

International Journal of Environmental Research and Public Health



Article Examining the Effect of the Environment and Commuting Flow from/to Epidemic Areas on the Spread of Dengue Fever

Shuli Zhou ^{1,2}, Suhong Zhou ^{1,2,*}, Lin Liu ^{3,4}, Meng Zhang ⁵, Min Kang ⁵, Jianpeng Xiao ⁶ and Tie Song ^{5,*}

- School of Geography and Planning, Sun Yat-sen University, Guangzhou 510275, China; zhoushul@mail2.sysu.edu.cn
- ² Guangdong Provincial Engineering Research Center for Public Security and Disaster, Guangzhou 510275, China
- ³ Center of Geo-Informatics for Public Security, School of Geographical Sciences, Guangzhou University, Guangzhou 510006, China; lin.liu1@yahoo.com
- ⁴ Department of Geography, University of Cincinnati, Cincinnati, OH 45221-0131, USA
- ⁵ Guangdong Provincial Center for Disease Control and Prevention, Guangzhou 511430, China; ccmeng0914@163.com (M.Z.); kangmin@yeah.net (M.K.)
- ⁶ Guangdong Provincial Institute of Public Health, Guangdong Provincial Center for Disease Control and Prevention, Guangzhou 511430, China; jpengx@163.com
- * Correspondence: eeszsh@mail.sysu.edu.cn (S.Z.); tsong@cdcp.org.cn (T.S.)

Received: 19 November 2019; Accepted: 6 December 2019; Published: 10 December 2019



Abstract: Environment and human mobility have been considered as two important factors that drive the outbreak and transmission of dengue fever (DF). Most studies focus on the local environment while neglecting environment of the places, especially epidemic areas that people came from or traveled to. Commuting is a major form of interactions between places. Therefore, this research generates commuting flows from mobile phone tracked data. Geographically weighted Poisson regression (GWPR) and analysis of variance (ANOVA) are used to examine the effect of commuting flows, especially those from/to epidemic areas, on DF in 2014 at the *Jiedao* level in Guangzhou. The results suggest that (1) commuting flows from/to epidemic areas affect the transmission of DF; (2) such effects vary in space; and (3) the spatial variation of the effects can be explained by the environment of the epidemic areas that commuters commuted from/to. These findings have important policy implications for making effective intervention strategies, especially when resources are limited.

Keywords: dengue fever; environment; commuting flow from/to epidemic areas; geographically weighted Poisson regression (GWPR)

1. Introduction

Dengue fever (DF) is a vector-borne infectious disease that is mainly transmitted by Aedes aegypti and Ae. Albopictus [1]. It has been the most rapidly spreading mosquito-borne disease globally [2]. Nearly 4 billion people worldwide are at risk of DF, and 390 million people are infected each year [3]. The cost of treatment and management during DF outbreak has brought a serious economic burden for public health systems [4–6]. How to enhance prevention and control is an important issue. Environments provide habitats for mosquito growth and influence virus replication. The link between environments and DF diffusion has been discussed for decades. Previous studies have shown that the meteorological environment, social–economic environment, and built environment could facilitate local infections [7–15]. Due to the limited flight range of mosquitos, which is usually

less than 400 m [16], human mobility is considered and proven to be another important driver for DF transmissions [16–25]. Therefore, understanding human mobility is key to controlling the spread of infectious diseases.

Human mobility is an important component of our daily life, whether commuting to work, traveling on business, or carrying out other routine activities such as shopping or leisure [26]. Human daily life is in a home-centered living space called the "daily life circle" [27–31]. In that daily life circle, commuting is considered to be the most important daily activity and largely accounts for daily mobility. With increased home-work separation caused by urban space expansion and suburbanization, urban residents have taken longer commute trips than before [32–34], which makes commuters may have a higher chance to be exposed to mosquitos, thus becoming susceptible to DF. When commuters acquire DF infections in epidemic areas, they become important carriers of the virus on the journey to work. A previous study [25] shows that there are two ways of disease transmission. First, people who live in epidemic areas may bring the virus with them when they go to other places; second, people who visit epidemic areas may become infected during their stay, carrying the virus back to their home. Therefore, commuting flows from/to epidemic areas may have a great impact on disease transmission. However, most studies about human mobility and DF are conducted at a large-scale (national scale or cross-city scale) [24,25,35,36]. Small-scale intra-urban commuting flows, especially those from/to epidemic areas, have rarely been addressed in the existing literatures. Mao [37] mapped the intra-urban transmission risk of DF in Shenzhen with cellphone data, but did not pay attention to commuting flows from/to epidemic areas. Examining the effect of commuting flows, especially from/to epidemic areas, on the spread of DF at a finer granularity would be helpful in identifying high-risk areas for effective prevention and intervention.

