 2000).

The life of vector and the transmission process of DHF disease are closely related with climate conditions before disease incidence; thus, studies related to climate have been increasing. The current study, however, has been directed to the relation between this disease and climate information related to climate change issues (Hales *et al.* 2002; Reiter 2001) and climate variability in order to anticipate both seasonal and annual incidence of such a disease (Focks *et al.* 1995; Schreiber 2001; Peterson *et al.* 2005; Sasmito *et al.* 2006; Sintorini 2006).

The models have been developed consisting of a mechanistic models (Fock *et al.* 1993, Focks *et al.* 1995, Reiter 2001, and Sintorini 2006), as well as empirical models (Hales *et al.* 2002, Schreiber 2001; Peterson *et al.* 2005; Sasmito *et al.* 2006). However, there has not been any prediction model on the number of DHF incidence used by the Department of Health in Indonesia. This is due to the consideration that the model is inaccurate, complicated in application, relatively costly in obtaining input parameter, or related to a specific location only. Model to be developed is a simple model that will be easy to apply. The model will be a combination of mechanistic and empirical models. Input variables are easily obtained.

The prediction model of DHF based on climate information is expected to be used as materials for an early warning system that is beneficial to develop strategies for anticipation and control for such disease; particularly the one in Indonesia. A number of reasons for this are, among others: (1) There is a climate observation station, particularly for rainfall, in every city/regency (2) Climate observation has been carried out routinely and institutionally, and (3) Climate determines the breeding places, activities of the vector (*Aedes aegypti*) and pathogen (*Dengue* virus) so that the incidence of DHF needs climate pre-condition.

In general, this study was aimed at developing dengue early warning model as the basis for determining the anticipation and control step upon dengue incidence which is related to climate occurrence.

MATERIALS AND METHOD

This research was carried out through three stages. The first stage was determining the length of mosquito's life cycle period. The second was developing a prediction model on dengue incidence rate by using climate variables. While, the third stage was an early warning model by using stochastic spreadsheet.

Determining the length of development stages period for *Aedes aegypti* mosquito and Dengue virus

The prediction on the length of periods for mosquito's development stages at one particular location was determined based on heat unit. The period length of one stage in mosquito's development (n days) was counted from heat unit value (HU C^{0}days), divided by the difference between the daily mean air temperature (T_a ^{0}C) in the study area and basic temperature T_b by using the following formula: $n = HU/(T_a - T_b)$. Such length of period was used as: (1) basis for determining the period for controlling mosquito's breeding sites (PSN) which consisted of the eradication of immature mosquito breeding sites (TPN, days) and mature mosquito's resting places (SND, days), and (2) basis for determinating of predictor's length period based on climate variables to predict IR.

Developing a prediction model for Dengue Incidence Rate (IR)

Incidence Rate of dengue (IR) data availability was weekly. Therefore, the analysis of climate variables to predict IR were also used in weekly period.

Predictors of climate variables were grouped into wetness and thermal data. The length of wetness period was determined from immature stage (PD) mosquito phase length in weekly ($n_{PD}/7$), whereas thermal length period was determined by the length of virus Extrinsic Incubation Period (EIP), also in weekly period ($n_{EIP}/7$).

Weekly wetness data (in cm/week) was obtained from the sum of daily rainfall data. Weekly thermal factors that consist of mean, maximum and minimum temperature (TR, TN and TX, in °C), were obtained by averaging daily data. Further analysis was conducted to calculate the data in the form of moving averages. Determining the period for moving averages analysis were based on PD for wetness data and EIP for thermal data.

Further analysis was also conducted to construct predictive models in the form of principal component regression of the best predictors obtained from the previous analysis. The data used were the ones from Indramayu regency (2002 - 2006). Meanwhile, the data used in validation process were taken from Indramayu (2007), Bogor (2003 - 2006), North Jakarta (1998 - 2002), and Padang (2003 -2005).

Developing early warning model using Stochastic Spreadsheet

The early warning model discussed here was the prediction of the optimum time model for **PSN** implementation, dengue Incidence Rate (**IR**), and the need for fogging. Model was developed in the form of stochastic spreadsheet by using Crystall Ball program package.

The prediction of the optimum time for PSN implementation refered to optimum time for the implementation of cleaning water tanks where immature mosquito (TPN) lives, and optimum time for the implementation of cleaning adult mosquito's breeding sites (SND). Each of TPN and SND was predicted based on the number of days in the period of PD mosquito and EIP virus using the daily mean air temperature as an input. In the case of PD and EIP prediction, the average daily temperature in a week was considered to represent the average daily temperature during the period of PD or EIP, so the prediction for the next few days could be done.

