

Re-Model the Relation of Vector Indices, Meteorological Factors and Dengue Fever

Yao-Ting Tseng¹, Fong-Shue Chang², Day-Yu Chao^{2*} and Ie-Bin Lian^{3*}

¹Department of Mathematics, National Changhua University of Education, Changhua, 50007, Taiwan

²Graduate Institute of Microbiology and Public Health, Nation Chung Hsing University, Taichung 40227, Taiwan

³Graduate Institute of Statistics and Information Science, National Changhua University of Education, Changhua, 50007, Taiwan

Abstract

Background: Dengue is the most rapidly expanding and spreading mosquito-borne viral disease in tropical and subtropical countries. In Taiwan, dengue incidence clustered in Southern part, especially Kaohsiung in the past decade.

Aim: The spatial and temporal patterns of dengue transmission in Taiwan from 2005 to 2012 were examined to investigate the occurrence of dengue fever (DF) patients and its association with immature and adult mosquito indices, and its interaction with meteorological factors and household density.

Methods: Three databases were spatially and temporally linked, including the comprehensive chart records of DF cases and vector surveillance data in Kaohsiung, as well as the meteorological and environmental information from 2005 to 2012. A case-crossover study design was used to explore the effects of mosquito indices and weather on the risks of DF, and conditional logistic regression was applied to estimate the odds ratios (OR).

Results: Results showed immature mosquito indices had significant positive association with DF in the medium and high household density areas (e.g., adjusted ORs of Breteau index were 1.04, 95% CI=[1.02, 1.06] and 1.06, CI=[1.04, 1.08] respectively), while adult mosquito index was significant to all low/med/high household densities (adjusted ORs of *Aedes aegypti* index were 1.29, CI=[1.23, 1.36]; 1.49, CI=[1.37, 1.61] and 1.3, CI=[1.21, 1.39] respectively). Meanwhile, combination with 2-week lag rainfall, 2-month lag rainfall, 2-week lag temperature and relative humidity, resulted better prediction of DF incidence.

Conclusion: Meteorological conditions affect DF occurrence in a nonlinear way, and a single time-point rainfall variable is insufficient to fit it. Our study suggested that short-lag (last 2 weeks) conditions of moderate rainfall, moderate temperature and high humidity, in combination with a long-lag heavy rainfall were related to higher probability of DF incidence. BI and CI are useful predictors for DF occurrence in medium and high household density areas, but not in the low density areas.

Keywords: Case-crossover study; Conditional logistic regression; Household density; Vector surveillance; *Aedes aegypti*; Meteorology

Introduction

Dengue is the most rapidly expanding and spreading mosquito-borne viral disease in tropical and subtropical countries [1]. This disease is mainly transmitted by *Aedes aegypti* and *Aedes albopictus* [2]. The incidence of dengue has increased by 30-fold in the past 50 years [1]. Approximately 2.5 billion people in more than 100 countries are currently under the risk of dengue viral infection, with the majority living in the Asia-Pacific region [3]. Dengue virus has four serotypes (DENV-1-DENV-4), resulting in a wide spectrum of clinical manifestations, including dengue fever (DF), dengue hemorrhagic fever, and dengue shock syndrome. No vaccine or anti-viral drug is currently available for dengue patients.

Transmission of DENV is maintained by horizontal transfer in an *A. aegypti*-human cycle, although vertical transmission has also been reported [4]. Mosquito infection begins when females imbibe viremic blood from a human host and survive an extrinsic incubation period of 7-14 days [5,6]. A few commonly used *Stegomyia* indices are as follows: the premise or house index (HI: percentage of houses infested with larvae and/or pupae), container index (CI: percentage of water-holding containers infested with larvae and/or pupae), and Breteau index (BI: number of positive containers per 100 houses) or oviposition trap (ovitrap) data. All these indices are intended to detect the presence or absence of *A. aegypti* rather than the relative abundance of adult virus transmitting mosquitoes [7,8]. Adult *A. aegypti* index (AI) can be determined by collecting mosquitoes with backpack aspirators or sweep

nets [9]. Although adult population density has been linked to the epidemiologically important dengue incident rate, the implementation is labor intensive and usually expensive under limited budget [10,11].