In addition, places can interact with each other through commuters' travel. For example, the probabilities of different commuters carrying the virus to the same workplace may be different depending on where they live. Those who come from high-risk areas might have a greater chance to affect the local disease outbreak [38]. Put differently, the concentration level of a disease at a local environment might also be related to where the commuters come from and where they residents commute. Unfortunately, previous studies mainly focus on the local environment while neglecting environments of the places, especially epidemic areas that people came from or traveled to [9,11–13,39–41]. In this study, the linkages between places are measured by the commuting flows from/to epidemic areas, and the environments of epidemic areas that commuters commuted from/to will be further examined. Specifically, this study seeks to answer the following three questions:

Question 1: *Do commuting flows from/to epidemic areas impact DF distribution?*

Question 2: *If the answer to the first question is a YES, does the impact vary in space?*

Question 3: If the answer to the second question is a YES, can the spatial variation be explained by the environment of epidemic areas that commuters commuted from/to?

To answer these questions, this study selected Guangzhou, a Chinese city experiencing a large outbreak of DF in 2014, as the study area. The number of DF cases in 2014 is 37,322, which is twice as much as the total accumulated cases in the city since the first reported case in 1978 [42]. The result of this study will greatly enhance our understanding of the DF transmission processes and help public health officers prioritize the limited resources for target prevention in the high-risk areas.

2. Materials and Methods

2.1. Study Area and Data Collection

2.1.1. Study Area

The data for the present research were collected from Guangzhou, a city located in southeast China. As the capital of Guangdong province, Guangzhou is one of the largest and most developed cities in China, with a total population of over 15 million and a total area of about 7400 square kilometers.

Guangzhou has a marine subtropical monsoon climate, and the temperature fluctuates between 15 and 32 °C. The study area is located in the southwest of the city, which is a highly developed area (Figure 1). It comprises 143 *Jiedaos* (the smallest government administrative unit). The average size of these *Jiedaos* is 22.39 km² with a standard deviation of 40.35 km².



Figure 1. Study area.

2.1.2. DF Outbreak in the Study Area

The DF case data were obtained from the China Information System for Disease Control and Prevention. All data are anonymous without individual identifiable information and aggregated to the *Jiedaos* level. According to the law of the People's Republic of China on the prevention and treatment of infectious diseases, all DF cases confirmed by any medical institution or hospital must be reported to the surveillance system in the local area within one day [42]. According to the diagnostic criteria for DF enacted by the Chinese Ministry of Health, a patient is considered as a confirmed case if the DF virus RNA is detected in their serum using the real-time PCR or if immunoglobulin M (IgM) against the DF virus is present [43]. During the outbreak in 2014, the first confirmed case was observed on 20 January, the epidemic peak with 1617 DF cases was observed on 1 October, and the last confirmed case was on 19 December.

2.1.3. Commuting Flow with Mobile Phone Data

The tracked data of mobile phone users are used to measure human daily mobility in this study. It is offered by one of the three major telecom companies in China, which has a market share of 22.5% [44]. The data contains hourly tracking information of the routes taken by the mobile phone users on Wednesday, 28 December 2016, which is a quite formal weekday in Guangzhou. The same tracked data has been used to measure human mobility [45]. To protect the privacy of the mobile phone users, the dataset was desensitized by the telecom company. It includes each mobile phone's identity (ID) number, and for each hour, the location of the cell tower that is the nearest tower most of the time during that hour. The dataset contains 10.2 cell tower hours/locations for each user on average. Fifty percent of mobile phone users had more than seven cell tower hours/locations, and 20% of mobile phone users have more than 20 cell tower hours/locations over the course of that day. The towers are densely distributed in Guangzhou, with the mean nearest neighbor distance of 136.4 m and a standard

deviance of 255.8 (min: 0.0; max: 5535.1). Each tower has a coverage area which is non-overlapping Thiessen polygon. A mobile phone user is connected to a tower when entering the tower coverage area, and the location of a tower will be recorded. The area of the largest tower coverage is smaller than that of *Jiedao* with the smallest area. Each *Jiedao* have multiple cell towers so that the spatial precision of individual location is good for the analysis at the *Jiedao* level.

Using the mobile phone trajectories, we first identified the location of the home and work of each mobile phone user. Local users between 18 and 60 years old were selected. The location where a mobile phone user spent the longest time during 21:00–07:00 was identified as their home, while the location where the mobile phone user spent the longest time during 10:00–17:00 was identified as work place. A commuting trip from home to work was identified as a general commuting flow in the study area. A commuting trip that started from/ended in epidemic areas was defined as a commuting flow from/to epidemic areas. Further, all general commuting trips were aggregated to the *Jiedao* level and into the two categories, FlowIn and FlowOut, as shown in Table 1. Similarly, commuting flows from/to epidemic areas were aggregated as EpiFlowIn and EpiFlowOut (Table 1). These four commute-related variables represent the number of different types of commuters for any *Jiedao*. Compared to FlowIn/FlowOut, EpiFlowIn/EpiFlowOut measures the commuting flows directly related to the epidemic areas in the city. The four variables will be compared later in the regression models.

