Policy Forum

Frequency, Duration and Intensity of Dengue Fever Epidemic Risk in Townships in Pearl River Delta and Yunnan in China, 2013*

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Dengue fever (DF), one of the neglected tropical diseases[1] also known as breakbone fever, is a mosquito-borne disease common in the tropics and subtropics. Dengue fever is transmitted primarily by *A.aegypti*, resulting in infection with any of four distinct but closely related virus serotypes[2]. The majority of infected people experience a self-limiting clinical course. A small proportion of cases develop into life-threatening Dengue Hemorrhagic Fever or Dengue Shock Syndrome[3]. Thus, DF imposes a heavy economic burden and negatively affects disability-adjusted life years (DALYs) worldwide[4-7].

The prevention and control of DF is difficult, as no vaccine or specific antiviral therapy is available[3,8], and no long lasting cross-immunity between the four distinct serotypes exists, although there is lifelong immunity to the same infected serotype. With increased population migration and the existence of silent or unapparent infections[9], people from non-endemic areas are more susceptible to DF, which makes the effective prevention and control of DF more difficult.

Instead of treatment, prevention and environmental control are the most effective ways to decrease the burden resulting from DF. The three classical approaches to preventing and controlling infectious diseases include controlling the source of infection, reducing the transmission route, and protecting the susceptible population. Different susceptible locations may require different targeted measures based on specific epidemic characteristics.

Previous epidemiological studies mainly focused on incidence and traditional descriptive analysis (such as the distribution of age or sex) at the county or prefectural level[10-13], which provided little information for directing targeted prevention and control measures. Wen et al.[14] proposed a new method to describe characteristics of a DF epidemic from 3 dimensions (frequency, duration, and intensity), which provided more comprehensive information for determining targeted measures. This method has been used to analyze the distribution of DF in Malaysia[15] and provided a convenient and efficient way to determine the targeted measures for controlling the transmission of DF[16]. In addition, it helped public health workers to understand the local epidemic situation within the entire epidemic-affected area. In the current study, we applied this method to describe the epidemic risk at the township level in priority areas of China, 2013 for the first time.

In China, DF is prevalent primarily in the southern provinces[17]. According to the National Notifiable Infectious Disease Surveillance System of Chinese Center for Disease Control and Prevention (founded in 2004), DF outbreaks were sporadic prior to 2013, but the outbreaks and number of cases observed in 2013 exceeded the totals for the previous 9 years, even spreading to central China[18]. The increased economic and medical burdens to patients during 2013 provided an opportunity to describe the epidemic risk characteristics of DF in China. Ninety percent of the cases in 2013 were distributed in Guangdong and Yunnan[10]. Specifically, 99% of the cases in Guangdong and Yunnan occurred in Pearl River Delta of China (PRD) and in two autonomous prefectures [Xishuangbanna Autonomous Prefecture (Xishuangbanna) and Dehong Autonomous Prefecture (Dehong)]. These 3 areas were chosen as our study areas to describe the epidemic risk characteristics of DF at the township level.

Study Area PRD, which is made up of 7 cities and 402 towns (Figure 1), is the low-lying area surrounding the Pearl River estuary. It is one of the most densely urbanized regions in the world and one of the main hubs of China's economic growth.

Xishuangbanna, famous for its tropical rain

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forest, is located in the southern part of Yunnan and is adjacent to Laos, Myanmar, Thailand, and Vietnam. Dehong is located in the western part of Yunnan and is adjacent to Myanmar. A total of 82 towns are located in these 2 autonomous prefectures (Figure 1). The countries adjacent to them all have high incidences of DF[19-20].

The case numbers at the township level for each study area are shown in Figures 2-4.

Data Source With approval and access from the Chinese Center for Disease Control and Prevention, case information was provided by the National Notifiable Infectious Disease Surveillance System based on the onset of DF from Jan 1st to Dec 31st in 2013, including laboratory confirmed cases and clinically diagnosed cases (a total of 2901 and 1408 cases for Guangdong and Yunnan Province respectively). All cases with permanent residential addresses (locations where cases had been living for more than 6 months) located in the study areas were included and used in subsequent statistical analysis.

The population data came from the National Bureau of Statistics of the People's Republic of China. As it concerned a notifiable infectious disease, this study was exempted from the institutional review board assessment.