Numerous efforts have been made to investigate the relationship between these mosquito indices and DENV transmission. However, several researchers repeatedly reported weak association and that DENV transmission frequently occurs even when *A. aegypti* population densities are low [8,12-16]. Different factors influence DENV transmission, including temporal and meteorological effects on mosquito life stages, larval mortality, heterogeneity in container productivity, variation in susceptibility of the human population to DENV infection, and spatial heterogeneities in vector density [8,11,15,17,18]. Failure to

***Corresponding author:** Ie-Bin Lian, Graduate Institute of Statistics and Information Science, National Changhua University of Education, Changhua, 50007, Taiwan, Tel: 886-4-7232105 ext 3201; Fax: 886-4-7211192; E-mail: maiblian@cc.ncue.edu.tw

Day-Yu Chao, Graduate Institute of Microbiology and Public Health, Nation Chung Hsing University, Taichung 40227, Taiwan, Tel: 886-4-22840694; Fax: 886-4-22852186; E-mail: dychao@nchu.edu.tw

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consider these factors may lower the prediction accuracy for DENV. Furthermore, administrative inconsistency among different spatial units may also cause geographical differences of the vector and dengue case data, which can mask potential relationship [19]. An ideal study design that considers the spatial and temporal aspects of these variables should provide better understanding on the relationship between *A. aegypti* population densities, DENV transmission, and disease incidence.

Kaohsiung City, a modern metropolis of 1.5 million people, has been affected by different serotypes of DENV and becomes the focus of DENV activity in Taiwan over the last decades [20-23]. During 2002-2011, Kaohsiung City had annual outbreaks of variable scales, resulting in more than 6,000 confirmed cases [24]. Since 2005, the Department of Health of Kaohsiung City Government has been initiating surveillance activities by using specially trained personnel. A previous study suggested that AI from 2005 to 2009 shows temporal correlation with the peak of the DF activity, with 1-2-month lag period [25]. However, the association between different vector indices and the occurrence of dengue cases has been not completely evaluated. In the present study, the case-crossover study design was applied to 8-year longitudinal data focusing on Kaohsiung City in Taiwan, where the most dengue incidences occurred. This study investigated the occurrence of dengue patients and its association with (1) different immature mosquito indices, (2) adult mosquito density, and (3) their interplay with meteorological factors and household density.

Aim

This study primarily depicted the association between the occurrence of DF and the vector surveillance factors including BI, AI, CI, and HI; the meteorological factors including rainfall, temperature, and relative humidity; and a few resident conditions including household density.

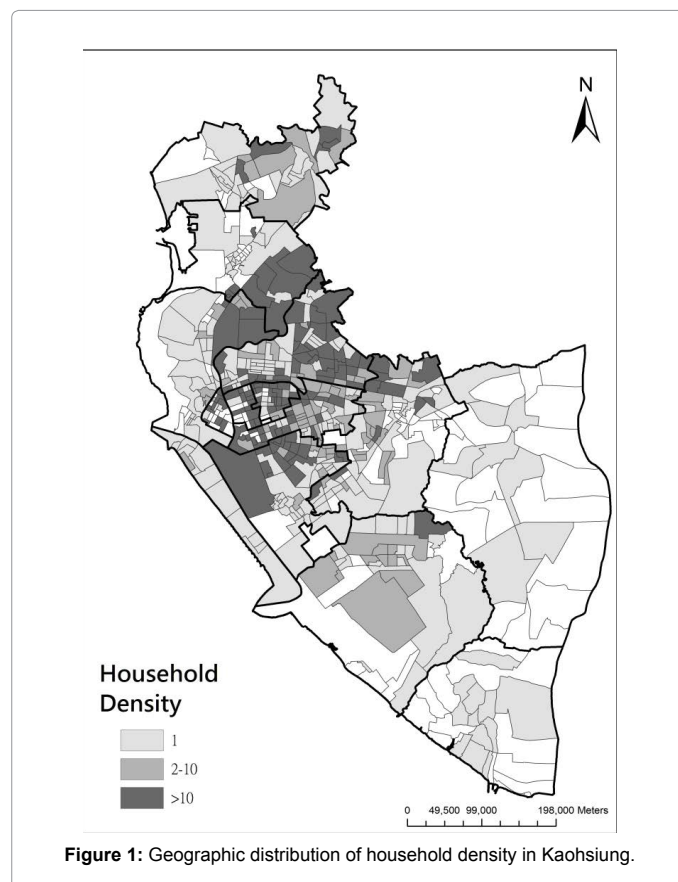
Materials and Methods

Study area

The government combined Kaohsiung City with Kaohsiung County into one unified administrative unit after December 25, 2010. Our study area includes the former Kaohsiung City and adjacent districts from the former Kaohsiung County, including Fongshan, Daliao, and Linyuan (Figure 1). The area is located from 120°10'32" to 121°01'15" east longitudes and 22°28' to 23°28' north latitudes. Kaohsiung City is a standard subtropical region, with annual average rainfall from 1796.7-2821.4 mm concentrated from May to September. In addition, the annual average temperature is from 24.9 °C-25.7 °C, with the lowest average of 11.6 °C in February and the highest average of 31.5 °C in June.