Categories	Variables	Description
Commuting Flow		Daily commuting flow
	FlowIn	The total numbers of commuters from other Jiedaos
	FlowOut	The total numbers of commuters to other Jiedaos
	EpiFlowIn	The total numbers of commuters from epidemic Jiedaos
	EpiFlowOut	The total numbers of commuters to epidemic Jiedaos
Local environment		Jiedao's local environment
	Local_popdens	Jiedao's population density
	Local_rioldhous	Jiedao's proportion of old houses (built before the 1990s)
	Local_NDVI	Jiedao's normalized difference vegetation index
	Local_riowater	Jiedao's proportion of water areas
Epidemic environment		The environment of the epidemic <i>Jiedao</i> s that interact with this local place through commuters
	Epi_env_from	The environment of the epidemic <i>Jiedaos</i> from which commuters came (or "come-from" epidemic <i>Jiedaos</i>)
	Epi_popdens_from	The population density of the "come-from" epidemic Jiedaos
	Epi_rioldhous_from	The proportion of old houses of the "come-from" epidemic Jiedaos
	Epi_NDVI_from	The normalized difference vegetation index of the <i>"come-from"</i> epidemic <i>Jiedao</i> s
	Epi_riowater_from	The proportion of water areas of the "come-from" epidemic <i>Jiedaos</i>
	Epi_env_to	The environment of epidemic <i>Jiedaos</i> to which commuters traveled (or "go-to" epidemic <i>Jiedaos</i>)
	Epi_popdens_to	The population density of the "go-to" epidemic Jiedaos
	Epi_rioldhous_to	The proportion of old houses of the "go-to" epidemic Jiedaos
	Epi_NDVI_to	The normalized difference vegetation index of the "go-to" epidemic Jiedaos
	Epi_riowater_to	The proportion of water areas of the "go-to" epidemic Jiedaos

Table 1. Detailed description of variables.

2.1.4. Environment Indicators

Previous studies have shown that population density [9,46], housing quality [10], vegetation [10,13], and water areas [47] can contribute to DF diffusion. Here, we used the proportion of the houses built before the 1990s to represent poor housing conditions. Both population data and housing data are from the sixth National Population Census. Vegetation is measured by the normalized difference vegetation index (NDVI). The original 30-m image dataset of NDVI was obtained from Landsat-8 and provided by the Geospatial Data Cloud site, the Computer Network Information Center, and the Chinese Academy of Sciences (http://www.gscloud.cn). The water body data was extracted from OpenStreetMap. The above four environment indicators were further calculated as local environment indicators and epidemic environment indicators. For one *Jiedao*, its local environment refers to its own environment, while its epidemic environment refers to the environment of the epidemic areas that interact with this local place through commuters. Further, we distinguished outbound commuters who traveled to epidemic areas from inbound commuters who came from epidemic areas. Therefore, each *Jiedao* has two types of epidemic environments: *Epi_env_from* and *Epi_env_to* (see Equations (1) and (2)):

$$Epi_env_from_{(i)} = \frac{\sum_{k}^{m} \left[EpiFlowIn_{(ik)} * local_env_{(k)} \right]}{EpiFlowIn_{(i)}}$$
(1)

$$Epi_env_to_{(i)} = \frac{\sum_{k}^{m} \left[EpiFlowOut_{(ik)} * local_env_{(k)} \right]}{EpiFlowOut_{(i)}}$$
(2)

In the above equations, $Epi_env_from_{(i)}$ means the environment of the epidemic areas from which commuters came (or "come-from" epidemic areas) for *Jiedao i*; $Epi_env_to_{(i)}$ means the environment of epidemic areas to which commuters traveled (or "go-to" epidemic areas) for *Jiedao i*. *m* is the total numbers of epidemic *Jiedaos*. $EpiFlowin_{ik}$ means the numbers of commuters from epidemic *Jiedao k* to the *Jiedao i*. $EpiFlowOut_{ik}$ means the numbers of commuters from *Jiedao k*. $local_env_k$ means the local environments of epidemic *Jiedao k*, which were further measured by population density, housing quality, NDVI, and water areas. All the variables used in this study are listed in Table 1.

2.2. Spatial Autocorrelation Analysis

Spatial autocorrelation analysis with the global Moran's I statistics is commonly used to analyze whether an observed spatial pattern, such as a spatial clustering, is formed due to chance. The values of Moran's I would be approximately between +1 (positive autocorrelation) and -1 (negative autocorrelation). Positive spatial autocorrelation means that similar values tended to occur in adjacent areas, while negative autocorrelation implies that nearby locations tend to have dissimilar values. Its local version—the Local Moran's I statistic [48]—maps local clusters and outliers. Based on the local Moran's I, a geographic area can be classified into five categories: high-high, low-low, high-low, low-high, and non-significant. The high-high areas in this study are defined as epidemic areas.

