DEVELOPMENT OF SPATIAL SURVEILLANCE MODELS FOR DENGUE FEVER AND DENGUE HAEMORRHAGIC FEVER PREVENTION AND CONTROL

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Abstract

The purpose of the study is to develop spatial models for surveillance of epidemics of dengue fever and dengue haemorrhagic fever (DF/DHF). Seasonal data of each sub-district in Ubon Ratchathani Province of Thailand related to the epidemics including rain, temperature, House Index (HI), Container Index (CI), and Breteau Index (BI) during 2001-2005 were used for analysis through mathematical equations. Epidemic probabilities related to temperature (P_t), rain (P_r), and larval index (I) were analyzed seasonally. These parameters were used as dependent variables in the regression analysis for the case prediction (y). The predicted cases were further transformed to be probabilities of occurrence (P) by logistic regression. The Delphi technique was employed to classify the probability of occurrences at 3 levels of risk: high, moderate, and low. An error matrix was used to verify the levels of predicted risk by spatially comparing them with data of the actual risk classified by the conventional method. From 18 seasons in those years, it revealed that 60%overall accuracy was achieved. The model outputs can be used as basic data for short-term and long-term planning in resources management and surveillance network operation.

Keywords: DF/DHF, surveillance models

Introduction

Dengue fever is a long known disease with high epidemic potential. The global burden of dengue has grown dramatically in recent decades due to unprecedented population growth, rapid and unplanned urbanization in tropical Asian countries, improved transportation, and globalization with modern transportation and an increase in air travel (Ungchusak and Kunasol, 1988; Gubler, 1998).

In 1998, Thailand experienced an exceptionally intense epidemic of DHF with 112,488 cases (23.3% increase from 1997) and 415 deaths (64.0% increase) (Chareonsook *et al.*, 1999), which was the second largest epidemic outbreak of dengue since 1987. Epidemics occur with a periodicity of between 2 and 4 years. These are of significant concern for the public health authorities. The trend of

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dengue has been increasing, especially in 2001 when there were 224.43 reported cases of dengue per 100000 of the population, the second highest rate during the past 40 years (1960-2001) (Barbazan *et al*., 2002). In 2005, the fatality ratio of dengue cases was 0.2% and the morbidity rate was 72.2 per 100,000 of the population, respectively, which was an increase of 18.1% when compared with the previous year.

Annually recorded epidemics in Ubon Ratchathani province, where the disease has been endemic since 1987, show a cumulative total of 35069 cases and 155 deaths (UOPH, 2006) as displayed in Figure 1. During the 1998 outbreak of DF/DHF, about 35% mortality was reported among children admitted to hospital, while a total of 4905 cases were hospitalized and 25 deaths recorded (UOPH, 2006). This epidemic peaked in August when an Aedes aegypti larval House Index (HI) of 30.50% was recorded. Since then, regular monitoring of the larval density of Aedes aegypti and dengue cases has been of interest in studying the trends and preventing any recurrence of an outbreak. In 2003, there were 3138 DF/DHF cases reported. The morbidity rate was observed at 173.82 per 100000 people. The DF/DHF incidences were recorded at the village level. The highest number of dengue incidences was recorded in the countryside with a morbidity rate > 50 per 100000 people. It was found that the highest number of cases occurred during March and August of 2001 to 2003. This indicated the seasonal dependence in the occurrence of DF/DHF cases, generally starting just before the rainy season and continuing until the end of the season as statistically recorded by Ubon Ratchathani Provincal Office of Public Health (UOPH) during 2000-2003.

To spatially monitor trends of dengue transmission for effective prevention and control, the objective of the study is to develop surveillance models of DF/DHF epidemics in Ubon Ratchathani. The developed models employed data on the larval index, climatic factors, and disease occurrence.

Materials and Methods

Study Area

Ubon Ratchathani province is located in Northeastern Thailand. It covers an area of 16112.61 km^2. The province comprises 25 districts, 219 sub-districts and 2469 villages. The province had a population of 1803754 at a density of 111.9/km^2 in 2006. The climate of this area during 1961-2001 had an average high temperature of 32.45°C and an average low temperature of 21.65°C. The rainy season in Ubon Ratchathani normally occurs from May to September. The average yearly rainfall was 1598.75 mm.