Data sources

We used the following four databases to collect data from 2005 to 2012: (1) dengue patient surveillance, (2) vector surveillance, (3) household registration, and (4) meteorological data. The first three databases were obtained from the Department of Health, Kaohsiung City Government, and the last database was archived from the databank of Environmental Protection Administration (EPA), Taiwan. The detailed description of each surveillance system can be referred to the EPA [26]. Noting that DF is classified as a legal communicable diseases in Taiwan, which means that all the cases have to be reported to the government. The county/city government is responsible for ascertaining each cases and reporting the record to Taiwan Center of Disease Control, as well as all the necessary measures for DF



prevention, including vector surveillance. Therefore the Department of Health of Kaohsiung has the most accurate DF surveillance data. Notably, considering the administrative change mentioned previously, the former Kaohsiung City has 8-year surveillance records, whereas the records of the districts from former Kaohsiung County started from late 2010. All the ascertained DF cases were collected via 3 types of surveillance: passive, active and semi-active. Most of the cases were mainly from passive and semi-active surveillance. In passive surveillance, dengue-like illness was reported by health care workers, and confirmed by local health authorities, while in semi-active surveillance, fever cases are investigated in residential areas, schools, and work places with epidemiological linkage, and specimens are taken once confirmed dengue cases are identified [27].

The records include the date of ascertainment, residency, age at the time of diagnosis, and gender. Notably, "Li" is the smallest administrative unit in Taiwan, and more than 900 Lis are present within the study area. In this study, the address of a patient is defined as Li. DF case is an acute febrile viral disease and fever (>38 °C), with at least two clinical symptoms, such as intense headache, nausea, fatigue, retro-orbital pain, myalgia, arthralgia, and skin rash [28].

Second, vector surveillance data including AI, BI, CI, and HI were summarized as the averaged measurement of 2-week period for each Li. However, we excluded the *Aedes albopictus* that activities at outdoor, because the Kaohsiung is an urban city [2]. The frequency of vector surveillance in Kaohsiung depends on the former DF incidence rate over the past years in each area. By the government definition, these Lis were considered to be of high incidence and surveyed once every week. The middle incidence and low incidence were surveyed in

monthly and tri-monthly basis, respectively.

To explore the effect of building style on DENV transmission, we divided all the Lis into three groups according to its household density levels. Notably, each doorplate of a building has its coordinates located by satellite and is shown in the geographical information system map. For each doorplate, we sum up the number of households with similar coordinates and classified them as “1 household,” “2-10 households,” and “>10 households.” For each Li, if the “1 household” building comprises more than 50% of all the buildings, then, the Li is regarded as low household density. For others, if a Li has higher proportion of “2-10 households” buildings than “>10 households,” then, the Li is regarded as medium household density; otherwise, the Li is classified as high household density.

Nine EPA monitor stations scattered in Kaohsiung collected the meteorological data. These data provide information, such as daily accumulative rainfall, daily mean relative humidity, and daily mean temperature. For each Li, its meteorological datum was calculated by using inverse distance weighting interpolation. All meteorological data were trisected into three levels (low, medium, and high), roughly according to the 33rd and 66th percentiles. As a result, the corresponding low, medium, and high accumulated rainfall of 8-14 days before diagnosis (i.e., 1-2 week lag) were 0-2.5 mm, 2.5-30.6 mm, and >30.6 mm, respectively. Moreover, the accumulative rainfall of 29-56 days before diagnosis (5-8 week lag) were 0-56.2 mm, 56.2-197 mm, and >197 mm. The 1-2 week lag average temperatures of the tripartitions were 16 °C-27.4 °C (low), 27.4 °C-29 °C (medium), and >29 °C (high). The 1-2 week lag average relative humidity percentages of the tripartitions were 52%-72.9%, 72.9%-77% and >77%.

Statistics analysis

A time-stratified case-crossover design [29-30] was used in this study. This method is used to investigate the effect of short-term exposure to risks that continuously change, occur, and measure. By using the self-controlled crossover design, cases act as their own control in periods when they are unexposed. Therefore, this method accounts for unmeasured confounding variables when these cases are constant over time within individuals. By using the same case in different (but insignificant) periods of time as its controls, the long-term effects, such as gender, social economic status, body mass index, habits, and household type, can be completely controlled.

