Heliyon 10 (2024) e27931

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Assessing the impact of emergency measures in varied population density areas during a large dengue outbreak

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ABSTRACT

Background: The patterns of dengue are affected by many factors, including population density and climate factors. Densely populated areas could play a role in dengue transmission due to increased human-mosquito contacts, the presence of more diverse and suitable vector habitats and breeding sites, and changes in land use. In addition to population densities, climatic factors such as temperature, relative humidity, and precipitation have been demonstrated to predict dengue patterns. To control dengue, emergency measures should focus on vector management. Most approaches to assessing emergency responses to dengue risks involve applying simulation models or describing emergency activities and the results of implementing those responses. Research using real-world data with analytical methods to evaluate emergency responses to dengue has been limited. This study investigated emergency control measures associated with dengue risks in areas with high and low population densities, considering their different control capacities.

Methodology: Data from the 2015 dengue outbreak in Kaohsiung City, Taiwan, were utilized. The government database provided information on confirmed dengue cases, emergency control measures, and climatic data. The study employed a distributed lag non-linear model (DLNM) to assess the effect of emergency control measures and their time lags on dengue risk.

Principal findings: The findings revealed that in areas with high population density, the absence of emergency measures significantly elevated the risks of dengue. However, implementing emergency measures, especially a higher number, was associated with lower risks. In contrast, in areas with low population density, the risks of dengue were only significantly elevated at the 1st week lag if no emergency control measures were implemented. When emergency activities were carried out, the risks of dengue significantly decreased only for the 1st week lag.

Conclusions: Our findings reveal distinct exposure-lag-response patterns in the associations between emergency control measures and dengue in areas with high and low population density. In regions with a high population density, implementing emergency activities during a significant dengue outbreak is crucial for reducing the risk. Conversely, in areas of low population density, the necessity of applying emergency activities may be less pronounced. The implications of this study on dengue management could provide valuable insights for health authorities dealing with limited resources.

1. Introduction

Epidemiological theory underscores that a pivotal determinant for a pathogen's ability to establish and endure within a population is the density of the host population [1,2]. In simpler terms, diverse population densities may manifest distinct disease patterns. Regarding vector-borne diseases (VBD), for instance, a study by Amelinda et al. demonstrated a significant correlation between population density and the incidence rate of dengue hemorrhagic fever in Indonesia [3], while another study in China identified factors such as population density and gross domestic product per capita as substantial predictors of the dengue incidence rate during the most recent and extensive dengue outbreak [4]. The reasons that densely populated areas play a role in VBD transmission include having

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https://doi.org/10.1016/j.heliyon.2024.e27931
Received 25 July 2023; Received in revised form 15 February 2024; Accepted 8 March 2024

more diverse and suitable vector habitats and breeding sites [5,6], increased human-mosquito contacts [7,8], as well as urbanization and land use changes [9,10].

In addition to population densities, climatic factors have been demonstrated to predict VBD patterns. Regarding dengue in Taiwan, minimum temperatures, relative humidity (RH), and accumulated precipitation are especially mentioned [11–16]. For example, during 2001–2008, the variable of minimum temperature was identified by Chen et al. as one of the predictors of dengue incidence rates in Kaohsiung City (KH) [17]. Another study by Chien et al. showed that dengue risk increased when minimum temperature increased in southern Taiwan, 1998–2011 [12]. In terms of RH, the study by Chang et al. found that RH and number of dengue cases positively correlated in KH, 2007–2011 [14]. RH also presented a negative correlation with indigenous case occurrences in southern Taiwan during 1998–2007 [15]. For accumulated precipitation, Chang et al. revealed that the number of confirmed cases exhibited notably positive correlations with rainfall in KH [14].

To control dengue, emergency responses focusing on vector management, such as space sprays, are facilitated during outbreaks [18]. One of the approaches to evaluate emergency responses to dengue is the application of simulation models [19–23]. For example, Wu et al. applied the Susceptible–Exposed–Infectious/Inapparent–Recovered (SEIAR) model to simulate the effectiveness of dengue interventions [23]. They concluded that the present control activities in China were practical. Applying simulation skills could explore

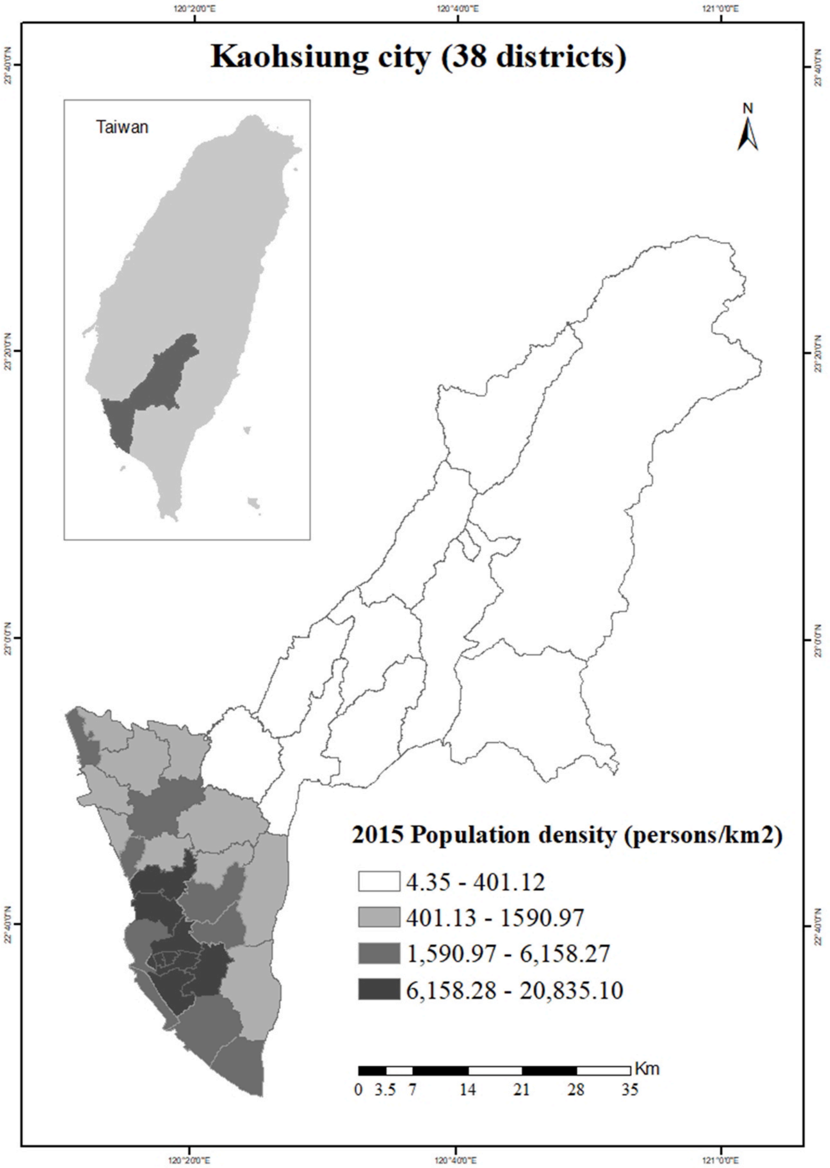

Fig. 1. Kaohsiung City, Taiwan, indicating the 38 districts of the city and population density in 2015. Inset shows location of Kaohsiung City in Taiwan.

many potential scenarios and identify critical game-changing variables in emergency responses. However, simulation models require assumptions to be made before analysis, and these assumptions may not be realistic. Taking Wu et al. as an example, the study assumed that the transmission rate from an infected mosquito to a susceptible person is homogeneous in the SEIAR model [23]. However, in reality, virus transmission rates to susceptible human populations could differ based on factors such as herd immunity [24,25], age [26,27], and gender [25,26,28].

