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Monthly district level risk of dengue occurrences in Sakon Nakhon Province, Thailand

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ABSTRACT

The paper deals with the incidence of the Dengue Virus Infection (DVI) in the 18 districts of Sakon Nakhon Province, Thailand, from January 2005 to December 2007. Using a statistical and autoregressive analysis to smooth incidence data, we have constructed yearly and monthly district level maps of the DVI distribution. It is found that the DVI incidence is very correlated with weather conditions and higher occurrences are observed in the three most populated districts Wanon Niwat, Sawang Daen Din and Mueang Sakon Nakhon, and the virus transmission period spans from mid-summer to mid-rainy seasons (from April to August). Employing a Generalized Linear Model (GLM), we found that the DVI incidences were related with current meteorological (monthly minimum temperature, past 2-month cumulated rainfall) and socio-economical (population of 0–4 years old, per capita number of public small water wells, and proportion of villages with primary schools) covariates. And using the GLM under the climate change conditions (A1B scenario of IPCC), we found that the higher risk of DVI spreads from the three most populated districts to less populated ones, and the period of virus transmission increases from 5 to 9 months to include part of winter, summer and rainy seasons (from March to November) during which 6%, 61% and 33% of districts will be at low, medium and high risk of DVI occurrences, respectively.

1. Introduction

Dengue Virus Infection (DVI) is a mosquito-borne disease with four distinct virus serotypes (DEN-1, DEN-2, DEN-3, and DEN-4), of the genus *Flavivirus*, with *Aedes aegypti* being the principal vector, which can cause a spectrum of disease ranging from mild infection (dengue fever, DF) to a severe deadly disease (dengue hemorrhagic fever/dengue shock syndrome) (World Health Organization, 1997). The first infection with one of these serotypes confers permanent immunity to that particular serotype, but only temporary and partial protection against the other three serotypes, and second or sequential infections are possible after a short time (Halstead, 1988). Infections with dengue virus are subclinical and several of them are missed as a large proportion of infections are asymptomatic (Poblap et al., 2006; Vaughn et al., 1997). Therefore, seropositivity is often used as an indicator of DVI. Many factors have been associated with the dengue transmission, including climatic factors, seasonal component, urbanization, water storage, socio-economic factors, population movement, and increase in discarded containers (Brunkard et al., 2007; Clark et al., 2005; Ligon, 2005; Nagao et al., 2008; Nakhapakorn and Tripathi, 2005; Siqueira et al., 2004; Vanwambeke et al., 2006; Wu et al., 2007, 2009).

The first outbreak of dengue hemorrhagic fever in Southeast Asia, including Thailand, appeared in the 1950s (Gubler, 1998). In the past four decades, the incidence of dengue fever has rapidly increased in Thailand with a cycle of 3–4 years (Cummings et al., 2004; Hay et al., 2000; Wearing and Rohani, 2006). Cases in the rural areas are reported from the district hospitals to the provincial public health centers and to the Ministry of Public Health. The dengue occurrences are however local events. All four serotypes, spreading from Bangkok, are widely distributed and permanently circulating over the country (Mangada et al., 2002; Nisalak et al., 2003; Sriprom et al., 2003; Thavara et al., 2006). Analyzing the climatic and socio-economic conditions of the dengue transmission intensities in Northwestern Thailand during 1996–2004, Nagao et al. (2008) came to the conclusion that the northwestern rural region had the highest intensity of transmission, suggesting that intense transmission of the dengue infection is not necessarily associated with urbanization. In 2005–2006, incidences of 36.7 and 69.2 per 100,000 people, respectively, from the northeastern region (including our study site, Sakon Nakhon Province) were reported (Bureau of Epidemiology, 2006). We focused on Sakon Nakhon Province where all the four dengue virus serotypes have co-circulated and where one finds one of the highest reported incidences of DVI (79.6 per 100,000) among the four provinces of public health zone 11 which borders Laos and Vietnam. Because of that, dengue fever is the first target of the vector-borne disease prevention program in Sakon Nakhon. In the last

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decade, the dengue transmission activity was taking place throughout the year with a seasonal peak from June to August and outbreaks occurring in 1–2 year cycles. Accordingly, the surveillance program was usually starting in June. The DVI incidence in the Sakon Nakhon Province peaked in 1998, decreased in 1999, continued to decline in 2000, and then arose to a peak again in 2002. The DVI incidence was 63 per 100,000 in 2004. Main areas at a risk of dengue transmission were located in three of the most densely populated districts, Mueang Sakon Nakhon, Wanon Niwat, and Sawang Daen Din. Based on the previous trends, it was even predicted that there will be a rise in the DVI incidence in 2006. Despite the increasing circulation of dengue infection, no analyses of the distribution of DVI prevalence in this province are available yet since the serologic component of the surveillance program in Sakon Nakhon has started in 2005.

Our objective in this study is twofold: provide a smooth distribution of DVI incidence and identify locations (at the district level) and periods of the year at risk of occurrence of DVI cases in Sakon Nakhon Province. For this purpose, we use data of DVI cases reported from 2005 to 2007 in the province and, like in Bicout et al. (2006), we employ the disease mapping approach to analyze the distribution of DVI across the study region. Next, we develop a Generalized Linear Model (GLM) to relate DVI occurrences with meteorological and socio-economical explanatory covariates. Finally, this latter GLM is used in the calculation of the probability or risk of occurrence of DVI cases. Based on this, the risk of DVI occurrences for the present meteorological conditions is computed and an estimate of that risk for one of the Intergovernmental Panel on Climate Change (IPCC) scenarios of climate change is provided.