Prediction of dengue incidence rate was conducted by using the best prediction model. The need for fogging was determined based on the critical boundary of IR figure determined by the Minister of Health namely, 20 patients per 100 000 inhabitants per year for an endemic regency.

RESULTS AND DISCUSSIONS

The length of development stages period for *Aedes aegypti* mosquito and Dengue virus

Focks *et al.* (1993) have shown that the higher the air temperature, the faster the gonotropic cycle and virus extrinsic incubation. In accordance to heat unit concept, Hidayati *et al.* (2007) revealed that the higher the air temperature, the faster the egg hatches and grows into adult mosquito, or, the faster the mosquito complete all of their life cycle stages, including their age. Furthermore, the heat unit of each development phase was relatively constant, thus, the higher the air temperature, the faster the heat unit that needs to be reached.

PD and EIP were determined based on the following formulation: $n = \frac{HU}{(T_a - T_b)}$

HU and Tb were heat unit and basic temperature which are suitable for immature stage and extrinsic incubation period. T_a was the daily mean air temperature in the study region. Basic temperature and heat unit value in mosquito's various development phases and their relation to dengue virus transmission are presented in Table 1.

Table 1. Basic temperature and heat unit at various stages of Mosquito's life

		Heat Unit (HU in C^0 days)	
Phase	**Tb (^{0}C)**	**Average**	**CV(%)**
Immature	15.0	224	27.4
EIP Virus	17.0	128	5.0
Gonothropic	17.5	36	6.4
Age	10.0	544	24.6

CV : Variation Coefficient (source: Hidayati *et al.* 2007).

DHF endemic regions are generally located at low altitude or city with dense population and relatively high temperature. Data on temperature in 4 research locations; namely, Indramayu, North Jakarta, Bogor and Padang were considered to represent data on air temperature of several big cities /regencies with endemic areas of DHF in Indonesia. In the weekly period, the average length of PD and EIP in four locations were nearly the same (Table 2); that is, 3 weeks for the phase of mosquito immature stage (PD) and 2 weeks for virus extrinsic incubation period (EIP).

Table 2. The average length of the phase of mosquito immature stage and virus extrinsic incubation period in four research locations

District/City	**Mean Air Temperature (^{o}C)**	**Immature Stage(PD)**		**Extrinsic Incubation Period (EIP)**	
		days	**weeks**	days	**weeks**
Indramayu	27.3	21	3	12	2
Jakarta Utara	28.0	20	3	12	2
Bogor	27.0	21	3	13	2
Padang	27.1	21	3	13	2

The most influential climate variable in PD period of mosquito was the existence of wetness (rain), while the dominant influence in EIP was temperature. Accordingly, to develop a relation model between dengue incidence rate and climate variables, there is a need to have 3 weeks moving average analysis, like the length of PD mosquito period for wetness variable, and 2 weeks moving average analysis, like the length of EIP for thermal variable.

Prediction model for Dengue Incidence Rate (IR)

The interview with the Head of Disease Eradication and Prevention Department, Health Office of Indramayu Regency (August 2006) revealed that the shortest period for about 2 weeks was required to be able to utilize the result of early warning in determining operational steps for controlling the diseases. Therefore, in selecting the best climate predictor variable, an interval of two weeks between climate occurence and diseases incidence was used.

Prediction based on Climate Variables only

Results of the analysis of all available climate variables, showd that the best subset of predictive models predictors in DHF incidence rate of two weeks after the climate incidence were rainfall (CH) and temperature (T) in the form of $CH3_{n-2}$, $CH3_{n-4}$, $CH3_{n-5}$, $TR2_{n-2}$, $TX2_{n-2}$, and $TN2_{n-2}$. Number 2 or 3 attached to variable CH (rainfall) and temperature including TR (average temperature), TX (maximum temperature), and TN (minimum temperature) were weekly periods for moving averages analysis. Index $_{\mathbf{n-i}}$ indicates the time of occurrence during $\boldsymbol{i}$ week before the IR occurrence that has been predicted. Actually, the rainfall and air temperature data were the easiest climate variable to be obtained.