Statistical Analysis The analysis was performed on towns in each study area individually, instead of regarding the 3 study areas as a whole.

(1) Spatial and Temporal Units to Perform Analysis: Town is the spatial statistical unit, as it is the smallest administrative unit in China. In 2013, 206 of 402 towns in PRD reported cases of DF, and 31 of 82 towns in Xishuangbanna and Dehong reported cases of DF.

As the incubation period for Dengue is 2-15 d, with an average of 6 d, we adopted the time period of a week as the temporal statistical unit, with 51 full weeks in 2013. In this study, a full week means 7 d from Monday to Sunday in the year 2013.

(2) Index Construction and Evaluation: Three indices were calculated for each town, including frequency (probability of occurrence, α), duration (duration of epidemic, β), and intensity (intensity of transmission, γ). A comprehensive index comprised of the 3 indices was then constructed for each town. The definitions and calculation methods of these indices are as follows:

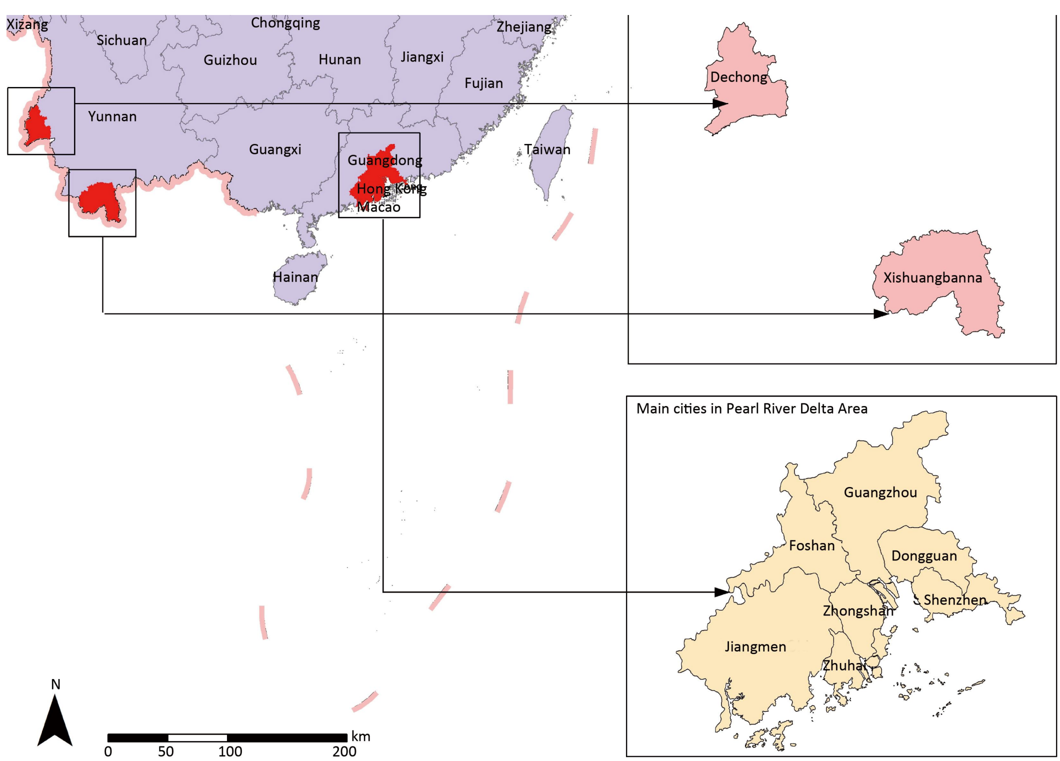

Figure 1. Study areas for Dengue Fever. Purpled area: southern part of China; Pinked parts: two area in Yunnan Province of China; Yellowed Area: main cities in Pearl River delta area, in Guangdong Province of China.