2.3. Geographically Weighted Poisson Regression (GWPR)

The traditional regression model (ordinary least square, OLS) is not applicable to spatial data if spatial autocorrelation exits between independent variables. The geographically weighted regression model (GWR) is a modeling technique that reveals the spatial heterogeneity among the independent and dependent variables, allowing the estimation of the regression coefficient to vary with location [49–51]. It has been widely used in disease mapping [46,52–54]. GWR is originally developed assuming a Gaussian distribution of the dependent variable, so it cannot be applied for count data such as DF cases. Poisson regression model is a standard model for multivariate analysis with count variables [55]. Compared with the general Poisson regression model, the geographically weighted Poisson regression (GWPR) not only quantifies the count variables. By examining the spatial distributions of the

coefficients, we can gain a better understanding of the spatial heterogeneity of the spatial processes [56]. Therefore, GWPR is considered as a suitable model for this research. The following was the equation:

$$\ln(A_i) = \ln(P_i) + \beta_0(u_i, v_i) + \sum_{k=1}^p \beta_k(u_i, v_i) X_{ik} + \varepsilon.$$
 (3)

In the equation, A_i is the amount of DF cases of *Jiedao i*; P_i is the population at risk of *Jiedao i*; (u_i, v_i) is the coordinate of *Jiedao i*; β_k is the coefficient of the *Jiedao k*. explanatory variable in *Jiedao i*, and it is a function changed by location.

In this study, five models are constructed by GWPR in order to test whether and to what extent the commuting flows from/to epidemic areas affect the spread of DF. Model 1 only considers four control variables. Model 2 includes FlowIn besides the four control variables. Model 3 replaces FlowIn with FlowOut. Models 4 and 5 include EpiFlowIn or EpiFlowOut besides the four control variables. At last, analysis of variance (ANOVA) is used to examine whether the environment of epidemic areas could explain the spatial variation of the commuting flows from/to epidemic areas.

3. Results

3.1. Exploratory Analysis

The distribution of DF in Guangzhou in 2014 is shown in Figure 2. The DF in Guangzhou mainly cluster in the conjunction of Baiyun, Tianhe, Yuexiu, Liwan, and Haizhu. The value of the global Moran's I test for DF is 0.17 with p < 0.001, indicating that there is a significant spatial clustering of DF in Guangzhou. Then epidemic areas (high-high clusters with p < 0.001) are detected by the local Moran's I and are shown in red in Figure 2b.



Figure 2. Distribution and cluster analysis of dengue fever in Guangzhou in 2014. (**a**) The spatial distribution of the dengue fever rate; (**b**) epidemic areas identified by local Moran's I.

Table 2 shows the descriptive statistics of the variables used in the regression models. The number of DF cases vary from 0 to 1445, with a mean value of 255 and standard deviance of 258. Commuting flows vary greatly among different *Jiedaos*. The spatial distributions of commuting flows are mapped in Figure 3. The darker the color, the larger the commuting flows. FlowIn (Figure 3a) and FlowOut

(Figure 3b) have a very similar pattern. There are several high general commuting flow areas in the north part, in the central part, and in the south part (Figure 3a,b). While compared to commuting flow, epidemic flows are mainly concentrated in the surrounding areas of the epidemic area (Figure 3c,d).

Categories	Variable	Min	Max	Mean	Std
Dependent variable DF cases		0	1445	255	258
	FlowIn	408	87,067	13,391	13 <i>,</i> 535
Independent variables	FlowOut	197	89,266	13,391	14,293
	EpiFlowIn	45	78,970	3038	8198
	EpiFlowOut	29	79,653	2867	8398
	local_popdens (10,000 people/km ²)	0.01	8.43	1.96	2.09
Control variables	local_rioldhous (%)	0.71	80.19	29.20	21.48
	local_NDVI	0.036	0.284	0.123	0.556
	local_riowater (%)	0.00	46.25	6.79	8.83





Figure 3. The spatial distribution of commuting flow. (a) Spatial distribution of FlowIn; (b) Spatial distribution of FlowOut; (c) Spatial distribution of EpiFlowIn; (d) Spatial distribution of EpiFlowOut.

3.2. GWPR Results

Before GWPR, four control variables and the commuting flow are put into Poisson regression. The result of Poisson regression shows that all the variables are significant with p < 0.05 and the Moran's I test of residuals is nearly 0.2 with p < 0.001, indicating that there is a significant spatial clustering and GWPR is suitable. AIC (Akaike Information Criterion) and percent deviance explained are considered as two important indicators for GWPR model fitness. A model with a lower AIC and a higher percent deviance explained is considered to be better. Table 3 compares the model fitness of the five models.

Table 3.	Geographically	weighted Poisson	regression (GWPR)	model results
----------	----------------	------------------	-------------------	---------------

Models	Variables	Percent Deviance Explained	AIC
Model 1	Four control variables	0.6702	7781.21
Model 2	Four control variables, FlowIn	0.7028	7029.15
Model 3	Four control variables, FlowOut	0.7091	6881.03
Model 4	Four control variables, EpiFlowIn	0.7437	6066.15
Model 5	Four control variables, EpiFlowOut	0.7523	5864.58

Notes: Four control variables include: local_popdens, local_rioldhous, local_NDVI, local_riowater.