All climate information consisting of those rainfall and temperature were calculated in terms of the relation between climate variable with dengue incidence rate of DHF by using the principle component regression analysis. By using this method, multikolinieriti among the climate data could be ignored. The result of the principle component regression analysis was:

$$IR_n = 0.920 + 0.157*CH3_{n-2} - 0.052*CH3_{n-4} + 0.066*CH3_{n-5} + 0.826*TR2_{n-2} - 0.387*TX2_{n-2} - 0.492*TN2_{n-2} \qquad \text{(equation 1)}$$

(R^2 adjusted = 52.1%; DWS = 0.634).

These results indicate that rainfall from 7 until 2 weeks before the week of disease incidence and air temperature at 3 and 2 weeks before the period of the disease incidents would determine the amount of IR. IR will be high if the rainfall in week 7, 3, and 2 is high, while in contrary low at week 6, 5 and 4.

The equation model obtained was not good enough with a determination coefficient only 52%, the DWS value stayed far below 2.0, that means that residual model still contained an obvious autocorrelation value at level 1 so that the model was not adequately stable when used for prediction (Selvanathan *et al.* 2004). The obstacle on the low accuracy of prediction model which only includes climate variables was also found by not only Schreiber (2001) for the weekly-scale model, but also Sasmito (2006) and Sintorini (2006) for the monthly-scale model. A better prediction model can be obtained by including non climate factor; that is, IR before prediction period. IR was chosen as a predictor variable by considering that IR was relatively easy to be obtained by the Health Office in Regency/City, and able to describe the level of inhibitant's susceptibility.

Prediction Based on the Combination between Climate Variables and IR before PredictionPeriod

Predictors comprised the combination of climate variables of two weeks before the dengue occurrance period, and IR one week before the disease incidence. By including IR aside from the climate variables consisting of rainfall, average temperature, maximum temperature, and minimum temperature, the equation of relation model obtained was reasonably good with the following form:

$IR_{n} = 0.744*IR_{n-1} + 0.070*CH3_{n-2} \quad 0.073*CH3_{n-4} + 0.042*CH3_{n-5} + 0.199*TR2_{n-2} - 0.115*TX2_{n-2} - 0.079*TN2_{n-2}$.

(R^2 adjusted = 78.4%; DWS = 2.151; $\varepsilon \sim N(0; 0.33; p{:}0.094)$.

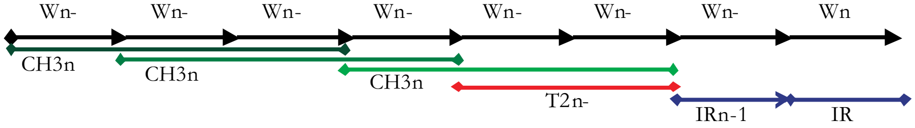
The next analysis result obtained by ignoring air temperature data did not reduce the model quality. If only rainfall was used as predictor, the equation produced would also be good. The form of its equation model is:

$\boldsymbol{IR_{n} = 0.795*IR_{n-1} + 0.067*ICH3_{n-2}}$, where $ICH3_{n-2} = CH3_{n-2} - 1.155*CH3_{n-4} + 0.702*CH3_{n-5}$ (equation 3)

If the model is developed based on predictor that consists of the combination of climate and IR at two weeks before the incidence, temperature has to be calculated together with rainfall in order to obtain a good equation model: (R^2 corrected = 70.3%; DWS : 1.182; $\varepsilon \sim N(0; 0.38; p{:}0.040)$. The form of the equation model is:

$\boldsymbol{IR_{n} = 0.612*IR_{n-2} + 0.111*ICH3_{n-2} + 0.315*IT2_{n-2}}$; $ICH3_{n-2} = CH3_{n-2} - 0.715*CH3_{n-4} + 0.244*CH3_{n-5}$, and $IT2_{n-2} = TR2_{n-2} - 0.577*TX2_{n-2} - 0.397*TN2_{n-2}$. (equation 4)

(R^2 adjusted = 78.0% ; DWS = 2.202 ; $\varepsilon \sim N(0; 0.33; p{:}0.064)$.