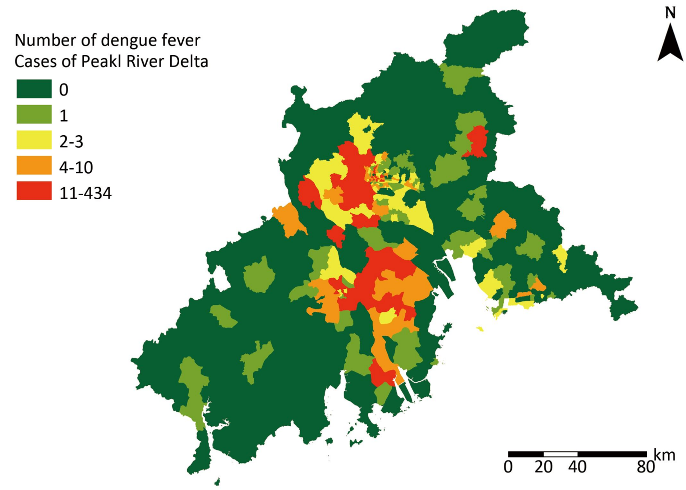

Figure 2. Township distribution of dengue fever cases in PRD.

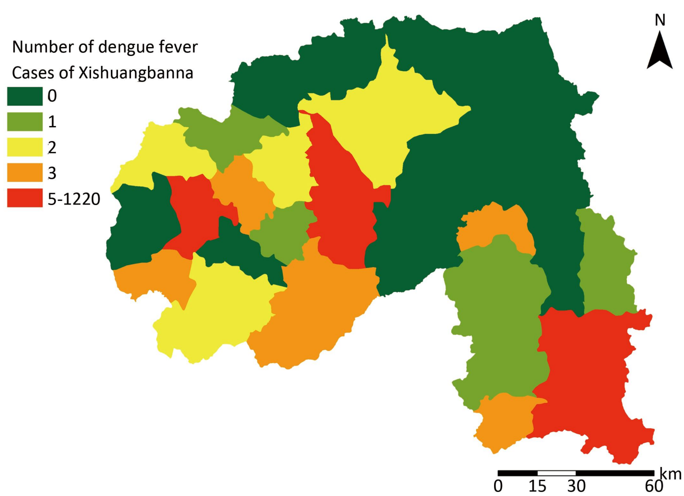

Figure 3. Township distribution of dengue fever cases in Xishuangbanna.

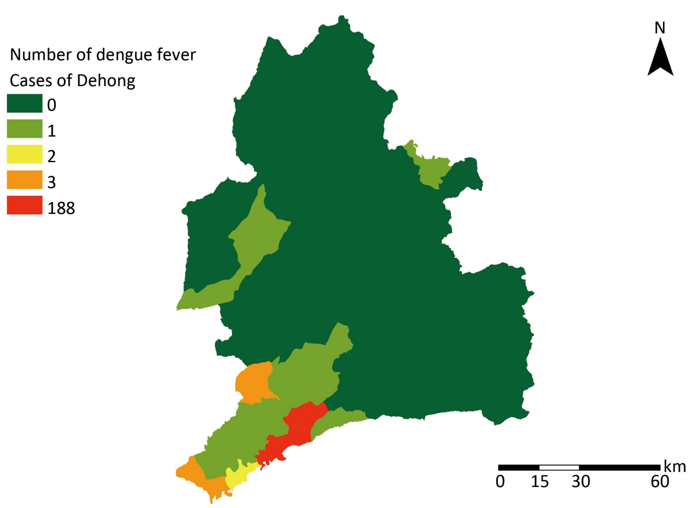

Figure 4. Township distribution of dengue fever cases in Dehong.

1) The probability of occurrence (α) measured how often the disease occurred and was calculated by dividing the number of weeks with one or more cases by the total number of full weeks for the year.

2) The duration of epidemic (β) calculated the average weeks an epidemic wave lasted. An epidemic wave was defined as the weeks during which cases successively occurred. β was arrived at by dividing the number of weeks with one or more cases by the total number of epidemic waves.

3) The intensity of transmission (γ) was calculated by dividing the incidence rate by the total number of epidemic waves to measure the severity of an epidemic.

All the towns in each study area were classified into high (H) or low risk (L) areas based on their deviations from the means of the corresponding study area for each individual index. Given an index, when the value was larger than the mean plus 1.5 times standard deviations (M + 1.5×SD), the town was classified as high risk (H); otherwise, it was classified as low risk (L). The 196 towns in PRD and the 46 towns of the 2 autonomous prefectures in Yunnan in which all 3 indices were 0 (towns with no case during the whole year of 2013) were denoted as 'zero value' towns.

4) The comprehensive index is the combination of the 3 indices described above, for which there were 8 possible values. The comprehensive index classifies a specific town (H or L) sequentially, according to the probability of occurrence, duration of epidemic, and intensity of transmission. For instance, a town with a comprehensive index of 'HLH' was classified as high risk (H) based on the probability of occurrence, low risk (L) based on duration of epidemic, and high risk (H) based on the intensity of transmission. The other possible values available in the comprehensive index can be deduced by analogy.