First, the null model (Model 1) that only contains the control variables is applied to examine to what extent DF can be explained only by the local environments. Then, the commuting flows are considered into Model 2 and Model 3 in addition to the control variables. The result shows that the percent deviance explained increases by 3% from 0.67 to 0.7, and the AIC declines by 752/900 from 7781 to 7029/6881. After the commuting flows from/to the epidemic areas were included into Model 4 and Model 5, the percent deviance explained increases by 4% or 5% from 0.7 to 0.74/0.75, and the AIC

reduced more (from 7029/6881 to 6066/5864). The results of Model 4 and Model 5 demonstrate a better model fitness, indicating that the commuting flows from/to epidemic areas has a better explanatory power in DF transmission than general commuting flows. The results of the five models answer Question 1.

The impacts of the commuting flows from/to epidemic areas on DF are summarized in Table 4 and mapped in Figure 4. Table 4 shows that the mean value of standardized coefficient for Epiflowin is 0.647 and the median value is 0.727, which is greater than the other coefficients (local_popdens, local_rioldhous, local_NDVI, local_riowater). Similarly, the mean value of the standardized coefficient for EpiFlowout is 0.977, and the median value is 0.842, which is far greater than the other coefficients. This again demonstrates that the commuting flows from/to epidemic *Jiedao* play an extremely important role in explaining DF outbreak (Question 1). Figure 4 shows that the impacts of commuting epidemic flows on DF are not homogeneous; they vary in space. However, the effects are stronger in the south and weaker in the north. This finding answers Question 2.

Models	Variable	Mean	Median	Min	Max	Std
	Pop_density	0.0695	0.0336	-0.7449 -1.4327	1.1678	0.3648
Model 4	NDVI	-0.0807	-0.1155	-0.6141	0.5604	0.1978
	Rio_water EpiFlowin	0.0925 0.6479	0.0724 0.7273	-0.2849 -0.3482	1.4412 2.3390	0.2249 0.5005
	Pop_density Rio_oldbouse	0.0564	0.0361	-0.7548 -1.4238	1.1754	0.3696
Model 5	NDVI Bio sustan	-0.0838	-0.0944	-0.6153	0.5648	0.2001
	EpiFlowout	0.0828	0.0553	-0.2789 -0.0385	5.1149	0.2218





Figure 4. The spatial distribution of coefficient of commuting flow from/to epidemic areas. (a) The coefficient of commuting flow from epidemic areas; (b) The coefficient of commuting flow to epidemic areas.

Why does the effect vary in space? Since the local environmental factors have been controlled, the main reason for the strong or weak effect may be related to two types of epidemic environments (*Epi_env_from* and *Epi_env_to*). To test this assumption, the coefficients of EpiFlowIn and EpiFlowOut are classified into four groups by geometrical interval in ArcGIS 10.3 (Esri, RedLands, CA, USA)

(Figure 4) and ANOVA is applied to find the difference of two types of epidemic environments among four groups. The analysis result is provided in the following section.

3.3. ANOVA Results

The mean *Epi_env_from* value of each group is shown in Table 5. Group 3 of EpiFlowIn has the strongest significant effect (1.219), while Group 1 has the weakest significant effect (0.144). Among the four groups, Group 3 ranks first in Epi_liv_popdens, Epi_liv_rioldhous, and Epi_liv_riowater, while it ranks last in Epi_liv_NDVI, indicating the inbound commuters of Group 3 who live in highly populated epidemic areas with poor housing conditions and more water surfaces and less vegetation. Obviously, the inbound commuters of Group 3 are more likely to be infected at home; thus, it is easy for them to bring the virus out when they go to work.

Group	β-EpiFlowIn	Epi_popdens_from	Epi_rioldhous_from	Epi_NDVI_from	Epi_riowater_from
0	No significance	1.6965 *	18.1868 *	0.0993 *	7.8068 *
1	0.144	1.6510 *	18.9830 *	0.1053 *	4.8462 *
2	0.7083	1.8057 *	23.1628 *	0.0975 *	8.7734 *
3	1.2198	2.3743	32.655	0.0885	10.728

Table 5. The mean value of "*Epi_env_from*" of each group.

* The mean difference of each group compared with Group 3 is significant at the 0.05 level.

The mean *Epi_env_to* value of each group is shown in Table 6. A very similar pattern is observed when compared to Table 5. Among four groups, Group 3 have the strongest effect (1.829), while Group 1 has the weakest significant effect (0.0606). The local commuters of Group 3 who work in highly populated epidemic areas with poor housing conditions and more water surfaces and less vegetation are more likely to be infected at the work place and bring the virus back home. The result of Tables 5 and 6 answer Question 3.

Table 6. The mean value of	"Epi_env_to"	' for each group.
----------------------------	--------------	-------------------

Group	β-EpiFlowout	Epi_popdens_to	Epi_rioldhous_to	Epi_NDVI_to	Epi_riowater_to
0	Nosignificance	1.9231 *	7.7114 *	0.0973 *	7.8192
1	0.0606	1.6194 *	22.3415 *	0.1037 *	3.6239 *
2	0.7232	2.1908 *	27.0545 *	0.0947 *	8.4258
3	1.8289	2.7388	39.1045	0.0866	10.3737

* The mean difference of each group compared with Group 3 is significant at the 0.05 level.