Note: W: week, CH: Rainfall period, T:Temperature period, IR: Incidence Rate period

Figure 1. Time frame period of IR prediction, climate variables and IR as predictors

The rainfall in Indonesia is, in fact, the most fluctuative climate variable which influences other climate variables including temperature, relative humidity, and incoming radiation. In developing IR model with a climate variable, the most obvious predictor was the rain. Hidayati *et al.* (2008) found that the pattern of monthly dengue proneness index in major parts of Indonesia was the same as the pattern of their monthly rainfall, except in some big cities where their maximum index experienced an interval two or three months after the maximum monthly rainfall. The temperature, indeed has an obvious impact, however, the data on temperature was relatively difficult to obtain. Based on the equations of prediction models on dengue incidence rate, equation 3 was the most potential to be used as a model for early warning since the information on rain together with IR_{n-1} could be used to predict the incidence of diseases for the next period.

The result of model validation showed that the model from equation 3 resulted in good IR prediction, not only in Indramayu, but also in Bogor, North Jakarta and Padang. RMSE relative value was in average less than 1, and the correlation value between prediction result and actual data was significantly high (Table 3). Furthermore, actual IR Plot and IR resulted from the prediction did not show significant difference. However, this model has been underestimated in predicting the high IR.

Table 3. Result of prediction model validation based on equation 3

Regency/ City	**Year**	**RMSE**	**RMSE/Average**	**Correlation Coefficient**
Indramayu	2007	1.272	0.601	0.75
Bogor	03 – 06	0.930	0.496	0.83
North Jakarta	98-02	1.693	0.603	0.90
Padang	03 – 05	0.724	0.601	0.75

In cities where the altitude was higher (> 500 m asl), or where mean air temperature was significantly lower (< 24 ^{0}C), the length of period for moving average calculation of climate variable needs to be adjusted to the heat unit concept. Furthermore, wetness variable also has to be adjusted to the length of PDN period, and thermal variable has to be tailored to the length of EIP. As an example, a place with an air temperature average of 21^{0}C, or at the height of about 1000 m asl, the moving average for wetness variable was approximately 5 weeks, and its thermal period was 4 weeks.

Thus, the rainfall variables that can be used in developing predictive models of IR are five weekly rainfalls ($CH5_n$). If we include the temperature in the model, then the form of temperature variables are 4 weekly temperature or $T4_n$ (modification of Fig. 1). However, the prediction model equations cannot be presented here in detail, because it is not sufficient supporting data are available. In general, a city located at an elevation > 500 m asl is not an endemic area.

Developing Early warning model Using Stochastic Spreadsheet

Early Warning Dengue Model

Stochastic spreadsheet model was developed using weekly time frame, consisting of Input cell, Assumption cell, Formula cell, and Prediction cell. Model inputs comprised the number of dengue cases one week before prediction period, the number of population, average weekly air temperature (TR_{n-1}) one week before prediction period (mm). The assumptions used in IR model were error model which was distributed normally with mean value of 0.00 and standard deviation of 0.33. The heat unit of immature mosquito stage was distributed normally with an average of 224 and with a standard deviation of 61. Likewise, the EIP heat unit was normally distributed with an average of 128.4 and standard deviation of 6.6. This assumption is built from the analysis of the mosquito life cycle heat units (Table 1) and the distribution of the IR. Thus, this assumption can be applied to most of the dengue endemic areas. The Formula cell was used to define IR at the present week, rainfall index, IR the week after, and the averages of PD mosquito and EIP virus periods.

In addition, Input, Assumption and Formula previously defined were then used to conduct a simulation in the Dengue Early warning model. Simulations which were carried out for several times would produce optimum prediction period for TPN and SND, IR value for the following week, and decision whether or not fogging at various confidence levels should be conducted. Each of the optimum period for PSN implementation was determined based on the length of both PD mosquito and EIP with confidence level (exceeded probability) of 90% or 75% in accordance with level of interest. Such value was obtained by filling out the certainty column with the display of simulation result. Fogging was suggested if the IR in this week was > 0.5 and predicted to raise in the following week; or if IR prediction for the following week was > 1.

Table 4. An example of the number of input for early warning dengue model

Input Parameter	**Value**
Average daily air temperature in the last one week	27.5
Number of patients in the last one week	15
Number of Population	1.500.000

Weekly rainfall (mm) in … week before (wb)					
7 wb	6 wb	5 wb	4 wb	3 wb	2 wb
0 mm	20 mm	75 mm	100 mm	80 mm	150 mm

As an illustration, the number of input as shown in Table 4, produced prediction values as presented in Figure 2. With confidence level of 90%, optimum period of TPN and SND cleaning were conducted in 7 days and 4 days after simulation time, or 14 and 11 days after previous cleaning, and IR prediction value in the following week would exceed the number of patients i.e. 1.6 persons per 100 000 population. Consequentrly, fogging is highly recommended.