The 3 indices were constructed with EXCEL and the correlation analyses were analyzed with SAS 9.3.

(3) Thematic Mapping. Based on the constructed indices, ArcGIS desktop (Esri Co. Ltd) was used to draw thematic maps for the 3 study areas separately. The map scale was 1:1,000,000 (one centimeter to 1 kilometer) using the World Mercator projection coordination system and the GCS_WGS_1984 geography coordination system.

The average probability of occurrence (α) was 4.13%, 5.09%, and 1.12%, for PRD, Xishuangbanna and Dehong, respectively, in 2013. These indices mean that there were 2.1 weeks, 2.6 weeks, and 0.6 weeks with one or more cases occurring among the 3 study areas, respectively. The maximum value of probability of occurrence was 39.20%, 37.25%, and 25.49% respectively (Table 1).

Excluding the 'zero value' towns, in PRD an epidemic lasted 1.68 weeks (β) on average, with a maximum of 19.00 weeks. The epidemics of in Xishuangbanna lasted on average 1.51 weeks (β) with a maximum of 6.33 weeks, and Dehong epidemics lasted on average 1.46 weeks (β) with a maximum of 6.00 weeks (Table 1).

Excluding the 'zero value' towns, the intensity of transmission (γ) in PRD was on average $9.25/10^5$ with a maximum of $300.24/10^5$. For Xishuangbanna the average value was $20.46/10^5$ with a maximum of $261.51/10^5$; and in Dehong, the average value was $14.03/10^5$ with a maximum of $82.99/10^5$ (Table 1).

The 3 aforementioned indices were highly correlated with each other in all 3 study areas ($P<0.01$) (Tables 2-4). In addition, the correlation coefficients were all >0.50; the smallest were in PRD while those in Dehong were the largest, with all correlation coefficients >0.90 (Tables 2-4).

Calculation of the comprehensive index showed that in PRD, there were 5 types of high risk towns (a total of 37 towns): HHH (5 towns), HHL (6), HLH (1), HLL (22), and LHL (3). Most of the high-risk towns were located within the prefecture boundary (Figure 5). A χ^2 analysis was used to test the hypothesis in all 402 towns in this area using SAS 9.3: whether a town was high risk was independent from whether it was located within the prefecture boundary. Results suggest high-risk towns were more likely to be located within the prefecture boundary ($P=5.18\times10^{-5}$).

Table 1. The Mean and Maximum Value of Epidemic Risk Indices among 3 Study Areas

Site	Frequency Index, α (%)		Duration Index, β		Intensity Index, γ ($/10^5$)	
	mean	max	mean	max	mean	max
PRD	4.13	39.20	1.68	19.00	9.25	300.24
Xishuangbanna	5.09	37.25	1.51	6.33	20.46	261.51
Dehong	1.12	25.49	1.46	6.00	14.03	82.99

Table 2. Correlation Coefficients of Epidemic Risk Indices for PRD

Indices	Frequency Index, α	Duration Index, β	Intensity Index, γ
Frequency index, α	1.00	0.77	0.53
Duration index, β	-	1.00	0.78
Intensity index, γ	-	-	1.00

Table 3. Correlation Coefficients of Epidemic Risk Indices for Xishuangbanna in Yunnan

Indices	Frequency Index, α	Duration Index, β	Intensity Index, γ
Frequency index, α	1.00	0.91	0.75
Duration index, β	-	1.00	0.85
Intensity index, γ	-	-	1.00

Table 4. Correlation Coefficients of Epidemic Risk Indices for Dehong in Yunnan

Indices	Frequency Index, α	Duration Index, β	Intensity Index, γ
Frequency index, α	1.00	0.97	0.96
Duration index, β	-	1.00	0.97
Intensity index, γ	-	-	1.00

In Xishuangbanna, there were 3 types of high-risk towns (of 5 total high risk towns): HHH (1 town), HHL (3), and HLL (1) (Figure 6). There was only 1 type of high-risk town (HHH for 1 town) in Dehong (Figure 7).