4. Discussion

Human mobility and environment have been considered as two important factors that drive the outbreak and transmission of DF. Since commuting is considered to be the main travel for urban residents, commuters provide many opportunities for the spread of infectious diseases via mosquitos' contact. This study examines the effect of the environment and commuting flows from/to epidemic areas on the spread of DF in 2014 at the *Jiedao* level in Guangzhou by using GWPR and ANOVA.

The analytical results suggest that intra-urban commuting flows from/to epidemic *Jiedaos* have a significant impact on DF diffusion and have a better explanatory power than general commuting flows in DF diffusion. An unexpected finding is that the effect of commuting flows from/to epidemic areas was much greater than the local environmental indicators such as population density, old housing conditions, NDVI, and water areas (Table 4). This finding suggests that intra-urban commuting flows from/to epidemic *Jiedaos* would be the main source of DF diffusion. Similar findings were also found in a few previous studies. One is Wen's study [18], where the author compared commuting and non-commuting DF cases in Tainan City of Taiwan and found that commuting was identified as a significant risk factor contributing to epidemic diffusion. Another recent study conducted by Huang [57] used weekday commuting network to construct an algorithm to analyze the diffusion of

two infectious diseases in Taiwan, and the result suggested the availability of the commuting network in predicting epidemic diseases. Besides, Rajarethinam [17] conducted a study about Zika epidemic in Singapore using mobile phone data and found that there were higher odds of Zika cases being reported in the areas that were visited by people from epidemic clusters.

Besides the effects of commuting flows from/to epidemic areas, this study demonstrates that the effects vary in space and comes up with the reasons for spatial heterogeneity by using ANOVA. The results suggest that the environments of the related epidemic areas contribute to infection diffusion through the move of the commuters. The results show that the Jiedaos whose commuters commuted to/from the epidemic areas that have higher population densities, older buildings, more water surfaces, and less vegetation coverage tend to be more influenced by the commuting flows than the Jiedaos whose commuters commuted to/from the epidemic areas with better conditions. Commuters in environments where mosquitos easily breed are more likely to be infected and bring the virus out when they commute to work or back home. Commuting flow is similar to a "bridge" linking other places to a local place and facilitating the interaction between places. The results suggest that the environment of other places in the "bridge", especially epidemic Jiedaos, could be an important cause of local infection. In contrast, previous studies mainly focused on the local environment [11–13,39–41] but neglected environments of the places, especially epidemic areas that commuters commuted from/to. This study bridges the gap and suggests that the living and working environment of commuters contribute to the source of infection diffusion. One recent study also demonstrates that an individual may often be infected at their home or other places where they spend significant amounts of time, such as their place of work, and homes and work places were suggested as possible transmission sources [58]. This finding suggests that the health management officers should pay attention to commute-related environments when combating a DF outbreak in a local place.

In a word, the findings from this study show us more insights into DF spread and help us better understand the transmission pattern of the disease, which provides useful guidance for targeted control strategies. In the past, DF control mainly relied on mosquito elimination and environmental management. Once an outbreak occurs, large-scale larval habitat elimination or campaigns using administrative boundaries as spatial units were carried out. This approach is time-consuming and less effective. Our results provide targeted strategies of interventions. For example, we would suggest that the spatial targeting should focus on the living and working environments of commuters. This helps us narrow the scope of the control and improve the effective control under limited resources for future outbreaks both in China and elsewhere.

However, this study has some limitations. First, meteorological indicators such as temperature, precipitation, and humidity were not included in this study. However, at a city scale (intra-urban), the meteorological difference among *Jidaos* was little and could be ignored. Second, the time when the mobile phone data were collected is not consistent with the onset of DF. We assumed that human daily commuting patterns do not change much from 2014 to 2016. Third, the spatial scale chosen at the *Jiedao* level is due to the limit of data availability; a finer-grained dataset may be expected in the future research. Last, the behavior of mosquitos was ignored, and mosquitos' density was not included in the analysis. There were few mosquito monitoring sites in Guangzhou in 2014. We assumed that vector density was even and the exposure to mosquitos was the same in each area of the city. In fact, even if human mobility was high, the probability of DF transmission caused by population mobility will be greatly reduced if the exposure to mosquitos was low or the density of mosquitos was low. In future studies, more risk factors and other routine activity places such as shopping or leisure places were expected to be taken into account in order for better understanding the spread of DF.

5. Conclusions

This study illustrates the impact of intra-urban daily commuting flow, especially those from/to epidemic areas, on DF transmission. The results suggest that (1) commuting flows from/to epidemic areas affect the transmission of DF; (2) such effects vary in space; and (3) the spatial variation of the

effects can be explained by the environments of the epidemic areas that commuters commuted from/to. Health management officers should pay attention to commute-related environments when combating a DF outbreak in a local place. These findings have important policy implications for making effective intervention strategies, especially when resources are limited.