Each patient presenting with DF for a specific condition was considered as a case on the date of diagnosis and as three possible controls on selected days, roughly 3, 6, and 9 weeks before the date of DF diagnosis. We defined “Week 1” as the first 7 days before the diagnosis, “Week 2” as the 8th-14th days before the diagnosis, and so on. For a case, the correspondent values of vector-borne (AI, BI, CI, and HI) were based on the surveillance measurement within the 2-week period before the diagnosis (i.e., Week 1 and 2). Similarly, the period of measurements for the first control was set to be 3 weeks ahead of the case and that of the second control was set to be 6 weeks ahead of the case, and vice versa.

As for the meteorological factors, we considered the following variables:

- **2-week lag rainfall:** for the case, this factor is defined as the average daily rainfall at the Li of the patient within the 2-week period prior to DF diagnosis (Week 1 to Week 2); and for the controls, this factor is the analogous average, but 3, 6, and 9 weeks earlier.

- **2-month lag rainfall:** the average daily rainfall from Week 5 to Week 8 (2 months prior to DF diagnosis).

- **2-week lag temperature:** the average daily temperature from Week 1 to Week 2.

- **2-week lag relative humidity:** the average daily relative humidity from Week 1 to Week 2.

Considering that a DF case and its matched controls are from the same patient, their long-term factors, such as living environment, habits, and chronic health conditions, are sufficiently controlled. The effects of vector-borne and meteorological factors were compared between case and control days by the following model:

$$\log \text{it} (Y) = \beta_0 + \beta_1 \cdot VI + \beta_2 \cdot RF_{11} + \beta_3 \cdot RF_{12} + \beta_4 \cdot RF_{21} + \beta_5 \cdot RF_{22} + \beta_6 \cdot Temp_1 + \beta_7 \cdot Temp_2 + \beta_8 \cdot RH_1 + \beta_9 \cdot RH_2$$

where Y = 1 for case, and = 0 for control, and VI is one of the vector-borne indices (AI, BI, CI, or HI). RF_{11} , $Temp_1$, and RH_1 are indicator variables, with a value 1 if the 2-week lag rainfall, temperature, and relative humidity are between the (overall) 33rd and 66th percentiles; otherwise, 0. Similarly, RF_{12} , $Temp_2$, and RH_2 have a value of 1 if the 2-week lag rainfall, temperature, and relative humidity are above the 66th percentiles. Furthermore, RF_{21} is an indicator variable, with value 1 if the 2-month lag rainfall is between the (overall) 33rd and 66th; otherwise, 0. Similarly, RF_{22} has a value of 1 if the 2-month lag rainfall is above the 66th percentiles.

Each stratum should ideally contain one case and three controls. However, the city government may not measure the indices every week in every Li. If any case does not have the vector measure in the correspondent Li in neither Week 1 nor Week 2, or if none of the controls have the measure during the correspondent period, then the stratum is deleted. By contrast, if more than one measurement is conducted within a week, then the average is selected. May to December is the DF prevalent season, with DF cases of 98.7% among all cases of a year, and surveillance data are more complete in this period. Thus, we only considered the cases that occurred between May and December. After the exclusion, 2453 out of the 4570 DF cases (strata) (54%) were used in the following analysis. We then estimated the association between vector-borne and the risk of DF using conditional logistic regression models, which was adjusted for the meteorological factors.

Each model contains only one index and adjusted by the meteorological factors to avoid the high co-linearity among the mosquito indices, namely, AI, BI, CI, and HI. All analyses were performed using the statistics software SAS 9.3. The study was approved by the Institutional Review Board IRB-R-05-002 of Taichung Hospital, Ministry of Health and Welfare.

Results

A total of 4570 indigenous dengue cases occurred during the period from 2005 to 2012 in Kaohsiung City, Southern Taiwan. Nearly 96% of the cases occurred from August 1 to December 31. Given the design of our study, only the cases with chronically and spatially matched vector indices data were recruited. As a result, only 2453 cases or 54% among all cases were analyzed, with mean ages of 46.6, 45.8, and 44.5 in low, medium, and high household density areas, respectively. The gender distribution of DF patients was composed of 46.9%, 51.2%, and 47.3% of males in low, medium, and high household density areas, respectively. Chi-square test was carried out, and no statistically significant differences were observed among all 4570 cases and the recruited 2453

dengue cases in terms of residential area (number of Li), gender, and age (Table 1). However, slightly more proportion (49.4%) of the studied cases was living in the low household density area, compared with that of all the cases (45.3%). Figure 2 shows the quartile distribution of four different mosquito indices. From this figure, difference was not observed among low, medium, and high household density areas.