This study described the epidemic risk characteristics (frequency, duration, and intensity) of DF in PRD in Guangdong, and in Xishuangbanna and Dehong in Yunnan, which were the most serious DF foci in 2013. This method, proposed almost a decade ago, still has value, especially when analyzing small areas:

1) It is a more comprehensive way to describe epidemics. Unlike traditional descriptive epidemiology that analyzes the demographic distribution of cases, this method depicts epidemic risk characteristics from 3 dimensions.

2) The indices used in the study could differentiate between epidemic scenarios. The indices (e.g., incidence, total case number) used in traditional descriptive studies have no ability to differentiate among epidemic patterns.

3) This method revealed the epidemic characteristics in towns for each study area and helped local public health workers understand the epidemic pattern for specific towns within the whole

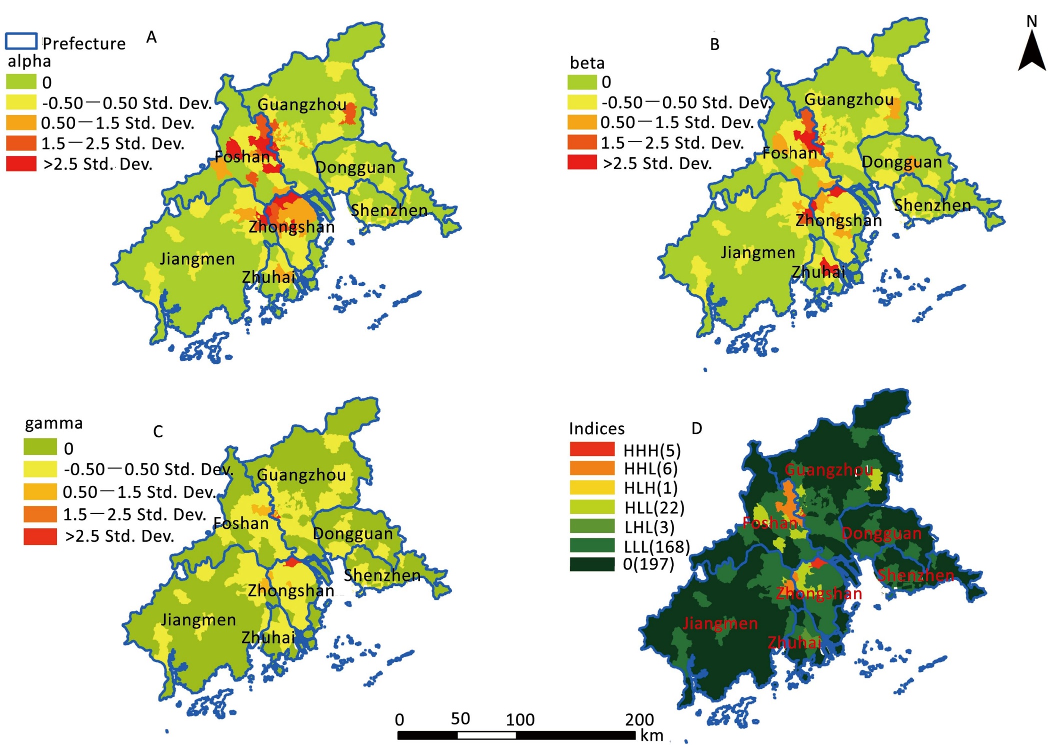

Figure 5. The distribution of the probability of occurrence (A), the duration of epidemic (B), the intensity of transmission (C), and comprehensive index (D) for dengue fever in PRD.