Another common approach to evaluating emergency responses to dengue is to describe empirical data regarding emergency activities and the results of implementing those responses [29–33]. For instance, Teng et al. provided a detailed description of the emergency applications, including the timeline of three insecticide space sprays and two source reductions over two months in Pingtung, Taiwan, in 2002 [33]. The results of the emergency activities showed a decrease in dengue cases from 27 to one. Evaluations using the descriptive approach can demonstrate how epidemics were controlled in detail. However, without analytical methods to quantify the relationships between emergency responses and dengue, details such as lag effects cannot be detected. The term "lag effects" implies that there is a temporal delay between the implementation of control measures and the measurable reduction in dengue risk. To the best of our knowledge, research using empirical data with analytical methods to evaluate emergency responses to dengue has been limited.

Kaohsiung City has been grappling with seasonal dengue outbreaks every year since the late 1900s [34]. In response to each confirmed case, emergency dengue measures are enacted once in residential areas and, if applicable, an additional time in workplaces. This implies that the frequency of emergency dengue responses may be once or, if applicable, twice, contingent on the specific circumstances and locations associated with each confirmed case. The quantity of responses is also significantly influenced by logistical factors such as the availability of human resources and spray equipment at the time. These actions are initiated and concluded within 1–2 days, covering areas within a 50-m radius of the locations linked to all confirmed cases [34].

In this study, control capacity is defined as the ratio of the number of emergency control measures to the number of cases in a

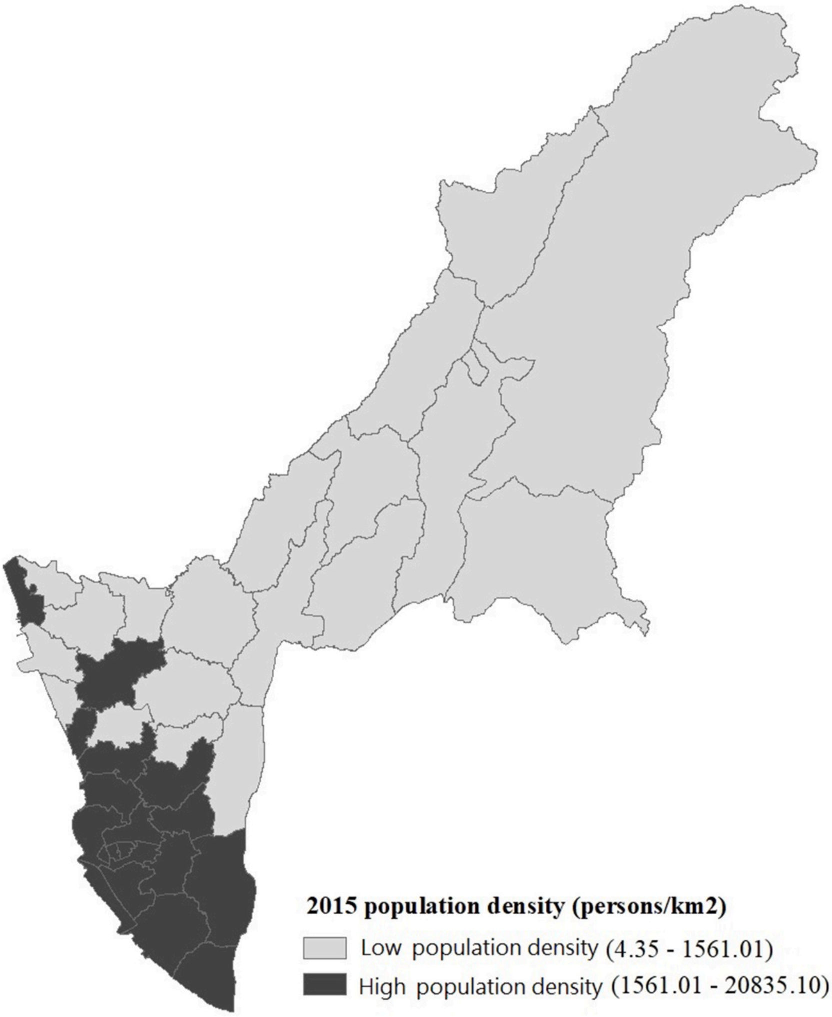

Fig. 2. The spatial distribution of districts with high and low population density in Kaohsiung City, Taiwan, 2015.

district during 2015. For example, if there were 12 instances of emergency control measures and 10 confirmed cases in District A during 2015, the control capacity would be 1.2. Consequently, if the control capacity is less than 1, those districts are categorized as insufficiently treated districts. Districts with control capacities ranging from 1 to 2 are labeled as sufficiently treated districts. If the control capacity exceeds 2 in districts, they are classified as over-treated districts.

This study aimed to evaluate the associations between various control capacities of emergency measures and dengue incidences during a significant outbreak. We employed a distributed lag non-linear model (DLNM) analyses in KH, Taiwan, in 2015. The study had two specific objectives. The first objective was to assess the relationships between dengue incidences and emergency control efforts, along with their respective time lags, in areas characterized by both high and low population densities. The second objective was to gauge the impact of different control capacities on dengue incidences in both high and low population density areas. All assessments were conducted while accounting for climate factors. The year 2015 was chosen as the focal point since it witnessed the most substantial outbreak in Taiwan over the last two decades.

2. Methods

2.1. Study area

KH is located in southern Taiwan and experiences a tropical monsoon climate. In 2015, the average temperature was highest at 30.6 °C in June, and the lowest was 19.9 °C in January [35]. Precipitation was observed to accumulate significantly, with 89.2% occurring between May and September [35]. The city has a population of 2.8 million spread across an area of 2950 km^2 [36], with population densities varying among its 38 districts, ranging from 4.4 to 20,835.1 persons/km^2 in 2015 (Fig. 1).

In this study, there were 19 districts characterized by high population density and an additional 19 districts characterized by low population density (Fig. 2). In KH, both *Aedes albopictus* (*Ae. albopictus*) and *Ae. aegypti* are responsible for dengue virus transmission, and they co-exist in all districts.

2.2. Dengue case

As dengue is classified as a Category 2 communicable disease in Taiwan, physicians are required to report detected cases of dengue or suspected cases within 24 h to the Centers for Disease Control, Taiwan (TW CDC) [34]. We use dengue confirmed cases as a proxy measure for dengue risk. According to TW CDC, cases were laboratory confirmed if blood samples met one of the following criteria, 1) dengue RNA was detected; 2) dengue virus was isolated; 3) IgM seroconversion occurred between paired sera; 4) IgG seroconversion or a fourfold IgG titer increase occurred between paired sera; or 5) NS1 was detected (Bio-Rad, France) [34]. The dengue surveillance system in Taiwan has been detailed described in the paper by Lin et al. [37].