Author Contributions: Conceptualization, S.Z. (Shuli Zhou) and S.Z. (Suhong Zhou); Formal analysis, S.Z. (Shuli Zhou); Funding acquisition, S.Z. (Suhong Zhou); Methodology, S.Z. (Suhong Zhou) and L.L.; Resources, M.Z., M.K., J.X. and T.S.; Software, S.Z. (Shuli Zhou); Validation, J.X. and T.S.; Writing—original draft, S.Z. (Shuli Zhou); Writing—revising and editing, S.Z. (Suhong Zhou) and L.L.

Funding: This research was supported under the National Key Research and Development Program of China (2018YFB0505500, 2018YFB0505503), National Natural Science Foundation of China (71961137003; 41871148) and Technology Key Project of Guangzhou (201804020016).

Acknowledgments: We thank Fang Ren from University of Redlands, Junwen Lu, the editor and the anonymous reviewers for helpful comments and suggestions.

Conflicts of Interest: The authors declare no conflict of interest.

References

- 1. Gubler, D.J.; Clark, G.G. Dengue/dengue hemorrhagic fever: The emergence of a global health problem. *Emerg. Infect. Dis.* **1995**, *1*, 55. [CrossRef] [PubMed]
- 2. World Health Organization. *Global Strategy for Dengue Prevention and Control 2012–2020;* WHO: Geneva, Switzerland, 2012.
- Bhatt, S.; Gething, P.W.; Brady, O.J.; Messina, J.P.; Farlow, A.W.; Moyes, C.L.; Drake, J.M.; Brownstein, J.S.; Hoen, A.G.; Sankoh, O. The global distribution and burden of dengue. *Nature* 2013, 496, 504. [CrossRef] [PubMed]
- 4. Castro, M.C.; Wilson, M.E.; Bloom, D.E. Disease and economic burdens of dengue. *Lancet Infect. Dis.* 2017, 17, e70–e78. [CrossRef]
- 5. Pang, T.; Mak, T.K.; Gubler, D.J. Prevention and control of dengue-the light at the end of the tunnel. *Lancet Infect. Dis.* **2017**, *17*, e79–e87. [CrossRef]
- 6. Katzelnick, L.C.; Coloma, J.; Harris, E. Dengue: Knowledge gaps, unmet needs, and research priorities. *Lancet Infect. Dis.* **2017**, *17*, e88–e100. [CrossRef]
- 7. Hsueh, Y.-H.; Lee, J.; Beltz, L. Spatio-temporal patterns of dengue fever cases in Kaoshiung City, Taiwan, 2003–2008. *Appl. Geogr.* **2012**, *34*, 587–594. [CrossRef]
- 8. Khormi, H.M.; Kumar, L. Modeling dengue fever risk based on socioeconomic parameters, nationality and age groups: GIS and remote sensing based case study. *Sci. Total Environ.* **2011**, *409*, 4713–4719. [CrossRef]
- 9. Delmelle, E.; Hagenlocher, M.; Kienberger, S.; Casas, I. A spatial model of socioeconomic and environmental determinants of dengue fever in Cali, Colombia. *Acta Trop.* **2016**, *164*, 169. [CrossRef]
- Cao, Z.; Liu, T.; Li, X.; Wang, J.; Lin, H.; Chen, L.; Wu, Z.; Ma, W. Individual and interactive effects of socio-ecological factors on dengue fever at fine spatial scale: A geographical detector-based analysis. *Int. J. Environ. Res. Public Health* 2017, 14, 795. [CrossRef]
- 11. Qi, X.; Wang, Y.; Li, Y.; Meng, Y.; Chen, Q.; Ma, J.; Gao, G.F. The Effects of Socioeconomic and Environmental Factors on the Incidence of Dengue Fever in the Pearl River Delta, China, 2013. *PLoS Negl. Trop. Dis.* **2015**, *9*, e0004159. [CrossRef]
- 12. Ren, H.; Zheng, L.; Li, Q.; Yuan, W.; Lu, L. Exploring Determinants of Spatial Variations in the Dengue Fever Epidemic Using Geographically Weighted Regression Model: A Case Study in the Joint Guangzhou-Foshan Area, China, 2014. *Int. J. Environ. Res. Public Health* **2017**, *14*, 1518. [CrossRef] [PubMed]
- Huang, C.-C.; Tam, T.; Chern, Y.-R.; Lung, S.-C.; Chen, N.-T.; Wu, C.-D. Spatial Clustering of Dengue Fever Incidence and Its Association with Surrounding Greenness. *Int. J. Environ. Res. Public Health* 2018, 15, 1869. [CrossRef] [PubMed]
- Chen, Y.; Zhao, Z.; Li, Z.; Li, W.; Li, Z.; Guo, R.; Yuan, Z. Spatiotemporal Transmission Patterns and Determinants of Dengue Fever: A Case Study of Guangzhou, China. *Int. J. Environ. Res. Public Health* 2019, 16, 2486. [CrossRef] [PubMed]
- 15. Yue, Y.; Liu, Q. Exploring Epidemiological Characteristics of Domestic Imported Dengue Fever in Mainland China, 2014–2018. *Int. J. Environ. Res. Public Health* **2019**, *16*, 3901. [CrossRef] [PubMed]