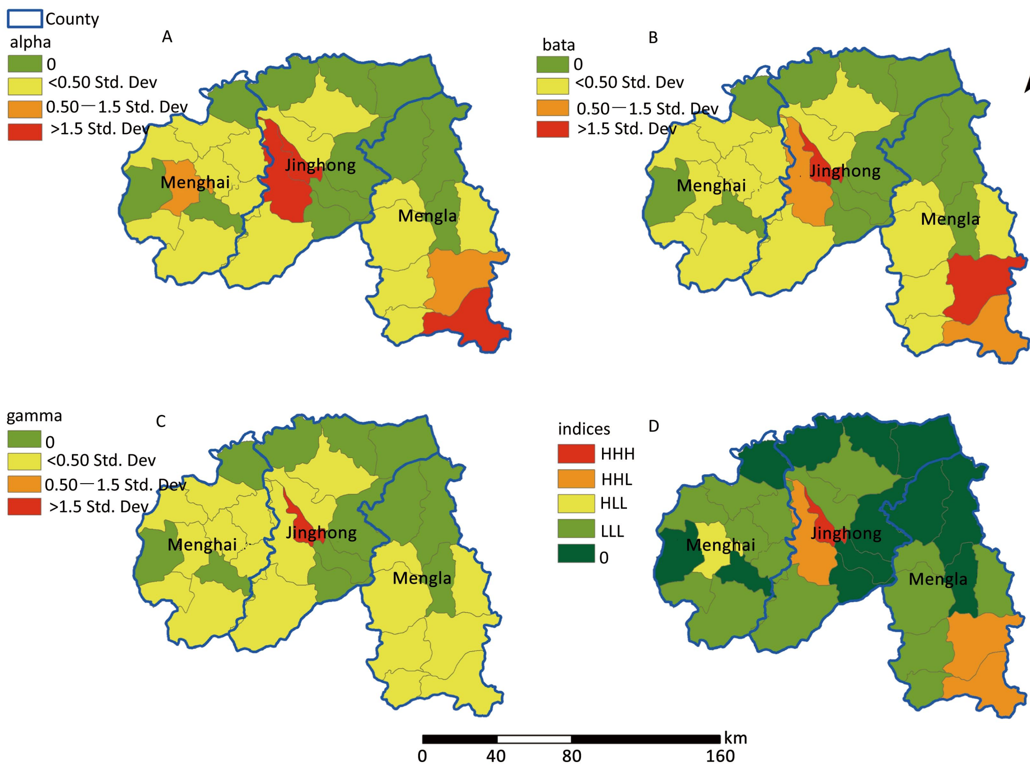

Figure 6. The distribution of the probability of occurrence (A), the duration of epidemic (B), the intensity of transmission (C), and comprehensive index (D) for dengue fever in Xishuangbanna.

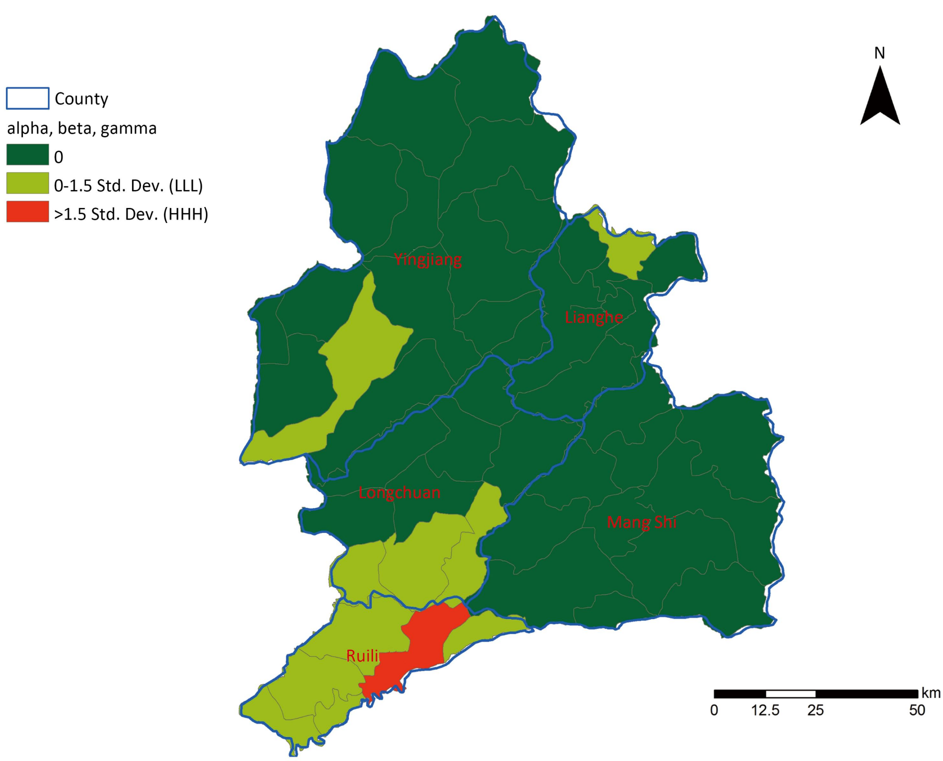

Figure 7. The distribution of the probability of occurrence, the duration of epidemic, and the intensity of transmission for dengue Fever in Dehong.

study area. For instance, public health officials did not put much emphasis on areas of type LHL (low frequency, high duration, low intensity), which were usually of low incidence, but the accumulated cases in these areas may contribute to DF outbreaks because of their long duration.