Spatial DF/DHF Prediction Models Formulation

To obtain surveillance models of DF/

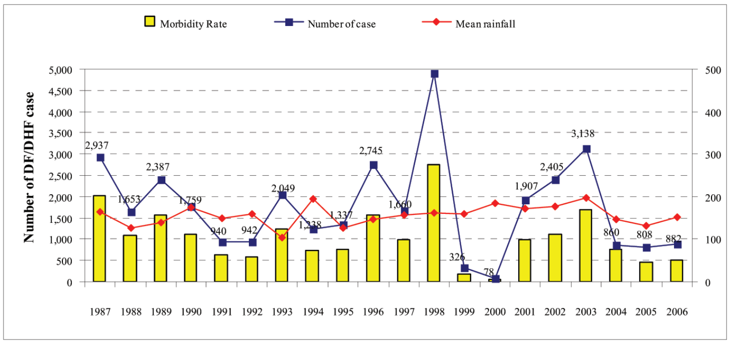

Figure 1. The number of DF/DHF cases, morbidity rate, and mean rainfall in Ubon Ratchathani, Thailand, (1986-2006)

DHF epidemics, the flow of a series of models for spatial DF/DHF prediction was formulated as displayed in Figure 2. Effective planning and implementation of the prevention and control of DF/DHF epidemics can be performed when the levels of risk for districts are known in advance. Therefore, the final output of the series of models used in the study was the rating of risk areas as low, moderate, and high, which were converted from the probability of risk areas using the Delphi technique. The performance of the logistic regression model conveyed the probability of risk areas from the predicted DF/DHF cases. The epidemic cases presented in the districts were influenced by the larval index and probabilities related to rainfall and temperature of the given districts. Both probabilities exhibit the likeliness of mosquito bites. With known sample cases, the epidemic cases and those variables had a linear regression relationship that allowed cases to be predicted while the larval index, temperature, and rainfall were recorded monthly and presented in terms of epidemic seasons which were classified to be pre-high incidence (January-April), high incidence (May-August), and post- high incidence (September-December).