Univariate analysis showed that BI, AI, CI, and HI were significant (p -values < 0.05), with odds ratios of 1.02, 1.33, 1.04, and 1.01, respectively. Further stratified by the household density, BI was significant only in medium and high household density areas, with odds ratios of 1.03 and 1.05, respectively. Notably, both had a p -value < 0.001. Similarly, HI was also significant (p -value < 0.05) only in medium and high household density areas, with odds ratios of 1.03 and 1.04, respectively. AI was significant among all low, medium, and high household density areas, with odds ratios of 1.29, 1.45, and 1.3, respectively. CI was also significant among all low, medium, and high household density areas, with odds ratios of 1.02, 1.03 and 1.08. All AI and CI among all areas had a p -value < 0.001 (Table 2).

Tables 3-5 show the estimates of odds ratio for each index (AI, BI, CI, or HI), with each model adjusted by functions of rainfall, humidity, and temperature. Based on the results, AI, BI, CI, and HI were significant, with odds ratios of 1.02, 1.31, 1.04, and 1.02, respectively. In addition, all indices had a p -value < 0.001. Further stratified by the household density, AI was significant among all low, medium, and high household density areas, with odds ratios of 1.29, 1.49, and 1.3, respectively. All had a p -value < 0.0001. BI was significant in medium and high household density areas, with odds ratios of 1.04 and 1.06, respectively. Notably, both had a p -value < 0.0001. CI was also significant in medium and high household density areas, with odds ratios of 1.03 and 1.1 respectively. Both had a p -value < 0.0001. HI was also significant in medium and high household density areas, with odds ratios of 1.07 and 1.04, respectively. Both exhibited a p -value < 0.001.

The effect of rainfall on the occurrence of dengue cases was classified into two. To consider the incubation period (3-8 days) after infection and the life cycle of mosquito, we regarded both the average rainfall of Week 2 before the diagnosis and that of Week 5 to Week 8 (5-8 week lag) before the diagnosis. A combination of a higher rainfall 5-8 weeks earlier and a lower rainfall 2 weeks earlier was related to higher probability of DF incidence. Meanwhile, higher relative humidity but lower temperature 2 weeks earlier was also related to higher DF incidence. Among all cases, p -value < 0.001 and the odds ratio between

DF and the three levels of rainfall, temperature, and humidity either increased or decreased in a monotonic order (Tables 3-5).

Discussion

The difficulties in predicting dengue is complicated by the interplay among the vector, climate, social, economic, household environment, infected serotypes, and the individual susceptibility and immunity conditions. Therefore, an inconsistent results on the association between immature mosquito indices and DENV transmission has been repeatedly reported. Some study had found that higher BI, HI and CI are positively correlated with DF occurrence [31]; while others [32-35] found no significant or even negative [36,37] association. Given that mosquito density is temporally dynamic and spatially non-stationary [36], the following reasons may cause the inconsistency. (1) Lack of control of numerous environmental and demographic factors. (2) The household density may have interaction effect with BI on DF incidence. In our study, the case-crossover design was spatially and demographically matched, so all the factors not changed in short period were well-controlled. To resolve reason (2), we conducted separate analyses for different household density areas. The results showed that BI and CI had significant positive association with DF in medium and high household density (2 or more households per doorplate) areas, but not in the low household density areas. All other studies used pooled analysis which may dilute the effect and produced non-significant association.

The inference on the association between temperature and DF incidence is also inconsistent. A few studies [37,38] also concluded that the temperature in a 3-month lag has negative association with the DF occurrence; and a study in Taiwan [39] also reported negative result. In contrast, Yu et al. [38] showed that minimum temperature in a 8-12-week lag is positively associated with DF cases. Shang et al. [27] demonstrated positive association in different lag periods. The inference on the association with rainfall is also inconsistent. Yu et al. [38] and Wu et al. [39] indicated that a 3-month lag rainfall is positively significant, whereas Chen et al. [37] described that the 3-month lag rainfall is negatively significant. Most of the results above reported negatively association between relative humidity and DF.

Our study integrated both meteorological and mosquito index data and suggested that both the short-lag (last 2 weeks, or 2-week lag) and long-lag (week 5-8 before, or 2-month lag) meteorological factors independently affect dengue case occurrence. Short-lag meteorological conditions of moderate rainfall, moderate temperature, and high humidity, in combination with a long-lag higher rainfall were related to higher probability of DF incidence. A possible explanation of the phenomenon is that the long-term heavier rainfall is responsible for creating a better environment for larvae to breed, and the short-lag moderate rainfall and temperature suitable for human's outdoor activities as well as for mosquito to feed. In contrast, short-lag heavy rainfall may be detrimental for mosquito.