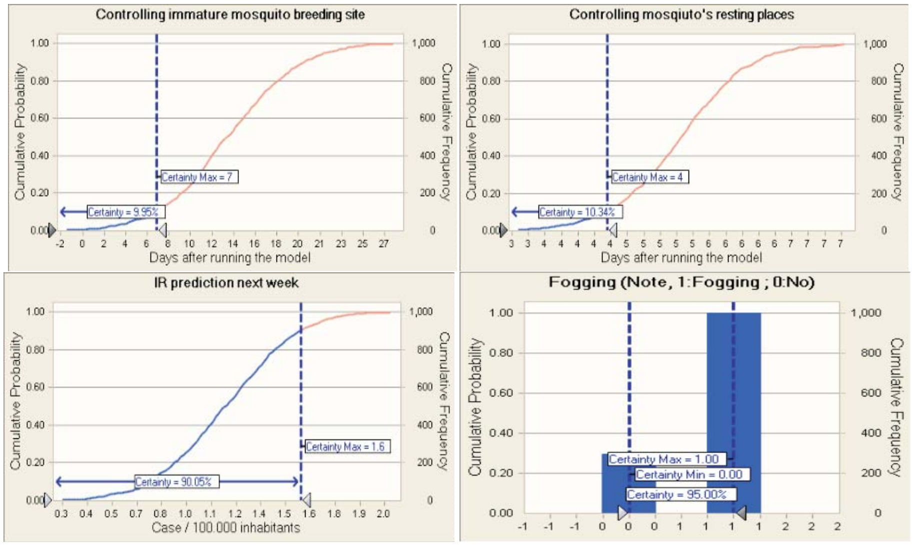


Figure 2. Output of dengue early warning model from 1000 times simulations

Anticipative Steps and Control of DHF Disease Incidence

In order to control DHF disease, the Decree of Minister of Health (KEPMENKES) No: 581 year 1992 suggested to prioritize activities on prevention and society empowerment by performing what is called: PSN 3 M PLUS (Eradicating mosquito's breeding site Drying, Covering, Burying, PLUS adding larvaside, raising fish, using mosquito net, and spraying). In wet tropical regions where the vegetation and fauna are varied, it was relatively difficult to eradicate *Aedes* mosquito. In order to suppress the number of DHF patients, therefore, PSN has to be carried out regularly and entirely. So that, mosquito's life cycle can be totally cut. As an effort to control *Aedes* mosquito, the optimum time for PSN implementation as resulted from the simulation can be used as guidance.

Based on the Decree of the Minister of Health (MENKES) 581/92 fogging was carried out when there was an outbreak, that is, when the number of cases doubled from the previous period, or when a case occurred in the region where previously none of such case was found. In order to suppress the number of patients not exceeding the critical limit as determined by the Ministry of Health, fogging is suggested to be carried out when the IR value early in the week is > 0.5. Based on rainfall data, it is predicted that IR will increase; and/or IR prediction in the following week is > 1.

The model operationalization should be conducted every week, particularly during rainy season, so that the IR prediction value and information whether or not fogging was performed will be available in each of the previous week. DHF disease season generally occurs from the beginning to the end of rainy season. Unlike the IR prediction and fogging, PSN simulation has to be performed one week after PSN was carried out.

The step for anticipation and control of the disease could make use of the result of IR value simulation one week after. Such a superficial model can be utilized by personnels who work in hospitals and City/Regency Health Offices as the basic for calculating both structure and infrastructure that need to be provided for nursing and treating the patients in the following week.

In the beginning of rainy season, where the number of DHF patients starts to rise, it is suggested to carry out PSN at time period in accordance with exceeded probability of 90%. In the season where the IR is relatively low, PSN period at probability level of 75% can be chosen (Fig. 3).