All confirmed cases were obtained from Government Open Data (TW GOV), managed by TW CDC [38]. For each case, data were included the date of onset, city of residence, and district of residence. The number of cases was the dependent variable in this study.

2.3. Routine control measures

Routine dengue control measures in 2015 involved information, education, and communication (IEC) and the activities were maintained throughout the year. The IEC activities were delivered by TW CDC. Health education activities were based on television advertisements, radio announcements, posters, internet or other social media platforms, and aim to increase the knowledge of self-protection, symptoms recognition and management of water holding containers on private properties. Regarding vector control, it was carried out by local authorities, mainly the health and environmental protection departments, and comprise of routine source reduction, larvicide treatment and vector surveillance [34]. Source reduction activities include the removal of water holding containers on government property. Containers that cannot be removed are treated with larvacides mainly *Bacillus thuringiensis israelensis*, methoprene, temephos, and pyriproxyfen [34]. There are 454 Lis, which are the smallest administrative units in TW, in KH. Each Li is monitored for immature vectors every 1–2 months [39]. Routine dengue control measures are conducted throughout the year, irrespective of whether emergency control measures are implemented.

2.4. Emergency control measures

Emergency control measures were implemented within 1–2 days of confirming each dengue case in the city [34]. The control activities included adulticide spraying indoors and outdoors, in conjunction with source reduction on private properties [40]. These activities were organized by the Department of Health, Kaohsiung City Government (DoHKH).

For buildings with five floors or less, emergency control activities were implemented for all households on each floor. For buildings with six floors or more, control activities were applied to two floors below the floor where the cases lived and the floor where the cases lived. Additionally, the spaces surrounding the buildings, such as alleys, were also treated. An emergency management team consisted of a supervisor, an entomologist, and a highly trained spray operator. Implementing emergency management activities involved multiple teams.

Data on emergency control measures were obtained from TW GOV and managed by DoHKH. The data included the date of the measures and the district where the measures were implemented. The adulticides used included deltamethrin and cypermethrin.

2.5. Climate data

Meteorological data for each district were recorded from the meteorological observation station in each district, and those data were obtained from the Central Weather Bureau [35]. However, there were no meteorological stations in Yancheng, Qianjin, Niaosong and Namasia districts. Therefore, we utilized the nearest meteorological stations to represent them. We used Gushan (station id: C0V690), Qianzhen (station id: C0V890), Fengshan (station id: C0V440), and Fuxing (station id: C0V210) for the Yancheng district, Qianjin district, Niaosong district, and Namasia district, respectively. The location of the meteorological observation stations is shown in Fig. 3.

2.6. Statistical analyses

DLNM is a statistical approach that evaluates the non-linear exposure–response associations and non-linear time lags simultaneously [41]. This method presents the exposure and the lag at once in a two-dimensional space by a ‘cross-basis’ function [41]. The “cross-basis” refers to combining two sets of basis functions, one for exposure levels and another for lags. DLNM results show the risk of a specific exposure level at specific time lag as compared to the risk at the referenced exposure level.

To understand the effect of emergency control measures on dengue cases in 2015, we applied DLNM to assess the relationships. As

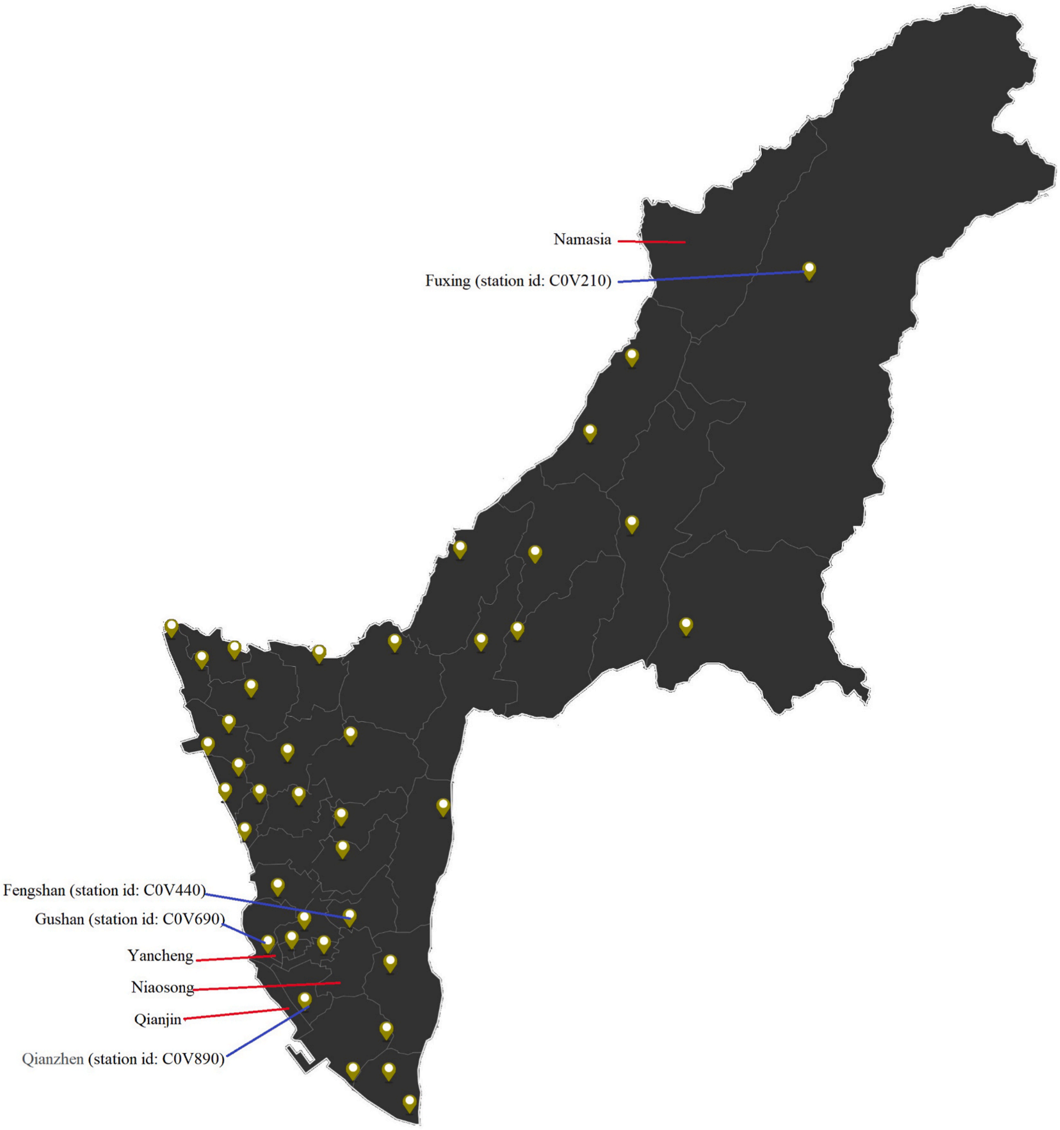

Fig. 3. The location of meteorological observation stations in each district, including districts without weather stations and the weather stations used to represent those districts in Kaohsiung City, Taiwan [35].