Limitations

Due to Privacy Protection Regulation, the exact address cannot be accessed and the finest geographical information we can obtain is "Li," which usually contains tens to hundreds of households. In addition, not all the Li's had frequent vector surveillance inspection. Some DF cases were forced to be excluded due to the incomplete vector surveillance in the residential Li within a month before the incidence. A potential selection bias was considered and missing at random was examined. No specific cluster or pattern was found with regard to the resident areas among the excluded cases.

Dengue subjects (Number)	Subjects recruited (2453)			All subjects (4570)		
	Low	medium	high	low	medium	high
Household Density ^a						
number of DF (%)	1212	565	676	2072	1082	1416
number of Li (%)	165	79	96	311	109	161
age (std ^b)	46.6 (19.5)	45.8 (19.7)	44.5 (19)	45.8 (19.2)	44.6 (19.6)	44.2 (18.3)
gender (% of male)	569:643 (1:1.13)	289:276 (1:0.955)	320:356 (1:1.11)	988:1084 (1:1.1)	542:540 (1:1)	650:766 (1:1.18)
population density (pop/km ²)	7998.36	12420.86	17408.46	5619.68	10484.72	17457.8

^alow household density: 1 household; medium household density: 2-10 households; high household density: >10 households.

^bstd: standard deviation

Table 1: Demographics of the studied cases by household density.

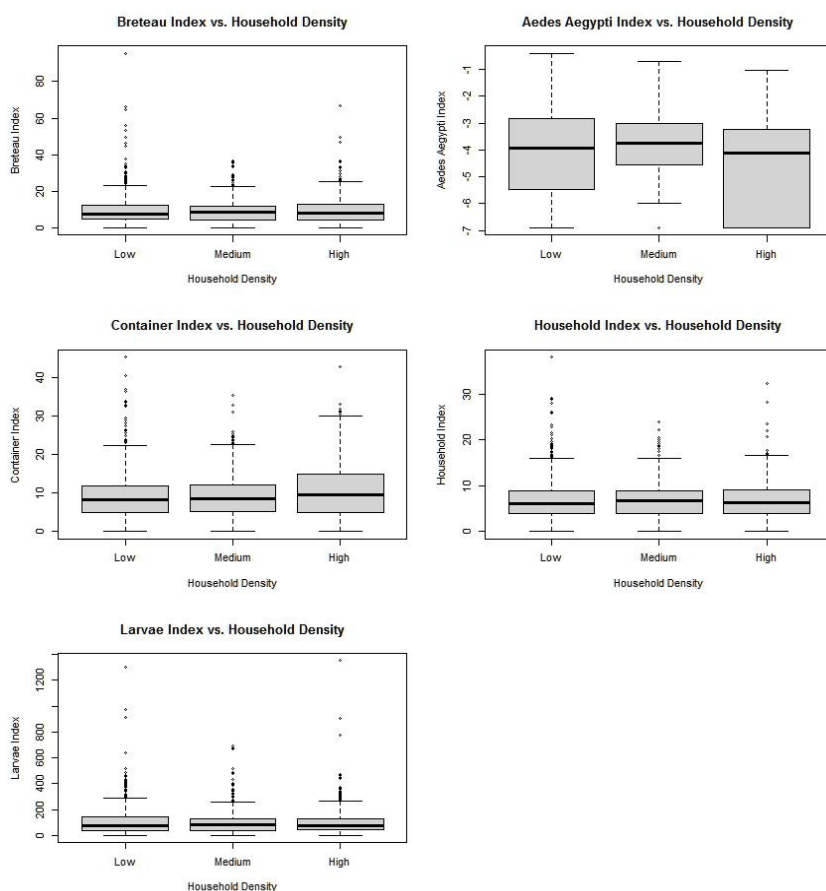


Figure 2: Box plots of various vector surveillance at low, medium, and high household density regions. *Aedes aegypti* index was log-transformed after adding 0.001 for avoiding infinity.

	Low household density		Medium household density		High household density	
	Odds ratio	(95% CI)	Odds ratio	(95% CI)	Odds ratio	(95% CI)
BI	1.002	(0.994, 1.01)	1.03 ^b	(1.01, 1.04)	1.05 ^a	(1.03, 1.06)
AI	1.29 ^a	(1.24, 1.35)	1.45 ^a	(1.36, 1.55)	1.32 ^a	(1.24, 1.39)
CI	1.02 ^b	(1.01, 1.03)	1.03 ^b	(1.01, 1.04)	1.08 ^a	(1.06, 1.1)
HI	0.992	(0.977, 1.01)	1.03 ^c	(1.01, 1.06)	1.04 ^b	(1.02, 1.06)

^a p-value < 0.0001

^b p-value < 0.001

^c p-value < 0.05

Table 2: Result of univariate conditional logistic regression on vector by household density.