4) The method used in the study may be helpful to direct targeted control measures for different risk types of DF. As described by Wen et al.[14], risk characteristics may suggest possible weaknesses in the 3 prevention and control strategies (infection source, transmission route, and susceptible population) to help direct targeted measures.

The comparison of epidemic risk characteristics between PRD and the 2 prefectures in Yunnan suggests socioeconomic factors may play a role in the DF epidemic as PRD is one of the main hubs of China's economic growth, while the 2 autonomous prefectures (Xishuangbanna and Dehong) in Yunnan are underdeveloped.

There were quite a few differences in the epidemic risk characteristics between PRD and the 2 autonomous prefectures, which may be associated with different economic modes. First, the cases were distributed widely in PRD, covering 206 towns, while DF had a narrow range in Yunnan, only covering 31 towns of the 2 studied prefectures. Adult mosquitos fly only short distances[21-23], so the developed traffic system may have contributed to the DF outbreaks[24]. It is possible that large traffic volume within PRD can partly explain the widely distributed DF cases in this area, since PRD of China has the most busy and developed transportation system in Guangdong. Yunnan does not have such a developed transportation system and experienced a much narrower range of DF outbreak during the same time period.

Second, the epidemic risk characteristics were more diversified in PRD, which had 5 types of high-risk towns based on the comprehensive index, while there were only 3 types of high-risk towns in the study areas of Yunnan. One explanation for this is that larger coverage might result in more variety.

Finally, high-risk towns were more likely to be located within the prefecture boundary in PRD, while there was no such pattern in the study areas of Yunnan. Prefecture boundary areas were usually badly managed with poor sanitary conditions, making residents more vulnerable to infection. In addition, economically developed regions generally create more job opportunities, which attract migrant workers from non-endemic area susceptible to DF. It is reasonable to speculate that migrant workers would be more likely to live in the prefecture boundary zone. Both poor sanitary conditions and large, susceptible populations may have an impact on the characteristics of DF epidemics. Conversely, in Yunnan, large numbers of tourists, rather than migrant workers, visited the area to enjoy the beautiful scenery; such tourists were more likely to reside in well-appointed hotels, where conditions were sanitary.

There were some limitations in our study. First, we did not bring up targeted measures for different types of risk areas as we did not conduct field surveys to help make inferences. The 3 indices used in the study have been applied to plan insect spraying areas in the past[16], but there is currently no confirming study evaluating the effects and utilizing the targeted measures to prevent and control DF as proposed by Wen et al. [14]. One reason for the dearth of confirmatory studies may be the lack of attention from the public health sector to the potential applications of this method of analysis. If local public health workers were to apply targeted measures based on the 3 epidemic risk indices and then evaluate the results, it would compensate for this limitation. Second, the underreporting rates and climatic factors in different study areas may be varied. This would not appreciably influence the results since the classification was performed on towns for each study area, and different towns in the same study area should have similar underreporting rates and climatic conditions. Furthermore, the comparison between rural Yunnan and PRD was based on risk types rather than estimated statistics. The inconsistencies in reported cases would not have a large effect on results. Third, this study analyzed the epidemic risk characteristics in one year only, and the risk type may be different during another time period. The results could suggest possible weaknesses in prevention and control measures. On the other hand, once measures were taken, the risk types would change. Therefore, the study is not only useful to direct targeted control measures, but also to provide an example to analyze the epidemic characteristics from 3 dimensions (frequency, duration, and intensity). Local public health workers can apply this method to discover appropriate targeted measures, take the measures, and then apply this method to update their targeted measures. This limitation would not depreciate the value of this study.

In conclusion, the current study constructed 3 indices to describe the epidemic risk of DF in PRD and 2 autonomous prefectures (Xishuangbanna and Dehong) in Yunnan of China; the epidemic risk characteristics between PRD and the 2 autonomous prefectures were quite different. The findings suggested that high-risk towns were more likely to be located within prefecture boundary areas in PRD, which is the most vulnerable zone of economic developed areas. There is no such pattern in the 2 studied prefectures in Yunnan, which were underdeveloped.

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