2. Methods

2.1. Study site

This study was conducted in the Sakon Nakhon Province, a 9605.76 km^2 province in the northeastern of Thailand, situated between latitudes 16°45′N and 18°15′N and longitudes 103°15′N and 104°30′N. It is located on the Khorat Plateau which is approximately 647 km from Bangkok and 90 km from Khong River, the border line between Nakhon Phanom Province and Lao People's Democratic Republic. The Sakon Nakhon Province is divided into 18 districts, 125 sub-districts, and 1485 villages. Yearly, Thailand's weather involves 3 seasons with 4 months duration: winter (from the beginning of November to the end of February) is a dry season relatively cold especially at night, summer (from the beginning of March to the end of June) is dry and hot, and rainy season (from the beginning of July to the end of October) is rainy and hot. The climate in the Sakon Nakhon Province is savannah with temperatures varying between 15 °C and 39 °C, and the average annual rainfall between 200 mm and 1600 mm (Sakon Nakhon Meteorological Office, 2005). Based on the 2005 data, the total population is about 1.1 million with a literacy rate of 90% and an average annual income of 641 US$ (Department of Disease Control, 2006). There are 20 hospitals and 166 health stations. The majority of the population is farming because of several rivers across the province and the quality of soil irrigation. The main natural water resource is Nong Han Lake, the biggest natural lake of northeast Thailand. Most of the inhabitants have electricity and have also inside piped-private water supply. They stored rain water for drinking within household containers (Sakon Nakhon National Statistical Office, 2005). Most of the public roads are non-asphalt road. The villages of Sakon Nakhon are concentrated around the public transportations.

2.2. Study data

In this province, DVI cases are reported from district hospitals to provincial public health office, and on to the Ministry of Public Health. This study is based on the data collected in 2005–2007 by the Sakon Nakhon Provincial Public Health Office. The patients hospitalized at the provincial hospital were identified DVI by medical doctors, and the positive test results for IgM antibody were confirmed at the department of medical science. To generate the distribution of infection with some factors, climatic and socio-economic factors were incorporated as the independent variables. Climatic data included the daily rainfall (mm), the minimum temperature, and the maximum temperature (in Celsius degree) between 2005 and 2007 were obtained from the Sakon Nakhon Meteorological Office which enrolled 19 weather stations. The socio-economic variables were averaged for each district under the initiative of the National Rural Development Committee of Thailand which can be accessed at http://www.vector-borne-diseases.org/ socio-economics Thailand (Nagao et al., 2008).

2.3. Statistical analysis

Spatio-temporal analyses of DVI incidence and relative risk calculations were done as follows. First, for each district "i" ($i=1,2,\cdots,18$), the reported data of the monthly number of DVI cases K_{it} ($t=1,2,\cdots,36$) are concatenated to form the number of cases at time scale ΔT as $Y_{i,p}=\sum_{t=1+(p-1)\Delta T}^{p\times\Delta T} K_{i,t}$ for $p=1,2,\cdots(36/\Delta T)$. Note that $Y_{i,p}$ coincides with K_{it} for $\Delta T=1$. In what follows, the analyses will be presented for $\Delta T=1$ (month) and $\Delta T=12$ (year). Now, assuming that Y_i,p can be described as a Poisson variable with intensity parameter $\lambda_p=\sum_{i=1}^{18} Y_{i,p}/\sum_{i=1}^{18} S_i$, where S_i is the population of district "i", and the number of expected cases under the homogeneous hypothesis is, $E_i,p=\lambda_p S_i$, the smoothed and estimated standardized incidence ratio $\mathrm{SIR}_{i,p}$ for each district "i" at time period "p", were computed like in Bicout et al. (2006) following the model, $\log(\mathrm{SIR}_{i,p})=-\log(E_{i,p})+\alpha_p+u_{i,p}+v_{i,p}$. At each time period "$p$", the model takes into account the overall random effect α_p of the SIR and incorporates both uncorrelated heterogeneities $v_{i,p}$ of each district and spatial correlations $u_{i,p}$ between districts. The software WinBUGS was used for Markov chain Monte Carlo simulations to find Bayesian estimates of $\mathrm{SIR}_{i,p}$. The smoothed number of cases $sY_{i,p}$ was obtained by inverting the relation defining the SIR, $\mathrm{SIR}_{i,p}=sY_{i,p}/E_{i,p}$. Next, for $\Delta T=1$ (month), we have constructed a Generalized Linear Model (GLM) relating $sY_{i,t}$ with meteorological and socio-economical explanatory variables. We used the following model: $\log(\langle sY_{i,t}\rangle)=\beta_{0,q}+\sum_{n=1}\beta_n x_{i,t,n}+\sum_{m=1}\sum_{n\neq m}\beta_{mn} x_{i,t,m} x_{i,t,n}$, where $\langle sY_i,t\rangle$ is the mean smoothed number of DVI cases in the district "i" at time t, $x_{i,t,n}$ is the n-th ($n=1, 2, \ldots$) normalized (value divided by the standard deviation) meteorological variable or socio-economical indicator for the district "i" at time t, β's are the GLM parameters associated to explanatory variables to determine. The intercept $\beta_{0,q}$ is allowed to vary at scale q larger than t. The best GLM model was chosen following 3 criteria: the Akaike Criterion, the Cook's distance repartition, and comparison of the model with an embedded one using the deviance analysis. The results report only the best model, and the number of DVI cases generated from this GLM is denoted by gY_i,t. All the regression calculations were performed using the software R-Project version 2.10.0 (R Development Core Team, 2009).