climate factors have been demonstrated to be predictors of dengue cases in Taiwan, meteorological parameters were adjusted in the regressions as well [11–16]. Also, temporal autocorrelation assessed by the partial autocorrelation function (pacf) was in the model. Here, the number of emergency control measures, minimum temperatures, average relative humidity, and accumulated precipitation were calculated on a weekly basis. The climate data were measured hourly. The minimum temperature on a weekly basis represents the lowest temperature recorded within each 7x24-h period. The average relative humidity on a weekly basis corresponds to the mean value within each 7x24-h period. Accumulated precipitation on a weekly basis is calculated as the sum of precipitation over each 7x24-h period. All predictors used the cross-basis functions. The number of emergency control measures, minimum temperatures, average relative humidity, and accumulated precipitation had lag effects on dengue incidences. The DLNM model equation was as follows:

$$\mathrm{Case_t} \sim \mathrm{Poisson}\ (\mu_t)$$

$$\log(\mu_t) = \alpha + \beta_1 f(\text{control measure}, \text{lag})_t + \beta_2 f(\text{temperature}, \text{lag})_t + \beta_3 f(\text{relative humidity}, \text{lag})_t + \beta_4 f(\text{precipitation}, \text{lag})_t + \beta_5 f(\text{week}) + \varepsilon_t$$

$$t = 1\text{–}53$$

Where $\mathrm{Case_t}$ was the number of confirmed cases in week t of onset and it followed a Poisson distribution; μ_t represented the weekly expected number of dengue in week t; α was the interception; β_1, β_2, β_3, and β_4 were coefficients of control measure, temperature, relative humidity, and precipitation, respectively; β_5 was the coefficient of temporal autocorrelation; ε is the error term. In this model, we specify the effect of control measure was linear, as the Pearson correlation coefficient was high. Meanwhile, natural cubic splines were applied for the effect of climatic factors and the temporal autocorrelation [12]. Regarding the lag functions, polynomial functions were set for control measure, temperature, relative humidity, and precipitation. We determined the lagged effects of control measure up to 5 weeks of lag, according to the time span of viremic, extrinsic incubation, and intrinsic incubation periods [42]. Moreover, the maximum lag of climatic factors were set to 20 weeks, based on previous studies [11–16]. We modeled overdispersed case data by the quasi-Poisson family. The result was presented as the estimated relative risk (RR) with a 95% confidence interval as compared to the median number of control measures. We used the median number due to a skewed distribution of emergency control measures.

The degrees of freedom (df) for natural cubic spline functions and degrees for polynomial functions were systematically searched from one to five, respectively, to obtain the best combination of models. The best models were identified using ANOVA approaches with a significance level set at 0.05. All models were developed, compared, and selected in R version 4.1.2 [43–45].

3. Results

3.1. Spatio-temporal distribution of cases and emergency control measures

We included a total of 19,871 confirmed dengue cases and 7716 emergency control measures in KH from week 1 in 2015 (December 29, 2014–January 4, 2015) to week 53 (December 28, 2015–January 3, 2016). Overall, the number of dengue cases in districts with both high and low population density increased steadily each week, reaching a peak in week 47 (Fig. 4). At week 47, the total number of cases was 2,487, with 2388 cases in districts with high population density and 99 cases in districts with low population density. In terms of emergency control measures, the highest numbers were recorded in Week 44, with a total of 631 measures: 593 in districts

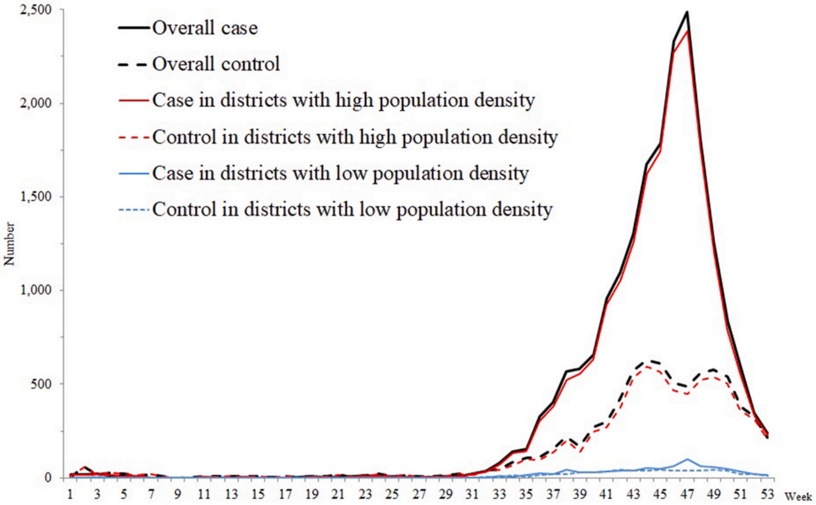

Fig. 4. Epidemic curve of confirmed cases of dengue virus infection by week of onset, and emergency control measures by week, Kaohsiung City, Taiwan, 2015.

with high population density and 45 in districts with low population density in Week 45 (Fig. 4).

Throughout the study period, both confirmed cases and emergency control measures were concentrated in districts with high population density (Figs. 2 and 5). In terms of control capacity, over 75% of the 38 districts were classified as insufficiently-treated (Table 1). All districts with high population density fell into the insufficiently-treated category. Among districts with low population density, 10 were classified as insufficiently-treated, 7 as sufficiently-treated, and 1 as over-treated (Table 1).

4. Emergency control measures in districts with both high and low population density

In districts with high population density, a total of 19,080 cases and 7112 emergency control measures were recorded over the 53-week period. The minimum number of cases per week was 0, while the maximum reached 2388. The median number of cases was 13. Regarding emergency control measures, the range varied from 0 to 593 times, with a median of 18. The weekly autocorrelation of dengue cases was 1. The best DLNM model was obtained with 3 degrees of freedom for natural cubic spline functions and degree 1 for polynomial functions.

In districts with high population density, when no emergency control measures were implemented (i.e., control = 0), dengue risks exhibited a significant increase over time lags compared to the scenario with 18 emergency control measures (Fig. 6). Conversely, when emergency control measures were implemented (i.e., control>0), the lag-response relationships revealed that higher numbers of emergency control measures corresponded to lower dengue risks (Fig. 7(a)), with significant differences observed (Fig. 7(a), (c), and 7 (d)), except for cases involving a low number of emergency control measures (Fig. 7(b)).

Concerning the 19 districts with low population density, there were 791 cases and 604 control measures recorded during the study period. Similar to the districts with high population density, the weekly autocorrelation of dengue cases was one week. The weekly number of cases in the districts with low population density ranged from 0 to 99, with a median of 1, and the number of control measures ranged from 0 to 45 times, with a median of 1. The best-fitting DLNM for the districts with low population density had a degree of freedom of 2 for the natural cubic spline and a degree of 2 for the polynomial functions, respectively.

The findings in the districts with low population density revealed that if no control measures were implemented, only the first week showed a significantly higher risk (Fig. 8). When emergency control measures were implemented, the measures were associated with Relative Risks (RRs) less than 1 in the first week (Fig. 9(a)), which was significant (Fig. 9(b), (c), and 9(d)). From lags 2 to 5, RRs steadily increased with the number of control measures, reaching the highest RRs at lag week 3 (Fig. 9(a)). However, the effects from lags 2 to 5 were not significant (Fig. 9(b)–9(e)).