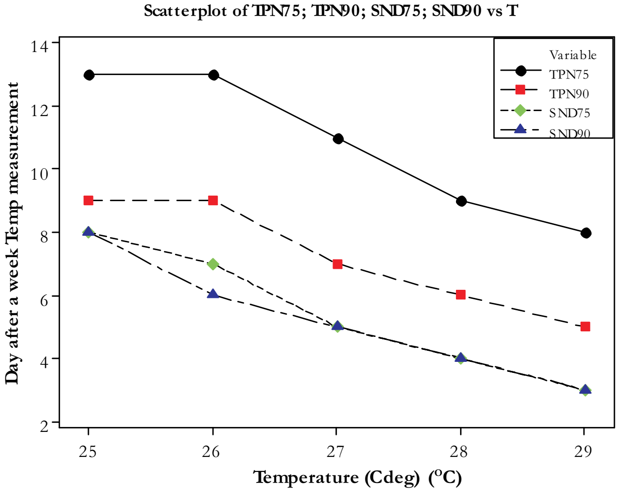


Figure 3. Period (days) of controlling Immature mosquito breeding sites (TPN) and Mature mosquito breeding sites (SND) recommendation for the dry season (75) and rainy season (90)

The result of IR value prediction simulation is needed as the base of calculation upon structure and infrastructure for controlling DHF diseases. Since treating DHF patients has to be immediately carried out, both supporting structure and infrastructure should be available in an adequate number, or even, higher number. To accommodate such needs, IR prediction is suggested to be below the exceeding probability levels; namely 10%, or 25% at the highest.

The implementation of fogging is highly suggested if the probability level to gain value of 1 in the simulation is higher . Each of the value, either 1 or 0 described the need to carry out fogging. From such description, it can be identified that the higher the ICH, the higher confidence value upon the suggestion to carry out fogging. Conversely, fogging will not be suggested if, naturally, climate supports the decrease of IR cases. Accordingly, although IR prediction is high , but naturally there will be a decrease untill less than 1, fogging is not really suggested.

The fogging of superficial model result (Fig. 4) has not been able to describe the characteristics of fogging: focused (on the selected/limited area), or mass (on an extensive area). Fogging can be carried out by the community or funds provided by the local government. Such a built model can only predict the incidence of one week ago (for the next week). As a result, fogging activities are suggested to be prioritized by the community independently under supervision or as a program of City/Regency's local Health Office.

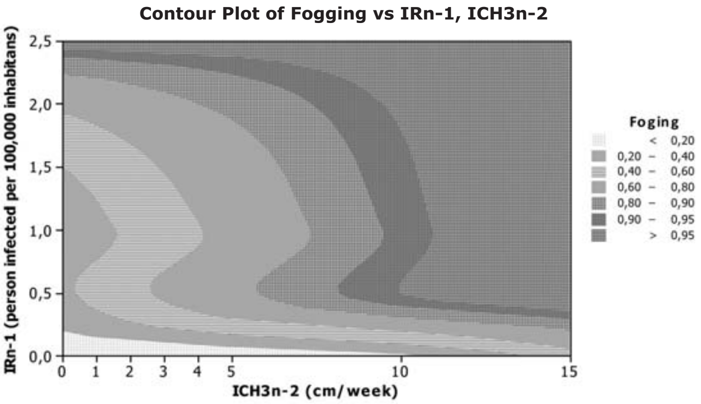


Figure 4. Level of fogging requirement

CONCLUSIONS

Early warning models can be developed based on (1) the weekly IR model prediction $IR_n = 0.795*IR_{n-1}+0.067*ICH_{n-2}$, and the optimum time for controlling mosquito's breeding sites (PSN implementation) models using heat unit concept, *i.e.* (2) $n\ (days) = 256\ ^{o}Cdays/((Ta-15)\ ^{o}C)$ for controlling immature mosquito's breeding site, and (3) $n\ (days) = 128\ ^{o}Cdays/(Ta-17)\ ^{o}C$ for controlling moquito's resting places. The rainfall index of week-nth ICH_n , is a function of three weeks moving averages rainfall (CH3), *i.e.* ($CH3_n$ -1.155*$CH3_{n-1}$ + 0.702*CHn-2), and IR_{n-1} is IR one week lead time. Model was developed in the form of the stochastic spreadsheet by using Crystall Ball program package, so that the confidence level of the model outputs can be demonstrated.

From the beginning of rainy season to the beginning of dry season, optimum period for PSN implementation of model superficial result is used with 90% exceeded probability, but from the middle to the end of dry season, simulation result with 75% exceeded probability can be used. The provision of both structure and infrastructure is recommended to be in line with IR prediction value at high estimated value with 10% exceeded probability, minimal at low estimated value in accordance with IR prediction value with 25% exceeded probability. Fogging activity is suggested if the simulation result of exceeded probability is more than or the same as 90%. A routine simulation model in the endemic region in the low altitude should be conducted every week, particularly in endemic regions. In mid and high altitude, models need to be evaluated.

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