		Low household density ^a		Medium household density ^a		High household density ^a	
		Odds ratio	(95% CI)	Odds ratio	(95% CI)	Odds ratio	(95% CI)
2-week lag rainfall ^c	BI ^b	0.998	(0.988, 1.01)	1.04 ^h	(1.02, 1.06)	1.06 ^g	(1.04, 1.08)
	low	1		1		1	
	medium	0.247 ^g	(0.198, 0.307)	0.584 ^h	(0.441, 0.773)	0.225 ^g	(0.165, 0.308)
	high	0.066 ^g	(0.048, 0.091)	0.078 ^g	(0.052, 0.119)	0.04 ^g	(0.025, 0.064)

2-month lag rainfall ^d	low	1		1		1	
	medium	3.39 ^a	(2.75, 4.15)	5.75 ^a	(4.04, 8.17)	3.68 ^a	(2.7, 5.02)
	high	7.42 ^a	(5.69, 9.69)	10.4 ^a	(6.96, 15.4)	5.04 ^a	(3.45, 7.36)
2-week lag temp ^e	low	1		1		1	
	medium	0.313 ^a	(0.253, 0.388)	0.451 ^a	(0.334, 0.61)	0.181 ^a	(0.131, 0.249)
	high	0.19 ^a	(0.149, 0.242)	0.117 ^a	(0.079, 0.175)	0.047 ^a	(0.032, 0.07)
2-week lag rh ^f	low	1		1		1	
	medium	2.75 ^a	(2.2, 3.44)	1.78 ^b	(1.31, 2.43)	2.72 ^a	(2, 3.69)
	high	6.82 ^a	(4.89, 9.5)	4.61 ^a	(3, 7.07)	5.09 ^a	(3.32, 7.8)

a low household density: 1 household; medium household density: 2-10 households; high household density: >10 households.

b BI: Breteau index

c 1-2-week lag rainfall: 8-14 day lag of accumulative rainfall. Low rainfall: 0-3.5 mm, medium rainfall: 3.5-32 mm, and high rainfall: >32.

d 5-8-week lag rainfall: 29-56 day lag of accumulative rainfall. Low rainfall: 0-65 mm, medium rainfall: 65-240 mm, and high rainfall: >240 mm.

e 1-2-week lag temp: 8-14 day lag of mean temperature (temp). Low temp: 18 °C-27.6 °C, medium temp: 27.6 °C-29.1 °C, and high temp: >29.1 °C.

f 1-2-week lag rh: 8-14 day lag of mean relative humidity (rh). Low rh: 60%-73.2%, medium rh: 73.2%-77.2%, and high rh: >77.2%.

g p-value < 0.0001.

h p-value < 0.001

Table 3 : Results of multivariate conditional logistic regression on BI and meteorological factors by household density

		Low household density ^a		Medium household density ^a		High household density ^a	
		Odds ratio	(95% CI)	Odds ratio	(95% CI)	Odds ratio	(95% CI)
AI ^b		1.29 ^a	(1.23, 1.36)	1.49 ^a	(1.37, 1.61)	1.3 ^a	(1.21, 1.39)
2-week lag rainfall ^c	low	1		1		1	
	medium	0.224 ^a	(0.178, 0.281)	0.636 ^b	(0.474, 0.854)	0.236 ^a	(0.173, 0.323)
	high	0.06 ^a	(0.043, 0.084)	0.092 ^a	(0.06, 0.141)	0.046 ^a	(0.029, 0.073)
2-month lag rainfall ^d	low	1		1		1	
	medium	3.1 ^a	(2.5, 3.85)	5.84 ^a	(4.03, 8.47)	3.89 ^a	(2.85, 5.3)
	high	6.99 ^a	(5.31, 9.2)	10.6 ^a	(7.01, 16)	4.9 ^a	(3.36, 7.15)
2-week lag temp ^e	low	1		1		1	
	medium	0.304 ^a	(0.244, 0.379)	0.474 ^a	(0.345, 0.65)	0.187 ^a	(0.136, 0.258)
	high	0.179 ^a	(0.139, 0.23)	0.12 ^a	(0.08, 0.18)	0.052 ^a	(0.035, 0.076)
2-week lag rh ^f	low	1		1		1	
	medium	2.54 ^a	(2.02, 3.18)	1.83 ^b	(1.32, 2.54)	3.11 ^a	(2.28, 4.25)
	high	5.88 ^a	(4.2, 8.25)	5.21 ^a	(3.36, 8.06)	5.56 ^a	(3.61, 8.57)

^a low household density: 1 household; medium household density: 2-10 households; high household density: >10 households.