2.4. Risk of occurrence of DVI cases

The number of DVI cases generated from the GLM is used to assess the occurrence risk of DVI cases as follows. For each district "i", the probability of observing at least "m" DVI cases at month "t" is given by the binomial, $Q_{i,t}(m)=1-\sum_{n=0}^{m-1}\binom{S_i}{n}q_{i,t}^n(1-q_{i,t})^{S_i-n}$, where $q_{i,t}=gY_{i,t}/S_i$ is the probability of single case occurrence. To compute the risk R_i, t of occurrence of DVI cases for each calendar month, we use the threshold of $m = 5$ cases (as lot of infectious cases are asymptomatic) in $Q_{i,t}(m)$ and perform the yearly average of $Q_{i,t}(5)$ for each month within a year to have, $R_{i,t} = \frac{1}{M}\sum_{j=1}^{M} Q_{i,t\ +\ 12\times(j-1)}(5)$, where M is the number of years (in our data, $M = 3$ for 2005, 2006 and 2007). The $R_{i,t}$ index is then used to identify districts and periods of the year at low ($R_{i,t} \leq 0.1$), medium ($0.1 < R_{i,t} \leq 0.5$) and high ($0.5 < R_{i,t} \leq 1$) risk of DVI cases. Likewise, the seasonal risk $R_{i,\mathrm{season}}$ of DVI cases was also calculated as a 4-month average of $R_{i,t}$ that are $R_{i,\mathrm{winter}}$ (from November to February), $R_{i,\mathrm{summer}}$ (from March to June) and $R_{i,\mathrm{rainy}}$ (from July to October).

3. Results

3.1. Epidemiological data and meteorological factors

Dengue is endemic in Sakon Nakhon. From 2005 to 2007, all four dengue virus serotypes were diagnosed from 1894 patients (male 52%) confirmed with Dengue Virus Infection in the Sakon Nakhon Hospital (see Table 1). Patient ages ranged from 4 months to 65 years of which 42% ranged from 10 to 14 years (mean 13.9 years). The general trend is an increase of DVI cases with years with the highest number of cases recorded in the three most populated districts; Wanon Niwat (WN), Sawang Daen Din (SDD) and Mueang Sakon Nakhon (MSN) (see Table 1). Interestingly, low populated districts like Song Dao (adjacent to SDD) and Phu Phan (adjacent to MSN) also exhibited large number of DVI cases in 2006 and 2007, respectively. This is to underline that the population density is not the only variable that matters in the DHF transmission (Nagao et al., 2008). Other variables like the vectorial capacity of mosquitoes and movement patterns of individuals between districts have a non-negligible role in the transmission of the disease since the force of infection (or the propensity for individuals of contracting the disease per unit of time) for each district "i" is given by, $\lambda_i = C_i \sum_j w_{ij} I_j$, where C_i is the vectorial capacity of *Aedes* mosquitoes, I_j is the population of infectious individuals of the district "j" with "j" running over all districts including the one under consideration, and w_{ij}, the probability matrix for population movements from the district "j" to the district "i", accounts for the spread of the transmission from district to district.

Table 1
Reported yearly cases of Dengue Virus Infection, 2005–2007, Sakon Nakhon Province, Thailand.

District			No cases		
Name	Symbol	Population	2005	2006	2007
Nikhom Nam Un	NNU	13,765	4	8	6
Tao Ngoi	TN	23,070	17	6	0
Kut Bak	KB	31,721	6	48	22
Song Dao	SD	32,516	9	105	14
Khok Si Suphan	KSS	33,693	20	7	11
Phon Na Kaeo	PNK	35,279	4	16	21
Phu Phan	PP	35,821	14	12	90
Kham Ta Kla	KTK	37,979	7	40	1
Charoen Sin	CS	42,374	10	13	7
Ku Su Man	KSM	45,036	8	15	17
Waritchaphum	W	51,126	11	10	11
Phang Khon	PK	51,499	12	12	25
Ban Muang	BM	67,003	18	44	64
Akat Amnuai	AA	67,464	5	15	9
Phanna Nikhom	PN	79,071	11	11	12
Wanon Niwat	WN	119,724	77	204	54
Sawang Daen Din	SDD	146,345	54	142	81
Mueang Sakon Nakhon	MSN	185,278	75	114	265
Total		1,098,764	362	822	710

Concerning the time distribution of cases, Fig. 1 shows that the total number of DVI cases is synchronized and qualitatively correlated with the rainfall and minimum temperature (see below for quantitative analysis). It can be seen in Fig. 1 that the number of DVI cases is almost zero during the winter (very low level transmission) and appears to peak during the wet and hot seasons from June to August, suggesting the onset of transmission in summer.

3.2. Yearly number of DVI cases

As already noted above, Fig. 2 shows that the incidence rate of DVI cases is clustered with a gradient of cases spreading from the three most populated districts WN, SDD and MSN to adjacent less populated districts. The highest incidence rates of DVI occurred in 2006 and the proportion of districts with incidence rate greater than 50 (100) were 17% (0%), 44% (22%), and 33% (11%) in 2005, 2006 and 2007, respectively (see Fig. 2).

3.3. Monthly number of DVI cases

The smoothed monthly number of DVI cases is displayed in Fig. 3, where the x-axis represents months from January 2005 to December 2007 and the y-axis the districts sorted in a decreasing order of population size from the bottom to the top. Fig. 3 shows that the number of DVI cases at the district level remains higher from June to August (during the peak of DVI transmission) for 3 years like in Fig. 2, and that the larger number of cases is generally observed in the three most populated districts WN, SDD and MSN (see Table 1 and Fig. 2), although several low populated districts do have more than 5 monthly DVI cases. Considering that the number of DVI cases is proportional to the force of infection times the population of exposed susceptibles, Fig. 3 underlines that the number of DVI cases scales with the district population but with a multiplicative factor scaled by the heterogeniety of the force of infection (that involves the vectorial capacity and the matrix of population movements between districts which accounts for the spread of the transmission from district to district). Let D be the mean duration of virus circulation period defined as the time span during which the number of monthly DVI cases is >5 (corresponding to dark colors in Fig. 3) averaged over the WN, SDD and MSN. We find that D is about 4, 5 and 6 months in 2005, 2006 and 2007, respectively, and the proportion of districts with the number of monthly DVI cases >5 at least once within the virus circulation period are 44% in 2005 and 56% in both 2006 and 2007.