Based on the aforementioned findings, distinct patterns of associations between dengue risks, emergency control, and lag efforts have been demonstrated in districts with both high and low population density. Next, we evaluated the impact of different control capacities on dengue cases in each setting. In districts with high population density, all districts were found to have insufficient treatment (Table 1). Therefore, the analysis of different control capacities focused on districts with low population density.

4.1. *Emergency control measures in insufficiently-treated districts with low population density*

Among the 10 insufficiently treated districts with low population density (Table 1), there were 634 cases and 380 control implementations during the study period. Similar to the overall areas with low population density (i.e., 19 districts), the weekly

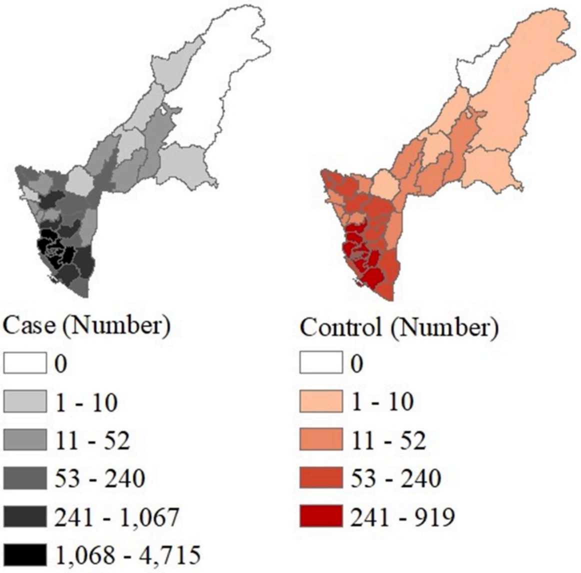

Fig. 5. The spatial distribution of confirmed cases of dengue virus and emergency control measures in Kaohsiung City, Taiwan, 2015.

Table 1
District distribution in Kaohsiung City: High and low population density across various control capacities, December 29, 2014–January 4, 2015.

Control capacity	Districts with high population density	Districts with low population density	Total
Insufficiently-treated[a]	19	10	29
Sufficiently-treated[b]	0	7	7
Over-treated[c]	0	1	1
Case = 0	0	1	1
Total	19	19	38

[a] number of control/number of case<1.

[b] 1≤number of control/number of case≤2.

[c] 2<number of control/number of case.

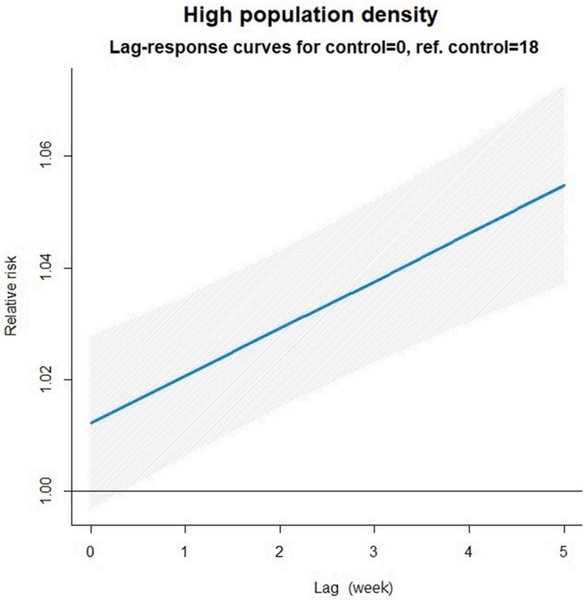

Fig. 6. Estimation of relative risk of dengue at each 1–5 lag week in the absence of emergency control measures in high population density districts of Kaohsiung City, Taiwan, 2015. The median number of emergency control measures in high population density districts is 18. The shaded region indicates its 95% confidence interval.

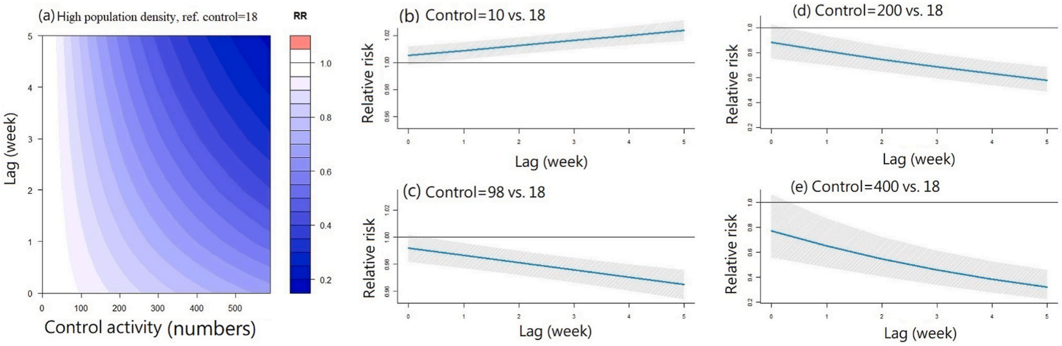

Fig. 7. The estimation of the relative risk of dengue at each 1–5 lag week under the application of different numbers of emergency control measures in the districts with high population density of Kaohsiung City, Taiwan, 2015. The different scenarios examined include: (a) overall, (b) 10 times of emergency control measures, (c) 98 times of emergency control measures, (d) 200 times of emergency control measures, and (e) 400 times of emergency control measures. The median number of emergency control measures in sufficiently-treated districts with high population density is 18. The shaded region indicates the 95% confidence interval.

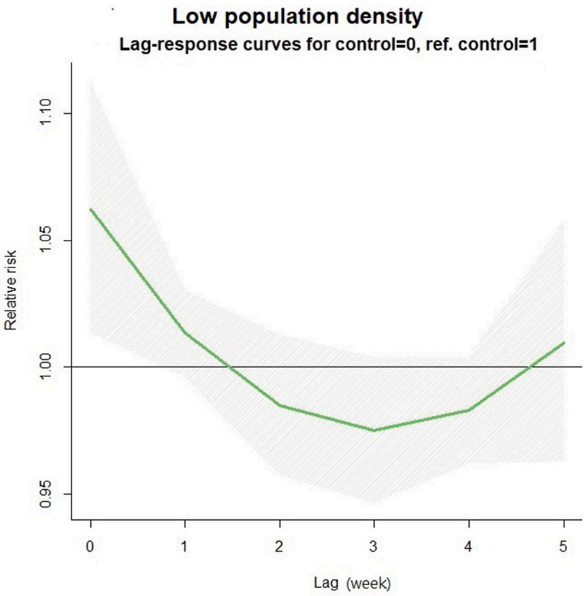

Fig. 8. The estimation of relative risk of dengue at each 1–5 lag week, under the absence of emergency control measures in low population density districts of Kaohsiung City, Taiwan, 2015. The median number of emergency control measures in low population density is 1. The shaded region indicates its 95% confidence interval.