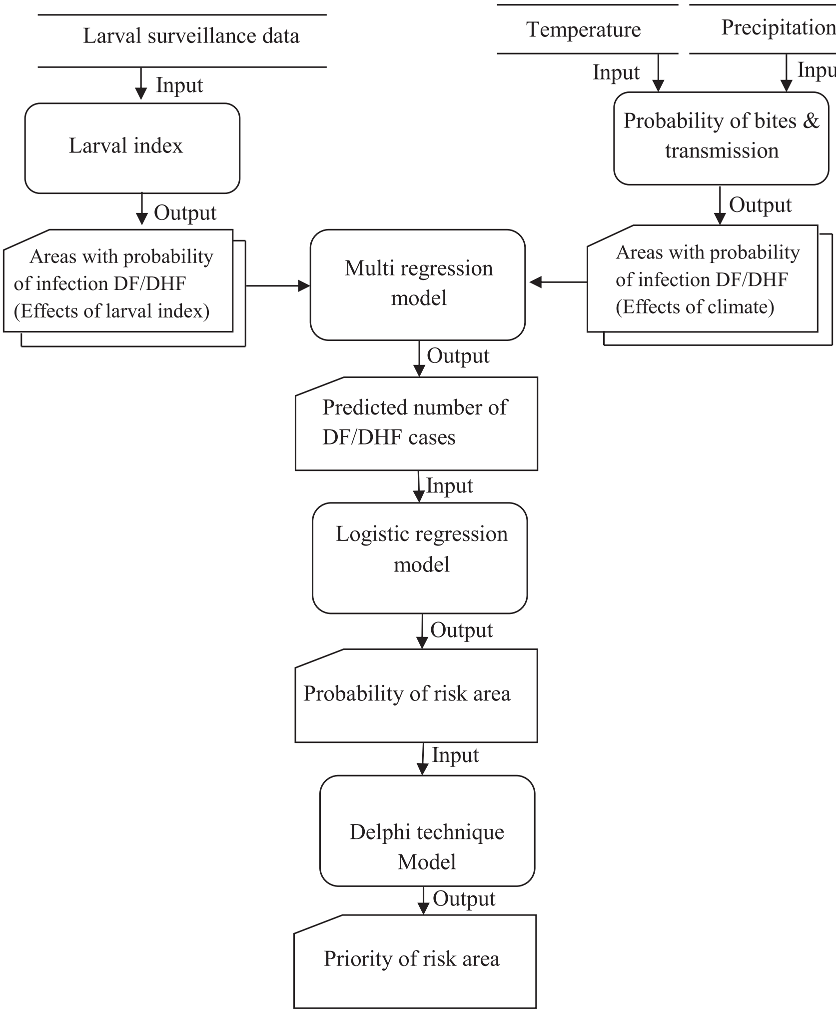

Figure 2. Flow diagram of DF/DHF spatial epidemic models

Prediction Model of DF/DHF Epidemic

Logistic regression is a part of a category of statistical models called generalized linear models (McCullagh, 1980). Logistic regression allows one to predict a discrete outcome, such as groups of membership from a set of variables that may be continuous (Kang, 1998). To apply it to DF/DHF epidemic prediction, the result of the analysis was the probability of predicted DF/DHF cases considered from epidemic–relevant variables-rainfall, temperature, and larval index, which are continuous spatially and temporally. The probability prediction model of a DF/DHF epidemic was performed by logistic regression analysis as expressed in Equation 1:

$$P = \frac{e^{(y)}}{(1 + e^{(y)})} \tag{1}$$

where P is the epidemic probability of DF/DHF, and y is the predicted number of DF/DHF cases (from Equation 2).

Risk Level Classification using the Delphi Technique

This Delphi technique permits obtaining a consensus from a group of experts regarding a certain phenomenon (Goodman, 1987; Hasson *et al*., 2000). The goal of this research in applying it was to reach a convergence of opinions to set the values, between 0 to 1, of the probability of predicted DF/DHF cases to be at 3 levels of risk: high, moderate, and low that they were comparable to the classification results using the conventional method.

Multilinear Regression Model of DF/DHF Incidence

The multilinear regression represented the independent contributions of each independent variable to the prediction of the dependent variable (Abraham and Ledolter, 1983; Focks *et al*., 1995; Alpana and Haja, 2001; Bohra, 2001). In the present study, climatic and surveillance independent variables such as rainfall, temperature, House Index (HI), Container Index (CI), and Breteau Index (BI) were related to the dengue cases in Ubon Ratchathani province. The model shows the relationship of the DF/DHF incidence and climatic factors including the larval index as expressed in Equation 2.

$$y = a_0+b_1(I)+b_2(P_r)+b_3(P_r) \tag{2}$$

where y is the predicted number of DF/DHF cases, I is the larval index which is the weighted linear combination of HI, CI, and BI (Equation 3), P_r is the probability of the rainfall effect, P_t is the probability of the temperature effect, ao is the intercept of the y-axis, and b_1, b_2, and b_3 are the coefficients for the larval index, rainfall, and temperature, respectively.

Dengue infection in Ubon Ratchathani province has been reported as a local endemic every year. The report showed that the maximum DF/DHF transmission started in the period of high rainfall (May-September) of each year studied. There was a positive correlation between the number of dengue cases and rainfall (Strickman and Kittayapong, 2002). This indicated the seasonal dependence in occurrence of DF/DHF cases, which generally starts just before the rainy season and continues until the end of the rainy season (Kittayapong and Strickman, 1993a).

Surveillance Data

The larval index (HI, CI, and BI) of Aedes aegypti density fluctuates according to seasonal climatic changes (Eamchan *et al*., 1989; Kittayapong and Strickman, 1993b; Ali *et al*., 2003). It rises in seasons with higher rainfall (Muttitanon *et al*., 2004) which leads to an increasing number of potential breeding sites.

Spatially varying secondary data on HI, CI, and BI at the sub-district level reported by the UOPH were calculated each season. They were normalized to be the larval index (I) for each sub-district using the weighted linear combination method (Banai-Kashani, 1989; Saaty, 1997; Malczewski, 2000) as expressed in Equation 3.

$$I = \frac{w_{(HI)}(x_{HI})w_{(CI)}(x_{CI})+w_{(BI)}(x_{BI})}{(w_{(CI)}+w_{(HI)}+w_{(BI)})} \quad (3)$$

where I is the larval index, x_{HI}, x_{CI} and x_{BI} are the seasonal indexes of HI, CI, and BI, and w_{HI}, w_{CI}, and w_{BI} are the weights of *Aedes aegypti* density for HI, CI, and BI, respectively.