3.4. GLM of number of DVI cases vs meteorological and socio-economical covariates

The best fit to the incidence rate of DVI with meteorological and socio-economical indicators was given by the following model:

$$\log\left(\left\langle sY_{i,t}\right\rangle\right) = \beta_{0,q} + \beta_1 T_t + [\beta_2 + \beta_{12} T_t] CR_{i,t} + \beta_3 V_{1,i} + \beta_4 V_{2,i} + \beta_5 V_{3,i}$$

where $\langle sY_{i,t}\rangle$ is the mean of smoothed number of DVI cases, T_t is the monthly minimum temperature, $CR_{i,t}$ is the past 2-month cumulated rainfall, and the definitions socio-economical variables and values of β's are given in Table 2. As a comparison check between the number of cases simulated from the GLM and the smoothed number of cases, we calculated the value of Δ which is the logarithm of the ratio of the simulated number on the smoothed number. The distribution of Δ and the cumulated frequency of $|\Delta|$ are reported in Fig. 4 showing that about 63% of data are contained within the interval $|\Delta| < \log(2)$, i.e., a factor smaller than 2 between simulated and smoothed values of number of cases.

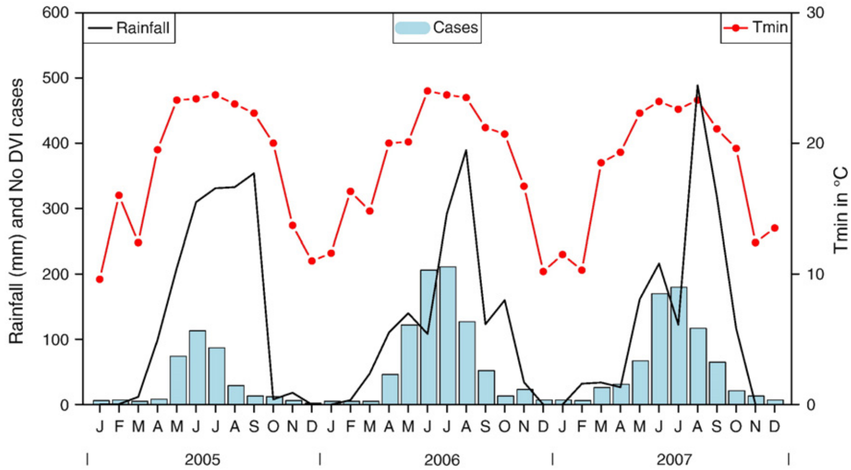

Fig. 1. Monthly rainfall (solid line), minimum temperature (line with symbols) and total number of cases of Dengue Virus Infection (histogram), 2005–2007, Sakon Nakhon Province, Thailand.

The GLM showed a significant effect of the year with the number of cases with a higher effect in 2006 and 2007 than in 2005 (see $\beta_{0,p}$, in Table 2), as already mentioned above (see Table 1, Figs. 1 and 3). Regarding the meteorological variables, the GLM indicates that the number of cases increases significantly with minimum temperature T_t and decreases (increases) with the rainfall $CR_{i,t}$ for $\mathrm{T_t}$ smaller (greater) than the compensation temperature T_c ($T_c = -\mathrm{SD}(\mathrm{T_t}) \times \beta_2 / \beta_{12} = 23.2$ °C) at which the effect of rainfall cancels out (see β_1, β_2 and β_{12} in Table 2). For the overall effect of meteorological variables given by, $Z_{i,t} = \beta_1 T_t + [\beta_2 + \beta_{12} T_t] CR_{i,t}$, we found that the number of cases in each district "i" significantly increases (decreases) with climatic factors for minimum temperatures greater (smaller) than the threshold temperature, $T_{th,i} = -\beta_2 CR_i \times SD(T_t) / (\beta_1 + \beta_{12} CR_i)$, indicating hence that $Z_{i,t} > 0$ ($Z_{i,t} < 0$) for minimum temperature $> T_{th,i}$ ($< T_{th,i}$) although the 2-month cumulated rainfall contribution is still negative in $T_{th,i} <$ minimum temperature $< T_c$, i.e., the increasing rate