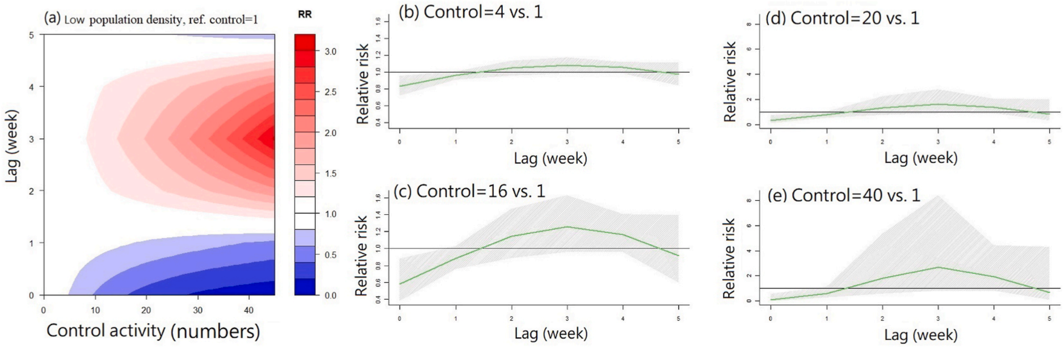

Fig. 9. The estimation of the relative risk of dengue at each 1–5 lag week under the application of different numbers of emergency control measures in the districts with low population density of Kaohsiung City, Taiwan, Taiwan, 2015. The different scenarios examined include: (a) overall, (b) 4 times of emergency control measures, (c) 16 times of emergency control measures, (d) 20 times of emergency control measures, and (e) 40 times of emergency control measures. The median number of emergency control measures in the sufficiently-treated districts with low population density is 1. The shaded region indicates the 95% confidence interval.

autocorrelation of dengue cases was 1. The weekly case numbers ranged from 0 to 87 with a median of 1, and the emergency control measures were implemented between 0 and 32 times, with a median of 1 time. The best-fitting DLNM for the areas with low population density had a df of 1 for the natural cubic spline and a degree of 4 for the polynomial functions, respectively.

The results showed that in insufficiently-treated districts with low population density, when no control measures were implemented, the lag-response analysis, using the reference value of 1 control measure, indicated that the RRs were consistently above 1 in each 1–3 week, which was significant. However, at the 4th and 5th weeks, the risk did not differ significantly from that of 1 control measure (Fig. 10). On the other hand, when emergency control measures were carried out, the lag curve demonstrated that the contributions of control measures on dengue risks were significantly positive, except at lag 4–5 weeks, where the significance was not observed (Fig. 11(a)–11(d)).

4.2. *Emergency control measures in sufficiently-treated districts with low population density*

In the 7 sufficiently-treated districts with low population density (Table 1), there were 154 dengue cases, with the weekly number ranging from 0 to 19 and a median of 0. In terms of emergency control measures, 216 interventions were implemented during the study

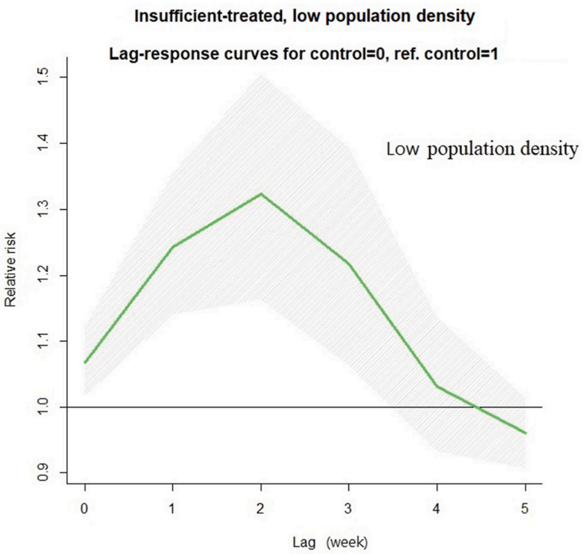

Fig. 10. The estimation of the relative risk of dengue at each 1–5 lag week in the absence of emergency control measures in the insufficiently-treated districts with low population density of Kaohsiung City, Taiwan, 2015. The median number of emergency control measures in the insufficiently-treated districts with low population density is 1. The shaded region indicates the 95% confidence interval.

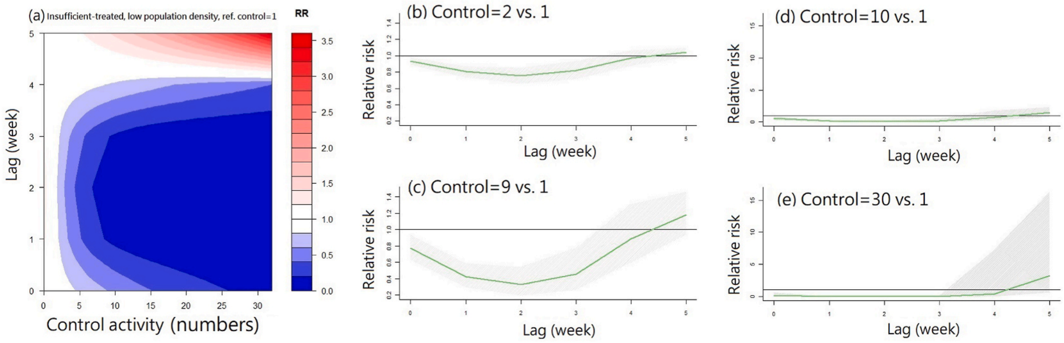

Fig. 11. The estimation of the relative risk of dengue at each 1–5 lag week under the application of different numbers of emergency control measures in the insufficiently-treated districts with low population density of Kaohsiung City, Taiwan, 2015. The different scenarios examined include: (a) overall, (b) 2 times of emergency control measures, (c) 9 times of emergency control measures, (d) 10 times of emergency control measures, and (e) 30 times of emergency control measures. The median number of emergency control measures in the sufficiently-treated districts with low population density is 1. The shaded region indicates the 95% confidence interval.

period. The weekly maximum and minimum numbers of control measures were 20 and 0, respectively. The median number was 1. The temporal autocorrelation for cases in these districts was 3 weeks. The best-fit model for the sufficiently-treated areas with low population density consisted of a degree of freedom of 3 in the natural cubic spline function and a degree of 1 in the polynomial function.

When control = 0, the lag-response associations demonstrated that dengue risks were significantly higher than when using the reference value of 1 control at lags 1–2 (Fig. 12). However, the RRs were not significant at lags 3–5. On the other hand, for control>0, the RRs of dengue were lower than 1 from lag 1 to lag 4, and higher than 1 at lag 5 (Fig. 13(a)). However, the RRs were only significant for the early weeks (lags 1 and 2) (Fig. 12(b) and (c)). The lag-response patterns were not significant at lags 3–5 (Fig. 12(d) and (e)).