The weights of these indexes can be obtained depending on the varying HI, CI, and BI as shown in Table 1 (Brown, 1974; 1977; Day and Curtis, 1989; Jetten and Focks, 1997). The higher the index means the higher the weight of transmission.

DF/DHF Data

In Figure 1, the DF/DHF cases of the province showed an increasing trend of continuous occurrence of DF/DHF from 2000 to 2003. Data on a number of cases were recorded seasonally for each district and sub–district by the UOPH. They were used as sample cases for Equation 2 so that the model could be set up for prediction.

Influence Factors

Key major factors for analysis of the number of DF/DHF cases were rainfall and temperature (Jetten and Focks, 1997).

Rainfall is the key to the direct increase of *Aedes aegypti* density in each period. It is related to the high abundance of mosquitoes (Day and Curtis, 1989) and most often leads to maximum feeding and outbreaks (Gratz, 1993; Patz *et al*., 1996; Martens *et al*., 1997; Githeko *et al*., 2000). Temperature plays an important role in the life cycle of mosquitoes and in the replication and transmission of diseases having an effect on matters such as population size, maturation period, feeding characteristics, and survival rate of *Aedes* mosquitoes (Watts *et al*., 1987; Jetten and Focks, 1997; WHO, 1997; Gratz, 1999; Focks, 2003; Nakhapakorn, 2005).

Rainfall and temperature data from 19 stations in the province were interpolated and averaged to represent each sub-district in each season during 2001-2005. Both data were further normalized to be in the forms of probability as follows:

Probability Related to Rainfall (P_r)

The probability related to the predicted number of DF/DHF cases based on rainfall data can be achieved from the below expression.

$$P_r = (Probability\ of\ bite)[P_{(trans)}] \quad (4)$$

According to the researches of Day and Curtis (1989) and Githeko *et al*. (2000), the

Table 1. Weight of *Aedes aegypti* density for each criterion index is displayed to show the priority of transmission

Weight of transmission	Container index (CI)	House index (HI)	Breteau index (BI)
1	0-2.99	0-3.99	0-4.99
2	3-5.99	4-7.99	5-9.99
3	6-9.99	8-17.99	10-19.99
4	10-14.99	18-28.99	20-34.99
5	15-20.99	29-37.99	35-49.99
6	21-27.99	38-49.99	50-74.99
7	28-31.99	50-59.99	75-99.99
8	32-40.99	60-76.99	100-199.99
9	> 41	> 71	> 200

probability of bite is 0.59 in pre-high incidence (January to April), 0.68 in high incidence (May to August) and 0.42 in post-high incidence (September to December).

$P_{(trans)}$ is obtained using the Mamdani model (Borke and Fisher, 1998). It is the maximum of the product of a rainy day and amount of rainfall as expressed in Equation 5.

$$P_{(trans)} = \max \left| x_1 y_1, x_2 y_2, x_3 y_3, \ldots x_n y_n \right| \quad (5)$$

where $P_{(trans)}$ is the probability related to the transmission of *Aedes aegypti*. n is a numerical of the month, x is the rainy days in a season, and y is the amount of seasonal rainfall.

Probability Related to Temperature (P_t)

Probability related to temperature (P_t) can be estimated using Equation 6.

$$P_t = (Probability\ of\ bite)\left[(w_t)(\bar{x}_t)\right] \quad (6)$$

where w_t is a weight of temperature in each season (Koopman *et al*., 1991; Boonmaging, 2004) as listed in Table 2, and x_t is an average temperature in each season. The same set of probability of bite from Equation 4 was applied to this relationship. P_t was later normalized to be between 0 and 1.

Models Verification

This procedure determines how well the risk areas classified by the model fit to the conventional classification. Error matrix was applied for this purpose.

Risk Level Classification by Conventional Method

The conventional classification method of risk area based on the epidemic status or case availability in a different number of consecutive weeks is illustrated in Table 3 and the following descriptions:

Code area A: there are cases in every week within at least 4 consecutive weeks; B: there are cases in at least 2 weeks within 4 consecutive weeks; C: within a week, there is a new case reoccurring in the area; D: there is a new case occurring in the area which has no case within the week before; E: there is a new case occurring in the area which has no case within 4 weeks before; F: there is a new case occurring in the area which has no case within 6 months before.