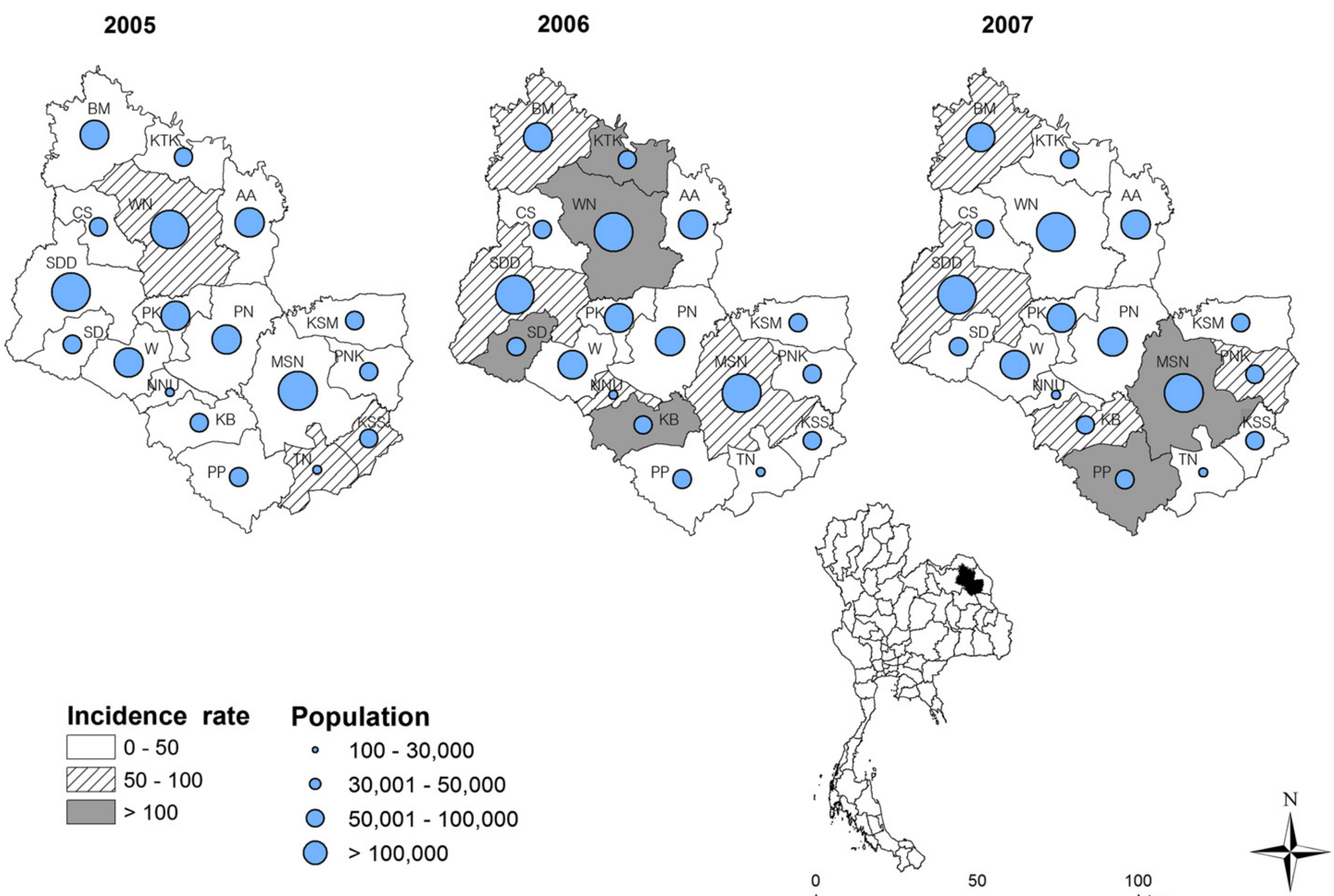

Fig. 2. District level distributions of the population and the (smoothed) incidence rate (number of new case for 100,000 people per year) of Dengue Virus Infection, 2005–2007, Sakon Nakhon Province, Thailand. See Table 1 for district symbols.

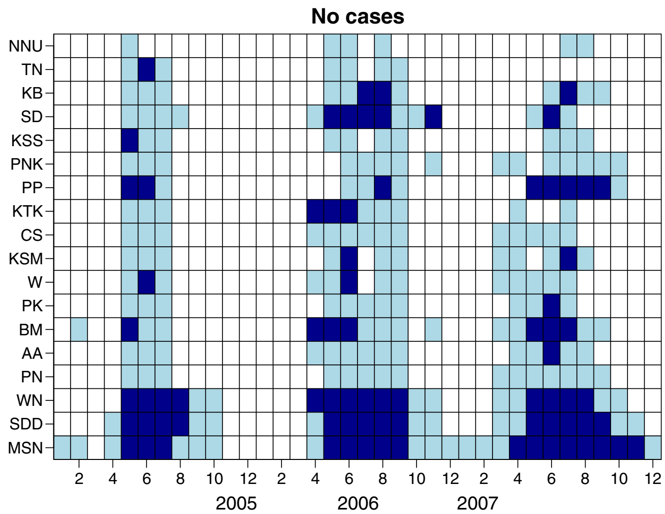

Fig. 3. Monthly time-series of the mean number of Dengue Virus Infection cases (mdvi) at the district level, 2005–2007, Sakon Nakhon Province, Thailand. The x-axis represents months from January 2005 to December 2007 and the y-axis the districts sorted in a decreasing order of population size from the bottom to the top. White colors correspond to mdvi ≤ 1, gray to 1 < mdvi ≤ 5, and dark to mdvi > 5.

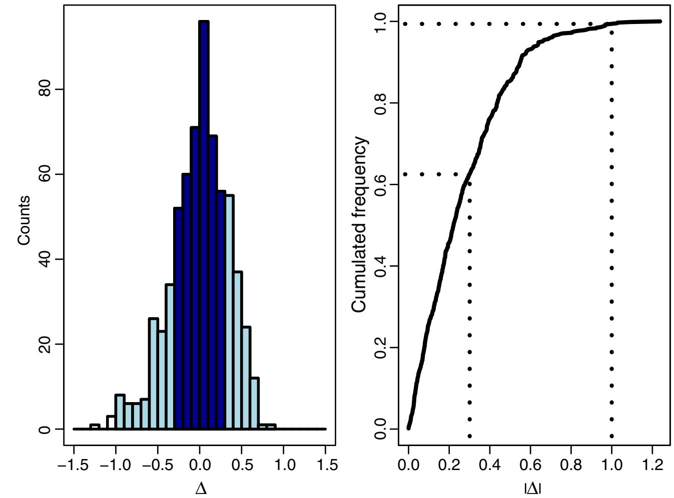

Fig. 4. Distribution (left panel) and cumulated frequency (right panel) of the deviation, Δ = log(number of cases simulated from GLM/smoothed mean number of cases), between simulated and mean number of cases of Dengue Virus Infection over all districts of Sakon Nakhon Province, Thailand, from 2005 to 2007. About 63% of the data is contained in dark histogram (left panel) and dashed line (right panel) corresponding to |Δ| = log(2), i.e., a factor of two between simulated and mean number of cases.

of $Z_{i,t}$ is higher for minimum temperature > T_c than for $T_{th,i}$ < minimum temperature < T_c. For instance, T_{th} = 10 °C and 14 °C for 2-month cumulated rainfall of 730 mm and 1400 mm, respectively. For socio-economic variables, the GLM indicates that the number of cases increases significantly with the number of children of 0–4 years old, while it decreases significantly with both the proportion of villages with primary schools and per capita number of public small water wells (see β_3, β_4 and β_5 in Table 2).