5. Discussion

This study focuses on evaluating the impact of emergency measures on dengue incidence during a significant outbreak in Kaohsiung City, Taiwan. To our knowledge, there has been a shortage of studies employing empirical data and analytical methods to assess emergency responses to dengue. Real-world data were utilized, applying DLNM approaches to the 2015 dengue outbreak in areas characterized by high and low population densities. The findings revealed that in areas with high population density, without the implementation of emergency measures, the risks of dengue were significantly elevated. However, the application of emergency measures, particularly a greater number of measures, was associated with lower risks. Conversely, in areas of low population density,

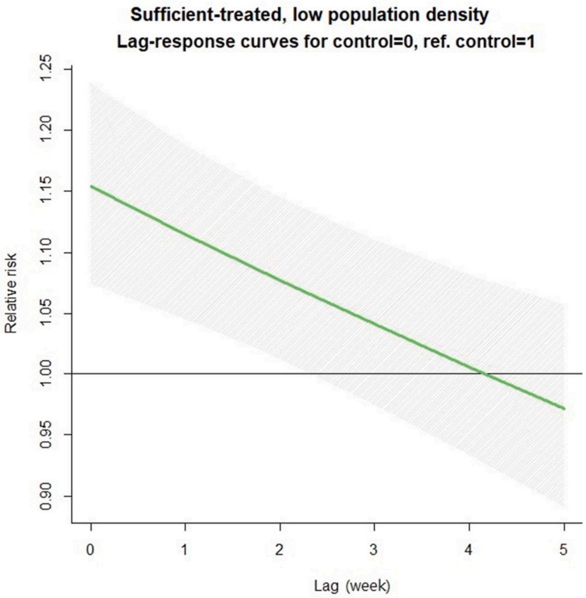

Fig. 12. The estimation of the relative risk of dengue at each 1–5 lag week in the absence of emergency control measures in the sufficiently-treated districts with low population density of Kaohsiung City, Taiwan, 2015. The median number of emergency control measures in the sufficiently-treated districts with low population density is 1. The shaded region indicates the 95% confidence interval.

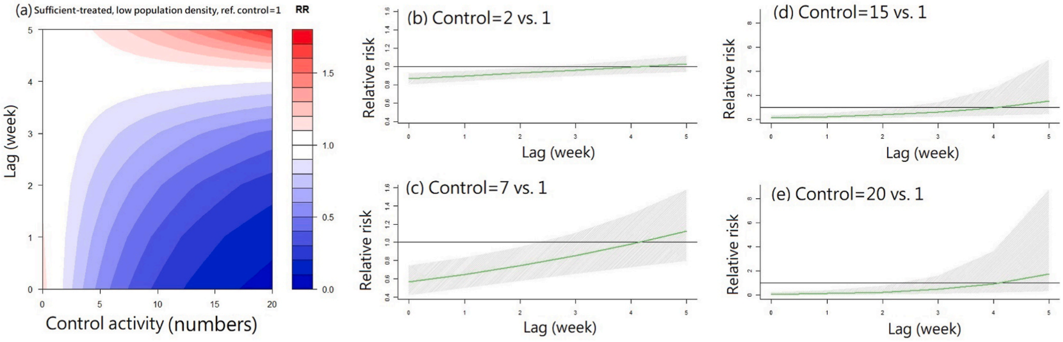

Fig. 13. The estimation of the relative risk of dengue at each 1–5 lag week under the application of different numbers of emergency control measures in the sufficiently-treated districts with low population density of Kaohsiung City, Taiwan, 2015. The different scenarios examined include: (a) overall, (b) 2 times of emergency control measures, (c) 7 times of emergency control measures, (d) 15 times of emergency control measures, and (e) 20 times of emergency control measures. The median number of emergency control measures in the sufficiently-treated districts with low population density is 1. The shaded region indicates the 95% confidence interval.

the risks of dengue were only significantly elevated at the 1st week lag if no emergency control measures were implemented. When emergency activities were carried out, the risks of dengue were significantly decreased only for the 1st week lag. Our findings demonstrate that the associations between emergency control measures and dengue exhibit different exposure-lag-response patterns in areas with high and low population density. Under routine control measures throughout the year, when a large dengue outbreak occurs, it is necessary to apply emergency activities to reduce the risk of dengue in areas with high population density. On the other hand, applying emergency activities in areas with low population density may not be deemed necessary. The impact of this study on dengue may assist health authorities in managing the disease under limited resources.

The DLNM is a statistical modeling approach commonly employed in epidemiology and environmental health research. This model possesses several strengths. Firstly, DLNMs enable the modeling of non-linear relationships between exposures and outcomes, particularly valuable when the relationship defies easy capture by simple linear models. Secondly, the model is specifically designed to account for delayed effects or lagged responses in the relationship between exposure and outcome. This proves crucial in numerous epidemiological studies, especially where the health impact of an exposure may not manifest immediately. Thirdly, DLNM can be extended to handle multiple exposures simultaneously, offering a means to assess the joint effects of multiple factors on health outcomes [46]. Fourthly, it excels in effectively modeling the temporal dependencies present in the data.

However, this modeling process also has its disadvantages. Firstly, the model is sensitive to the assumptions made during model specification, including the choice of lag structure, degree of non-linearity, and the form of the cross-basis functions. Small changes in these assumptions can lead to different results. Secondly, DLNM is associational and not necessarily causal. While it can identify associations between exposures and outcomes, establishing causation requires additional evidence and consideration of potential confounding factors. Thirdly, this approach requires a large amount of data to estimate lag and non-linear relationships accurately. In situations where data are limited, the model may struggle to provide reliable results. Fourthly, estimating DLNM models can be computationally intensive, especially for large datasets and complex models. This can be a limitation for researchers with limited computational resources.

We chose only one year, 2015, to study the lag effects of emergency measures on dengue for two reasons. One is the 2015 dengue outbreak was one of the largest dengue outbreaks during the recent decade in KH (Fig. 14). The other one is the year 2015 was the first year that emergency measures data could be obtained from TW GOV [38]. Therefore, for the purpose of assessing the associations between emergency control measures and dengue incidences in a large outbreak, the 2015 outbreak was chosen.

Based on the transmission of the dengue virus between humans and mosquitoes, if the time interval between two confirmed cases with illness onset dates was less than 2 weeks, it is unlikely that the second patient was infected through the bites of the infective female mosquito from the first patient [42]. In other words, the effects of emergency control measures on dengue would be evident with lags of 3–5 weeks.

In this study, a lower risk of dengue was observed in association with the implementation of more emergency measures, specifically in districts with high population density, at each 3–5 lag week (Fig. 7). The findings suggest that applying emergency control activities is linked to reducing dengue risks in areas with high population density. In those areas, all districts had insufficient treatment (Table 1). One reason leading to insufficient treatment in those districts was logistical factors, such as the unavailability of human resources and spray equipment at that moment.

Similar reasons have been demonstrated in the review by Horstick et al., which indicated that inadequate emergency measures, due to factors such as a lack of entomologists, limited mosquito control operations [48]. While limited mosquito control operations have been suggested as a reason for increasing dengue, in this study, the application of insufficient emergency activities was associated with lower dengue risks. It could be a fact that, in Taiwan, emergency control measures include not only spraying with pesticides, as is common in most countries [48], but also incorporate environmental sanitation in governmental and private properties [40]. This approach simultaneously reduces both immature and adult *Aedes* mosquitoes, which could be the reason why emergency management can reduce dengue risks.