Accuracy Assessment of Model Result Using Error Matrix

The statistics of fit for various predicted results and conventional classification with the same period of time can be calculated using error *matrix* (Pumplin and Stump, 2001). The overall accuracy can be calculated according to the following equation:

$$\text{Overall accuracy} = \left(\frac{D}{N}\right) 100 \quad (7)$$

where D is the total number of sub-districts in all classes of risk areas (high, moderate, and low where the predicted results are consistent with the ones classed by the conventional method), and N is the total

Table 2. Weight of temperature

Temperature	January to April		May to August		September to December	
	probability of bite	w_t	probability of bite	w_t	probability of bite	w_t
>35°C, <28°C	0.59	1.5	0.68	1.5	0.42	1.5
30°C	0.59	4.0	0.68	4.0	0.42	4.0
28-29°C, 31-35°C	0.59	3.0	0.68	3.0	0.42	3.0

number of sub-districts in the error matrix.

For this study, the models are verified and acceptable if the accuracy is ≥ 60%, or moderate to strong agreement.

Results and Discussion

Multilinear Regression and Logistic Regression Models

The multilinear regression model was performed on 18 seasonal data sets of the years 2001-2005 and their average to evaluate the correlation among the DF/DHF incidence rate, climatic variables (probability related to temperature (P_t) and rainfall (P_r)), and larval index *(I)*. The seasonal regression equations were derived as shown in Table 4. The most-fit equation is for the May-August season for which the coefficient of determination (R^2) is 0.72.

The correlation coefficients of the seasons fell in the range of 0.63-0.7 which was acceptable to be able to state that those variables had a high linear relationship. However, in the case where the input data covered more years, the cyclic pattern might be expected and the relationship should be reconsidered.

The spatial DF/DHF predictions were finally input through logistic regression analysis (Equation 1) and resulted in the seasonal epidemic probability or risk of DF/DHF of each sub–district for those years. To compare the risks resulting from the models with the ones from the conventional classification, they were classified into 3 classes i.e. high, moderate, and low using Delphi's technique. The result showed that the range of epidemic probability of the low, moderate, and high risks is 0.00-<0.40, 0.40-< 0.70, and 0.70-1.00, respectively.

Conventional and Predicted Risk Levels of Sub-districts

Risk areas of each sub–district resulting from the conventional classification and the predicted models of each season during 2001-2006 are displayed as maps in Figure 3. The risk trending resulting from both methods are displayed as a comparison graph for each risk level and each season in Figure 4.

For moderate and low risk areas, only the season of May to August shows obviously different trending from 2005 to 2006. The trending of the rest (seasons and years) is well consistent with each other.

According to Figure 5, the predicted moderate risk areas show an obviously smaller number than in the conventional one while for the high risk areas the predicted one shows a

Table 3. Conventional classification of DF/DHF risk area

Code area based on epidemic status		
A B C D	E	F
High risk area (A+B+C+D)	Moderate risk area (E)	Low risk area (F)

Table 4. The seasonal multi linear regression equations

Season	Seasonal multi linear regression equation	Correlation coefficient	Coefficient of determination (R^2)
Jan to Apr	$y = -15.87 + 2.66I - 0.125P_t - 0.01768P_r$	0.69	0.70
May to Aug	$y = -49.41 + 7.73I - 0.273P_t - 0.00051P_r$	0.70	0.72
Sep to Dec	$y = -14.77 + 2.21I + 0.008P_t - 0.0018P_r$	0.63	0.65

somewhat bigger number of areas in each season. When the high and moderate areas were grouped together as shown in Figure 4, it shows a higher correlation between the conventional and the predicted results, particularly in the second and the third seasons of the years. Not only are the numbers of risk areas of these 2 levels very close but also those areas (districts) are in the same set. It confirms the spatial precision of the prediction. Therefore, this can imply that the lower limit of epidemic probability of the high risk areas achieved from Delphi's technique is so low that many conventionally moderate risk districts are switched to be predicted as high risk areas.