3.5. Risk of DVI occurrences

As described in Methods section, the risk of DVI occurrences, as shown in Figs. 5 and 6, were calculated using the output of the GLM in which involves meteorological variables minimum temperature T_t and past 2-month cumulated rainfall $CR_{i,t}$. To assess the impact of the climate change on the risk of DVI occurrences, we used the data from the fourth report of the IPCC (Core Writing Team, 2007) providing results of multi-model averages based on the SRES A1B scenario. For the North-Eastern region of Thailand and for the period 2090–2099, relative to 1980–1999, the A1B scenario predicts an increase of the surface temperature by about 1.75 °C and a change in precipitation patterns with a rainfall increase by about 10% from June to August and a rainfall decrease by about 10% from December to February. To account for this climate change in our calculations, we have assumed that the meteorological sequences in the future will remain the same to the current ones excepted that i) the minimum temperature with climate change will rescale to $Tcc_t = T_t + 1.75$ °C, and ii) the rainfall (RF) with climate change will be modified to RFcc = 0.9 × RF from December to February, RFcc = 1.1 × RF from June to August, and RFcc = RF for the remaining months.

Fig. 5 shows the monthly risk of DVI occurrences under current and future (A1B scenario) meteorological conditions. The districts at higher risk under the current climate are the three most populated districts WN, SDD and MSN, and the period of virus transmission spans from the mid-summer (from April to may) to the end of rainy season (October) during which 33%, 50% and 17% of districts at low, medium and high risk, respectively. On the other hand, under the climate change conditions, the higher risk of DVI spreads from the

Table 2
Estimated GLM coefficients (all with p < 0.001) for the associations between the smoothed mean number of Dengue Virus Infection cases with meteorological and socio-economical variables, 2005–2007, Sakon Nakhon Province, Thailand. SD and SE stand for the standard deviation and standard error, respectively.

Covariate			GLM coefficients		
Definition	Symbol	SD	β	Value	SE
Intercept 2005			$\beta_{0,1}$	−3.745	0.343
Intercept 2006			$\beta_{0,2}$	0.584	0.078
Intercept 2007			$\beta_{0,3}$	0.697	0.080
Monthly minimum temperature	T_t	4.82	β_1	0.990	0.050
2-month cumulated rainfall	$CR_{i,t}$	368	β_2	−1.773	0.246
Temperature–rainfall interaction	T_t: $CR_{i,t}$		β_{12}	0.363	0.056
A1pop	V_1	3091	β_3	0.693	0.033
Pubpon_p	V_2	0.0009	β_4	−0.143	0.033
Primarysch_v	V_3	0.101	β_5	−0.113	0.033

A1pop = population of 0–4 years old.
Pubpon_p = Per capita number of public small water wells.
Primarysch_v = Proportion of villages with primary schools.

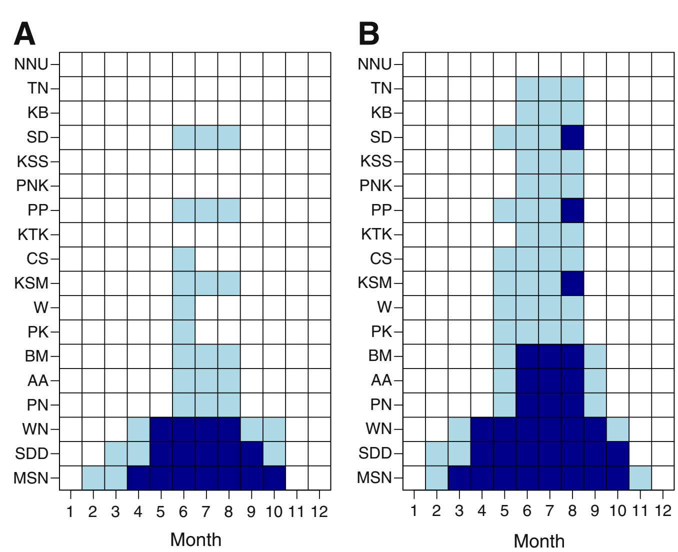

Fig. 5. Monthly risk $R_{i,t}$ of occurrence of dengue cases over the year under current (panel A) and future (climate change A1B scenario of IPCC) (panel B) meteorological conditions. White colors correspond to $R_{i,t} \leq 0.1$, gray to $0.1 < R_{i,t} \leq 0.5$, and dark to $0.5 < R_{i,t} \leq 1$.