^b AI: log *Aedes aegypti* index and plus positive small value.

^c 1-2-week lag rainfall: 8-14 day lag of accumulative rainfall. Low rainfall: 0-3.5 mm, medium rainfall: 3.5-32 mm, and high rainfall: >32.

^d 5-8-week lag rainfall: 29-56 day lag of accumulative rainfall. Low rainfall: 0-65 mm, medium rainfall: 65-240 mm, and high rainfall: >240 mm.

^e 1-2-week lag temp: 8-14 day lag of mean temperature (temp). Low temp: 18 °C-27.6 °C, medium temp: 27.6 °C-29.1 °C, and high temp: >29.1 °C.

^f 1-2-week lag rh: 8-14 day lag of mean relative humidity (rh). Low rh: 60%-73.2%, medium rh: 73.2%-77.2%, and high rh: >77.2%.

^g p-value < 0.0001.

^h p-value < 0.001

Table 4 : Results of multivariate conditional logistic regression on BI and meteorological factors by household density

		Low household density ^a		Medium household density ^a		High household density ^a	
		Odds ratio	(95% CI)	Odds ratio	(95% CI)	Odds ratio	(95% CI)
CI ^b		1.01	(0.995, 1.02)	1.03 ^b	(1.01, 1.06)	1.1 ^a	(1.08, 1.12)
2-week lag rainfall ^c	low	1		1		1	
	medium	0.246 ^a	(0.198, 0.307)	0.59 ^b	(0.446, 0.78)	0.202 ^a	(0.147, 0.279)
	high	0.065 ^a	(0.048, 0.09)	0.079 ^a	(0.052, 0.12)	0.041 ^a	(0.025, 0.067)
2-month lag rainfall ^d	low	1		1		1	
	medium	3.35 ^a	(2.71, 4.13)	5.68 ^a	(3.99, 8.08)	3.15 ^a	(2.3, 4.31)
	high	7.23 ^a	(5.53, 9.44)	10.3 ^a	(6.93, 15.4)	4.5 ^a	(3.06, 6.62)

2-week lag temp ^e	low	1		1		1	
	medium	0.316 ^a	(0.255, 0.391)	0.454 ^a	(0.335, 0.613)	0.171 ^a	(0.123, 0.237)
	high	0.19 ^a	(0.15, 0.242)	0.123 ^a	(0.083, 0.182)	0.048 ^a	(0.032, 0.072)
2-week lag rh ^f	low	1		1		1	
	medium	2.69 ^a	(2.16, 3.37)	1.8 ^a	(1.3, 2.46)	2.72 ^a	(2, 3.7)
	high	6.67 ^a	(4.79, 9.28)	4.91 ^a	(3.21, 7.51)	5.14 ^a	(3.33, 7.94)

^a low household density: 1 household; medium household density: 2-10 households; high household density: >10 households.

^b CI: Container index.

^c 1-2-week lag rainfall: 8-14 day lag of accumulative rainfall. Low rainfall: 0-3.5 mm, medium rainfall: 3.5-32 mm, and high rainfall: >32.

^d 5-8-week lag rainfall: 29-56 day lag of accumulative rainfall. Low rainfall: 0-65 mm, medium rainfall: 65-240 mm, and high rainfall: >240 mm.

^e 1-2-week lag temp: 8-14 day lag of mean temperature (temp). Low temp: 18 °C-27.6 °C, medium temp: 27.6 °C-29.1 °C, and high temp: >29.1 °C.

^f 1-2-week lag rh: 8-14 day lag of mean relative humidity (rh). Low rh: 60%-73.2%, medium rh: 73.2%-77.2%, and high rh: >77.2%.

^g p-value < 0.0001.

^h p-value < 0.001

Table 5: Results of multivariate conditional logistic regression on CI and meteorological factors by household density.

Conclusion

Meteorological conditions affect DF occurrence through the changes of mosquito density and biting behavior with a nonlinear relationship, and a single time-point rainfall variable in linear model may insufficiently fit. Our study suggested that short-lag conditions of moderate rainfall, moderate temperature and high humidity, in combination with a long-lag heavy rainfall were related to higher probability of DF incidence. BI and CI are useful predictors for DF occurrence in medium and high household density areas, but not in the low density (one households per doorplate) areas.

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