In areas with high population density, the findings also indicated that in the absence of emergency control measures, dengue risks were elevated in all 5 weeks (Fig. 6). In other words, relying solely on routine vector control activities was not sufficient to suppress dengue cases in areas with high population density. In Taiwan, one of the routine control measures is source reductions on government property [34]. Transmissions of dengue did not cease by removing *Aedes* habitats in this study align with Southeast Asian studies [49]. One of the reasons for routine control measures was not sufficient could be because the most *Aedes* productive containers have not been controlled. *Aedes* immature tended to aggregate in specific habitats, so fail to remove those could maintain dengue transmissions [50, 51]. In high population density areas of KH (i.e., urban KH), entomological surveys by Lin et al. revealed that containers on private property had more *A. aegypti* compared to those on government property [52]. However, the routine control measures, conducted by the KH government, mainly reduce breeding sites on government property, which would leave actual productive habitats on private property. In addition to aquatic containers on private property, unapparent spaces and cryptic habitats in urban could serve as productive habitats. For instance, in storm drains systems which are the integral part of urban setting, stagnated water often exists in the cryptic spaces of underground pipes and channels. A survey conducted from Wilke et al. showed that significantly more *Ae. aegypti* pupae were in storm water drains as compared with discarded tires in Florida [53]. The study by Seidahmed et al. also revealed that higher drainage densities were significantly associated with higher number of *Ae. aegypti* breeding sites in Singapore [54]. Another reason could be people unintentionally provide suitable habitats for *Aedes*. A field study conducted in the residential urban areas showed that the original *Ae. aegypti* breeding sites were replaced by other water-holding containers after three months, even though similar number of *Ae. aegypti* habitats existed in Florida [55]. The last reason is larvicide treated containers or source reduction come up with delayed control of adult *Aedes* [49]. That is, the current female vectors with dengue virus will not reduce their numbers by environmental sanitations, and hence only rely on source reduction may not suppress the dengue transmission [49].

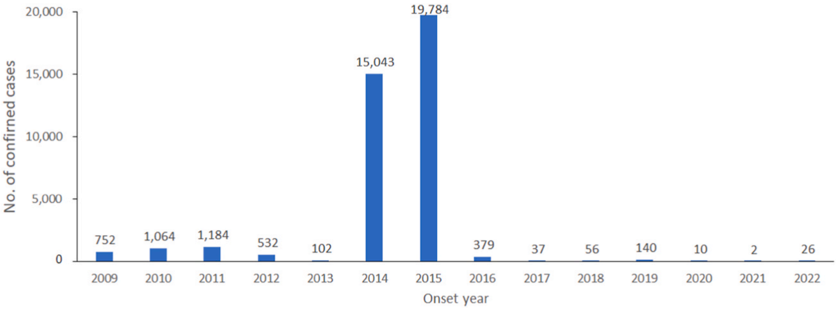

Fig. 14. Epidemic curve of confirmed cases of dengue virus infection by year, Kaohsiung City, Taiwan, 2009–2022 [47].

Unlike high population density areas, where emergency control measures play a crucial role in reducing dengue risks, the current study suggests that emergency control measures may not be as effective in low population density areas. This conclusion can be drawn from the overall findings in areas of low population density or specifically in areas of low population density with sufficient treatment, where emergency control measures did not exhibit significant effects on reducing dengue risks during the 3–5 lag weeks (Figs. 9 and 13). Even in areas of low population density with insufficient treatment, emergency control measures were only associated with a significantly higher risk during the 3rd lag week (Fig. 11). The lack of significant effects of emergency control measures in areas of low population density may imply that conducting routine control measures is sufficient. This implication is supported by the statistically non-significant risks observed during the 3–5 lag weeks when no emergency control measures were in place (Fig. 8).

Routine control measures in Taiwan include routine source reduction and larvicide treatments [34]. One possible explanation for the effectiveness of these routine measures is that residents in rural areas are more likely to comply with policies and collaborate with the government. For instance, a study conducted in Thailand showed that families in rural provinces were more willing to cooperate with volunteers conducting larvicide treatments to control severe dengue compared to those in urban communities [56]. Another study also indicated that people in rural areas were more likely to reduce household visitations during national lockdowns in response to the COVID-19 pandemic compared to residents in urban cities in England [57]. Another explanation could be that adult *Aedes* species have lower vectorial competence for transmission in rural areas. *Ae. albopictus* is the predominant species in rural districts in Kaohsiung city, while *Ae. aegypti* is predominant in urban districts [38]. As dengue virus transmission is less effective through female *Ae. albopictus* compared to female *Ae. aegypti* [58], targeting the immature stages of *Ae. albopictus* to prevent them from becoming adults as part of routine control measures could be sufficient in rural districts. It is worthwhile to note that the findings of this study were based on the assumption that routine control measures were carried out equally in all districts throughout the year.

While this study did not reveal differences in dengue risk between areas with high and low population densities associated with climate variables, it is worth noting that climate factors have been shown to contribute to variations in risk among areas with different population densities, either directly or indirectly. For instance, higher temperatures would have positive effects on mosquito growth rate, population, and incubation period, regardless of human population densities [59–62]. Despite this, the likelihood of exposure to infectious mosquito bites is higher in situations where households are crowded [63,64]. Therefore, temperature could play an indirect role in dengue risk among areas with different population densities.

Moving on to precipitation, the relationship between rainfall and dengue outbreaks has been demonstrated in previous studies in Taiwan [11,52,65]. Studies conducted by Lin et al. show a greater availability of *Ae. aegypti* and *Ae. albopictus* breeding sites in the wet season compared with the dry season, supporting a direct relationship between an increase in habitat numbers, higher vector abundances, and increased risk of human-vector contact [52,65].

This study suggests distinct control strategies for dengue and other *Aedes*-borne diseases in areas with high and low population densities. In areas with low population density, especially in countries or regions where *Ae. albopictus* predominates, such as France, Spain, Japan, and Hong Kong [66–68], it is crucial to implement routine vector management activities to combat *Aedes*-borne diseases such as chikungunya and Zika. These routine activities include monitoring *Aedes* mosquitoes and diseases, conducting health education and awareness campaigns, and implementing environmental sanitation measures. Emphasizing the reduction of immature *Aedes* mosquitoes should be a primary focus in rural areas with low population density. Conversely, in urban areas with high population density, where *Ae. aegypti* mosquitoes are abundant, relying solely on routine dengue control measures is insufficient to reduce risks. In addition to routine control activities, the application of chemical adulticides is necessary, and it is crucial to monitor insecticide resistance as well. There are some limitations in this study. First, in order to address the issue of overrepresented weeks with no dengue cases, we used only quasi-Poisson methods. Although we attempted to apply other models such as negative binomial or zero-inflated models, none of them could be converged. Second, this study relied on confirmed dengue cases to assess dengue risks. However, it is important to note that most dengue infections are asymptomatic or mild, which means that the risks may be underestimated [69]. Third, while we had information on when and where emergency control measures were implemented, the quality of each measure executed was unknown. Fourth, even if all measures were executed with the same quality during the study period, it is unclear whether the concentrations of insecticides were sufficient to combat resistance. Studies have shown that mosquito resistances can vary across districts in KH [70,71]. Fifth, we incorporated climatic factors, such as minimum temperature, on a weekly basis into the model, aligning with the findings from the reviewed literature in Taiwan. However, other climatic factors, such as the diurnal temperature range, might yield varied risk results. Finally, if multiple cases were confirmed in the same building or household on the same date, a single emergency response would be conducted. This situation could introduce bias, particularly in areas with high population density [72]. However, areas with low population density may also have clusters in households.

CRediT authorship contribution statement

Chia-Hsien Lin: Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Conceptualization. **Tzai-Hung Wen:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

This research was supported by the grants from the National Science and Technology Council in Taiwan (NSTC 110-2410-H-002-131-MY3 and NSTC 112-2121-M-002-002) and the Infectious Diseases Research and Education Center, the Ministry of Health and Welfare (MOHW) and National Taiwan University (NTU).

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