Considering the high risk areas, it is found that the number of risk areas in the first season have an influence in increasing the number in the second season which in turn did the same in the third season. Even though the number of risk areas in the second and the third seasons are almost the same, it shows a significant influence because the second season is the peak of the epidemic and normally

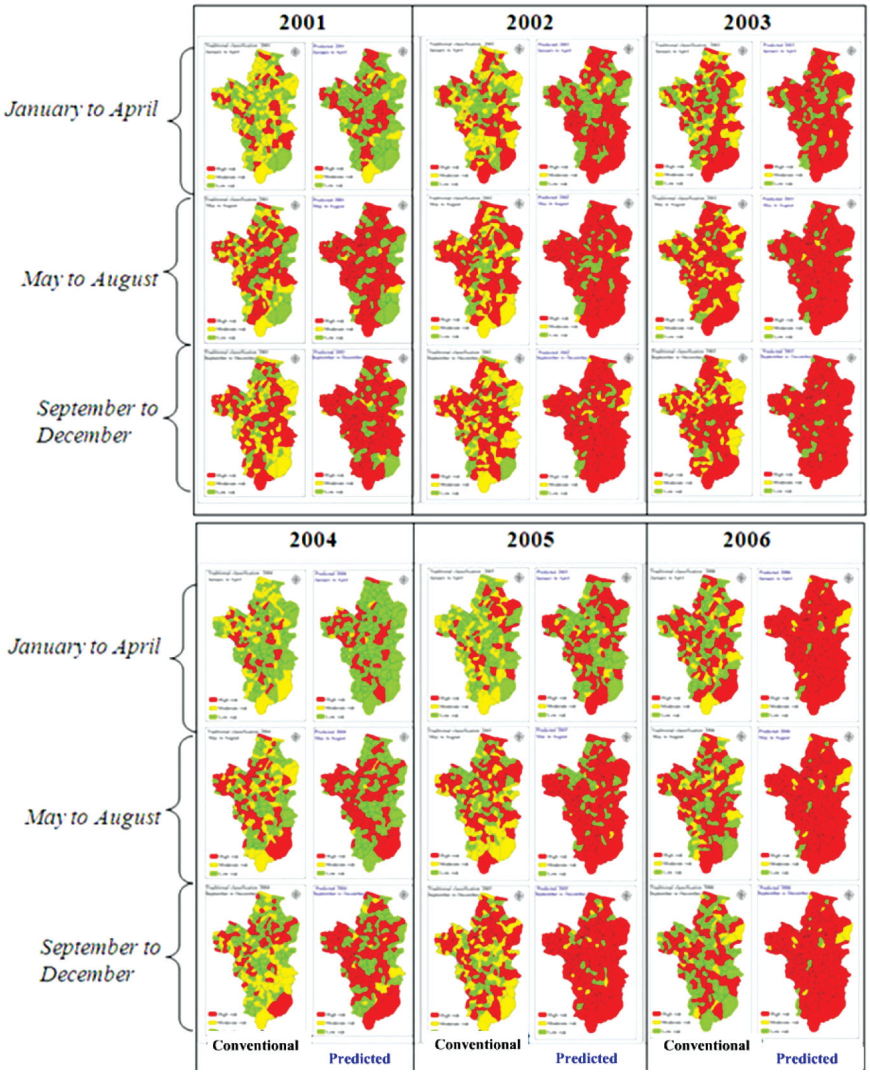

Figure 3. Risk areas resulting from conventional classification and predicted models

there is a tendency to have more cases than in the third season.

The low risk areas of the conventional and the prediction models show little difference in terms of the number of areas. However, to confirm the precision of the spatial predictions, they fall into almost the same set of districts.

Accuracy Assessment of the Predicted Model

The concluded accuracy assessment of the comparison of the risk areas between the conventional and predicted results of each season using the error matrix is expressed in Table 5. It shows that almost all the seasons during 2001-2005 have an overall accuracy above 60%. Only the accuracy of the last season in 2005 and the seasons in 2006 are lower, between 49.32-59.82%. This matter can be explained. According to the historical records of the UOPH, the epidemic circle will always occur in every third year. Plus there were constant increasing numbers of epidemic cases in Ubon Ratchathani during 2001-2003, and the UOPH therefore strengthened the control program in years 2005-2006. This resulted in reducing the intensity of epidemic cases in the areas and negatively affected the accuracy of the prediction results in the years as mentioned above. For example, in Dech Udom district the actual cases were reduced from 32 from January to April and 61 from May to August 2005 to be 13 and 23 for the same seasons in the year 2006. Without this strengthened control program, the prediction result should be more accurate.