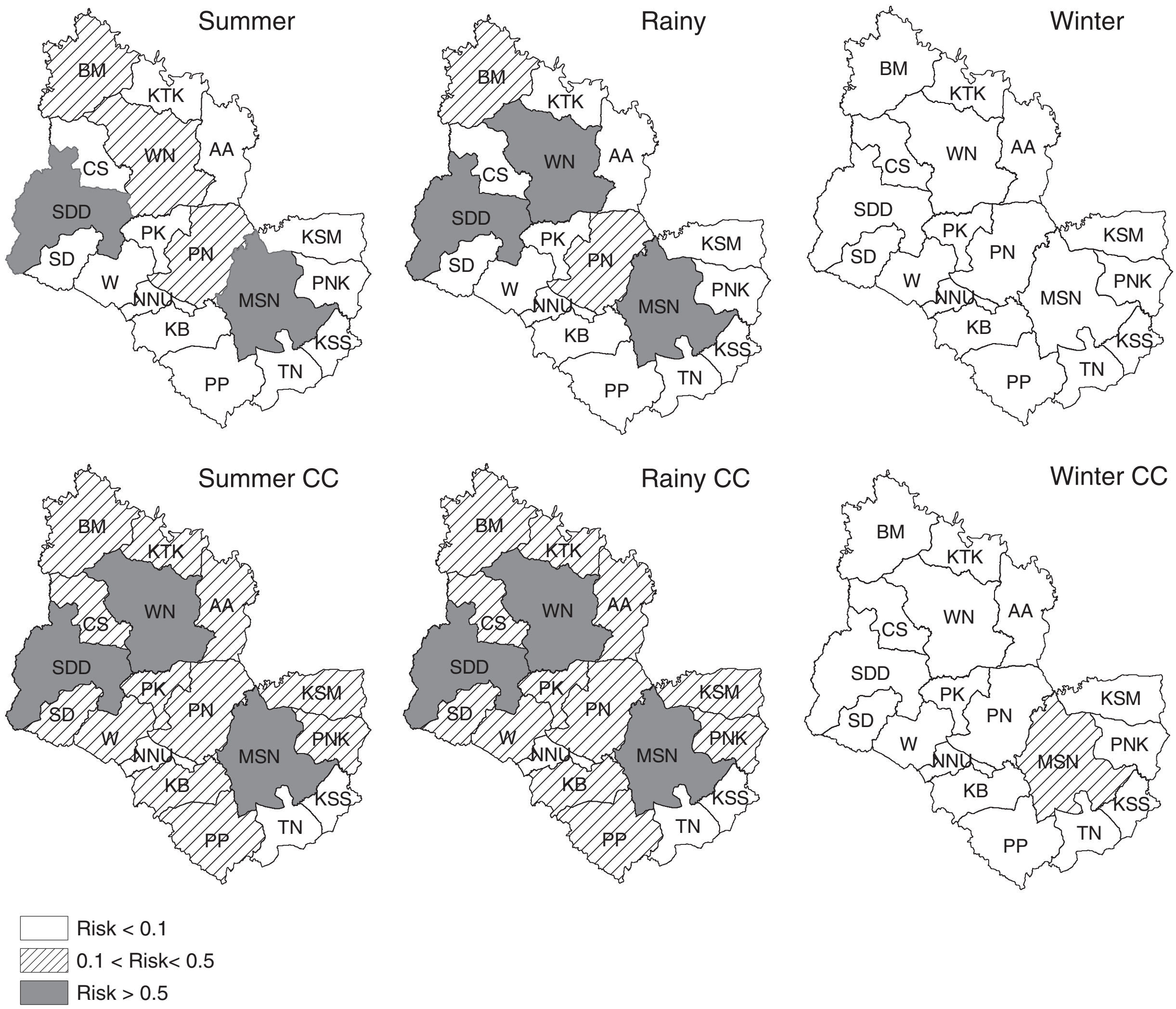

Fig. 6. Seasonal risk of occurrence of dengue cases under current (top) and future (climate change A1B scenario of IPCC) (bottom) meteorological conditions for summer, rainy and winter seasons (CC stands for climate change). White colors correspond to the risk ≤ 0.1, gray to 0.1 < risk ≤ 0.5, and dark to 0.5 < risk ≤ 1.

three most populated districts to less populated ones, and the period of virus transmission increases to include part of winter, summer and rainy seasons (from February to November) during which 6%, 61% and 33% of districts are at low, medium and high risk, respectively. This trend in the enhancement of the risk of DVI occurrences under climate change is also illustrated in Fig. 6. It can be seen that the proportion of districts at a seasonal risk >0.1 is 28% in summer and rainy seasons and 0% in winter for the current climate, while it is 89% in summer and rainy seasons and 6% in winter under climate change conditions.

4. Discussion and conclusion

Three aspects of the incidence of the Dengue Virus Infection (DVI) in the Sakon Nakhon Province have been considered in the analyses developed above.

In first, we have dealt with the yearly and monthly distributions of DVI incidence at the district level. We found that the averaged figure of the DVI in Sakon Nakhon Province during 2005–2007 is summarized as follows: 1) the incidence of DVI cases is clustered in the three most populated districts; Wanon Niwat (WN), Sawang Daen Din (SDD) and Mueang Sakon Nakhon (MSN), with a gradient of cases spreading from the most populated districts to adjacent less populated districts like Song Dao (adjacent to SDD) and Phu Phan (adjacent to MSN), and 2) the period of dengue virus transmission last about 5 months (from April to August) during the wet and hot (summer and rainy) seasons where more than 50% of districts in average are found with a number of monthly DVI cases >5. The apparent spread of the transmission from most populated districts to less populated ones may result from either i) heterogeneity in the population of exposed susceptibles, or ii) heterogeneity in the force of infection, or iii) a combination of i) and ii). However, this study does not allow to identify which kind of heterogeneity scenario is taking place.

In second, we investigated the relationships between DVI incidences and weather conditions and socio-economical variables. Using a regression approach, we found that 63% of the data were described by the developed GLM in which the DVI incidences were significantly related with a constant year effect, with monthly minimum temperature and past 2-month cumulated rainfall, for meteorological variables, and with the population of 0–4 years old, the per capita number of public small water wells, and the proportion of villages with primary schools, for socio-economical covariates.