Conclusions and Recommendations

The study offers spatial regression and logistic regression models for seasonally predicting the number of DF/DHF cases and the probability of risk in sub–districts of the Ubon Ratchathani Province of Thailand during 2001-2005. The larval index, temperature, and rainfall data analyzed in the regression model have revealed that the period of May-August is the most suitable season in Ubon Ratchathani Province for predicting the number of cases with a 0.72 coefficient of determination.

The classified seasonal probability of risk of each sub-district resulting from logistic regression was spatially compared to the conventional classification using the error matrix.

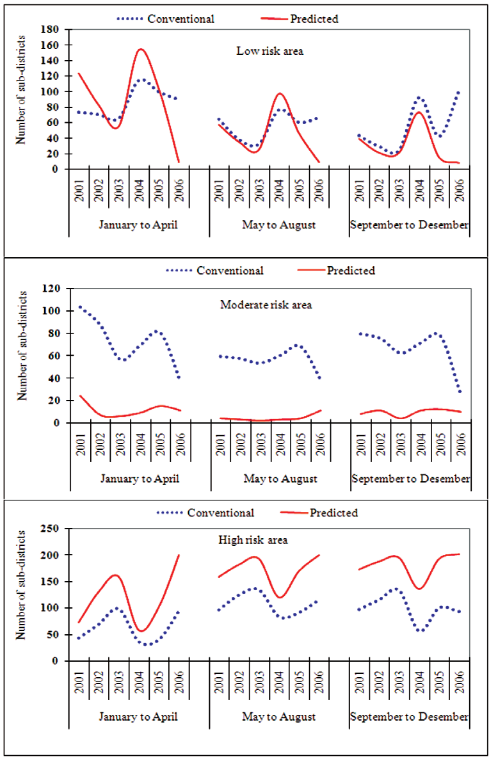

Figure 4. Graphs showing trends of high risk area, moderate risk area, and low risk area resulting from prediction models and conventional classification of each season in years 2001-2006

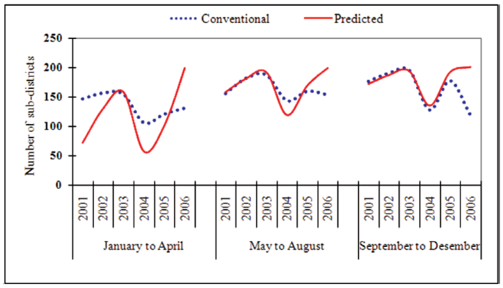

Figure 5. Comparison on the trending of the number of high and moderate risk areas between conventional and predicted results of each season during 2001-2006

Table 5. Comparison percentage of overall accuracy resulted from predicted models in year 2001-2006

Time period Year	January to April (%)	May to August (%)	September to December (%)
2001	63.92	71.68	65.75
2002	66.67	73.97	67.12
2003	72.60	73.52	71.69
2004	72.60	73.97	63.92
2005	70.32	64.38	57.59
2006	51.14	59.82	49.32

This accuracy assessment has conclusively revealed that almost all seasons during 2001-2005 have an overall accuracy above 60%. The period of May-August provides the highest overall accuracy while the period of September-December provides the lowest. However, if the grouped high and moderate risk areas were considered, the correlation between the conventional and the predicted results was obviously higher.

The resulting seasonal risk map of DF/DHF for each sub–district is useful information for the UOPH in both the short and long terms to enable proper allocating of resources for epidemic prevention and control activities particularly with regard to the recurrence of the same risk level in the next season and the same season of the next year. For example, the sub-districts predicted to be high and moderate risk areas should be subject to the routine prevention and control program of the UOPH such as using smoke, the elimination of water holding containers, and warnings through public relations for cooperation in the prevention of mosquito breeding and protection from mosquito bites, etc. All details of activities have been set up clearly as a standard implementation guideline for public health officers.

It is important to maintain the current status of input data of the spatial models in order to detect early DF/DHF epidemics more accurately. Meanwhile, past activities should be systematically recorded in order that the trend and the cycle of epidemics can be effectively observed.

In fact, to study the DF/DHF epidemic effectively, other factors should be considered such as the immunity of people and serotype changing of the dengue virus in that area. These data are generally required for an area having very intensive, continuous, and vital cases of the epidemic. To this date, the epidemic cases at that level have never existed in Ubon Ratchathani Province. Therefore, data related to these factors have never been recorded and reported.

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