The year effect of the DVI incidence can be attributed and accounted for the immunity status of host populations, the cycle of DVI and/or other factors related to population of dengue virus vectors. The DVI incidences were found to be positively associated with the monthly minimum temperature in consistency with the literature. Note that in the Sakon Nakhon area, the amplitude of yearly variations of the monthly minimum temperature is larger than that of the monthly maximum temperature (Sakon Nakhon Meteorological Office, 2005). Globally, the vector-borne diseases and associated vector activity are positively associated with temperature (<40 °C) (Deubel and Rodhain, 1999). There are numbers of studies in the literature dealing with relationships between temperature and dengue occurrences and dengue vector abundance (Nagao et al., 2008; Nagao et al., 2003; Nakhapakorn and Tripathi, 2005; Wu et al., 2009; Wu et al., 2007). In Thailand, for example, Nagao et al. found a positive association between the average daily pan evapo-transpiration and the inverse of mean age of DHF cases (Nagao et al., 2008) or a positive association between the larval abundance indices of the *Aedes* mosquitoes and the monthly means of daily minimum and maximum temperatures (with an optimum of 33–34 °C), and the increase of mean precipitation in the two previous months (Nagao et al., 2003). Likewise, Nakhapakorn and Tripathi (2005) reported that the dengue occurrences in Thailand were positively associated with rainfall and negatively associated with temperature and humidity, while during the rainy season they were positively associated with rainfall and temperature and negatively with humidity. Similarly, in Taiwan, Wu et al. (2007) found a positive association between the number of dengue occurrences and the monthly maximum or minimum temperature and the cumulative rainfall with a lag of two months. These observations are coherent with the biology of vectors of viruses. It was shown in many regions that the minimum temperature is the most critical factor for the threshold of mosquito survival and developing rate in sustaining the population density (Wu et al., 2009), and for the extrinsic period as the virus would not amplify in the vector when the temperature is less than 18 °C (Watts et al., 1987).

Regarding the rainfall, we found the DVI incidences to be negatively associated, for the monthly minimum temperature <23.2 °C, and positively associated, for the monthly minimum temperature >23.2 °C, with the past two months cumulated rainfall. The association of the DVI incidences with the cumulated rainfall of the two previous months in our GLM rather than with the cumulated rainfall of the current month is similar to the findings of other authors (Nagao et al., 2003; Wu et al., 2007). For monthly minimum temperatures <23.2 °C, the combined effect of minimum temperature and cumulated rainfall is heterogeneous over districts with the district DVI incidences positively (negatively) associated with climatic factors for minimum temperature $>T_{th,i}$ ($<T_{th,i}$), where the threshold minimum temperature $T_{th,i}$ depends on the 2-month cumulated rainfall in each district. In contrast, for monthly minimum temperatures >23.2 °C, the impact of climatic factors is positive and homogeneous over all districts. This suggests that increasing the monthly minimum temperature will likely increase the DVI incidences of districts and expand the transmission period in weakly endemic (less populated) districts.

The DVI incidences were found to be positively associated with the number of young children (less than 5 years) per district (A1). The number A1 is a function of both the total population (A) of the district and the proportion of young children in the district that can be related as, $A1 = 0.0686 \times A + 51.54$, corresponding in average to about 7% of young children per district. The larger the district population is the larger the number of case as underlined above in yearly and monthly analyses of DVI incidence. The incidence rate in young people can be higher than in older ones (Halstead, 2005; Rotela et al., 2007; Suwandono and Kosasih, 2006) as the mean age of infectious cases decreases with the infection rate intensity. In Thailand, dengue is an endemic disease and the mean age is relatively low (9 to 20 years old) (Nagao et al., 2008).

Negative associations between the DVI incidences and the per capita number of public small water wells and the proportion of villages with primary schools were also found to a lesser extent. These associations are less obvious. We remind that these covariates can be either a risk indicator or a risk factor of DVI incidences. In any case, one may hypothesize that the increase of per capita number of public small water wells to be related with the decrease of the need of containers for collecting and storing rainwater which form very favorable breeding sites for dengue vectors. In their study of the relation between *Aedes* infestation and social factors in the northern part of Thailand, Nagao et al. (2003) found negative and positive associations with the per capita private and public wells, respectively. The authors explained such associations with the necessity to store water (e.g., with large earthen drinking water container which are commonly used in Thailand).

The negative association between DVI incidence and the proportion of villages with primary schools can be related with the educational level of the population. More educated people are more aware and more careful in following policies of control measures. Similarly, Nagao et al. (2003) also found a negative association between dengue occurrences and the proportion of village with primary schools.

These findings on where and when the dengue virus circulation occurs are useful information that can be used by provincial health officials in designing and targeting control measures. Indeed, the breeding grounds for the *A. aegypti* mosquitoes, the main vectors of dengue virus, is the stagnant water found in discarded tires, tin cans and plastic cartons, or also bowls of water in which legs of food storage shelves are placed in order to prevent the stored cooked food from insect (ants) invasions. Thus, health workers from the provincial health office can visit the districts at a risk of DVI for surveillance and medical treatment, and for applying mosquito control measures like emptying containers after rainfall and reminding villagers to put salt in the dish bowls. Targeting the districts for actions reduces the number of districts to treat and therefore make the control measures more feasible in terms of both manpower and funding. The surveillance would have to be ongoing to determine any changes in where and when the control measures would have to be applied. Based on these findings, we may suggest the following recommendations to public health services: 1) start the surveillance system earlier in April when weather conditions are favorable (i.e., minimum temperature smaller than $T_{th,i}$ or 23 °C), 2) prioritize the surveillance efforts and control measures from most to least populated districts, and 3) promote the increase of the number of private wells.

And, in third, we used the GLM to investigate the changes in the patterns of DVI incidence under the climate change conditions (A1B scenario of IPCC). We found that the higher risk of DVI spreads from the three most populated districts to less populated ones, and the period of virus transmission increases from 5 to 9 months to include part of winter, summer and rainy seasons (from March to November) during which 6%, 61% and 33% of districts will be at low, medium and high risk of DVI occurrences, respectively. Everything being equal elsewhere, the climate change conditions as included above result in increasing the force of infection for each district.

Finally, recall that we have developed a GLM for the DVI incidences that involves only meteorological and socio-economical variables, and we found that the GLM correctly described 63% of the data. The remaining 37% of data not described by the GLM may account for the immunity status of host populations, the cycle of DVI and/or other factors related to population of dengue virus vectors. To include such additional variables of the problem into the analysis will require both the knowledge of these variables from raw data and to substantially improve our GLM to more advanced regressions or develop a mechanistic epidemiological model. This though task is out of the scope of this paper.

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