- Zhu, G.; Liu, T.; Xiao, J.; Zhang, B.; Song, T.; Zhang, Y.; Lin, L.; Peng, Z.; Deng, A.; Ma, W.; et al. Effects of human mobility, temperature and mosquito control on the spatiotemporal transmission of dengue. *Sci. Total Environ.* 2019, 651, 969–978. [CrossRef]
- 17. Rajarethinam, J.; Ong, J.; Lim, S.-H.; Tay, Y.-H.; Bounliphone, W.; Chong, C.-S.; Yap, G.; Ng, L.-C. Using Human Movement Data to Identify Potential Areas of Zika Transmission: Case Study of the Largest Zika Cluster in Singapore. *Int. J. Environ. Res. Public Health* **2019**, *16*, 808. [CrossRef]
- Wen, T.; Lin, M.; Fang, C. Population Movement and Vector-Borne Disease Transmission: Differentiating Spatial–Temporal Diffusion Patterns of Commuting and Noncommuting Dengue Cases. *Ann. Assoc. Am. Geogr.* 2012, 102, 1026–1037. [CrossRef]
- 19. Stoddard, S.T.; Morrison, A.C.; Vazquezprokopec, G.M.; Paz, S.V.; Kochel, T.J.; Kitron, U.; Elder, J.P.; Scott, T.W. The role of human movement in the transmission of vector-borne pathogens. *PLoS Negl. Trop. Dis.* **2009**, *3*, e481. [CrossRef]
- 20. Teurlai, M.; Huy, R.; Cazelles, B.; Duboz, R.; Baehr, C.; Vong, S. Can human movements explain heterogeneous propagation of dengue fever in Cambodia? *PLoS Negl. Trop. Dis.* **2012**, *6*, e1957. [CrossRef]
- 21. Stoddard, S.T.; Forshey, B.M.; Morrison, A.C.; Paz-Soldan, V.A.; Vazquez-Prokopec, G.M.; Astete, H.; Reiner, R.C.; Vilcarromero, S.; Elder, J.P.; Halsey, E.S. House-to-house human movement drives dengue virus transmission. *Proc. Natl. Acad. Sci. USA* **2013**, *110*, 994–999. [CrossRef]
- 22. Zhu, G.; Xiao, J.; Zhang, B.; Liu, T.; Lin, H.; Li, X.; Song, T.; Zhang, Y.; Ma, W.; Hao, Y. The spatiotemporal transmission of dengue and its driving mechanism: A case study on the 2014 dengue outbreak in Guangdong, China. *Sci. Total Environ.* **2018**, 622–623, 252–259. [CrossRef] [PubMed]
- 23. Adams, B.; Kapan, D.D. Man bites mosquito: Understanding the contribution of human movement to vector-borne disease dynamics. *PLoS ONE* 2009, *4*, e6763. [CrossRef] [PubMed]
- 24. Bengtsson, L.; Gaudart, J.; Lu, X.; Moore, S.; Wetter, E.; Sallah, K.; Rebaudet, S.; Piarroux, R. Using mobile phone data to predict the spatial spread of cholera. *Sci. Rep.* **2015**, *5*, 8923. [CrossRef] [PubMed]
- 25. Wesolowski, A.; Eagle, N.; Tatem, A.J.; Smith, D.L.; Noor, A.M.; Snow, R.W.; Buckee, C.O. Quantifying the impact of human mobility on malaria. *Science* **2012**, *338*, 267–270. [CrossRef] [PubMed]
- 26. Weber, J.; Kwan, M.P. *Mobility and Travel Activity Patterns*; Elsevier Inc.: Amsterdam, The Netherlands, 2015; pp. 636–639.
- 27. Chapin, F.S. *Human Activity Patterns in the City: Things People do in Time and in Space;* Wiley-Interscience: Hoboken, NJ, USA, 1974; Volume 13.
- 28. Golledge, R.G. Spatial Behavior: A Geographic Perspective; Guilford Press: New York, NY, USA, 1997.
- 29. Chai, Y.; Zhang, X.; Sun, D. A study on life circle planning based on space time behavioural analysis: A case study of Beijing. *Urban Planning Forum.* **2015**, *3*, 61–69.
- 30. Yuan, J.-D.; Sun, Z.-J.; Zhang, N.; Zhao, Z. Reconstruction of Urban Region System in China Based on Daily Life Circle. *Sci. Geogr. Sin.* **2005**, *1*, 17–22.
- 31. Zuopeng, X.; Yanwei, C.; Yan, Z. Overseas Life Circle Planning And Practice. Planners 2014, 10, 89–95.
- 32. Zhou, S.; Liu, Y.-L. The situation and transition of jobs-housing relocation in Guangzhou, China. *Acta Geogr. Sin.* **2010**, *65*, 191–201.
- 33. Zhou, S.; Yan, X. The Impact of Commuters' Travel Pattern on Urban Structure: A Case Study in Some Typical Communities in Guangzhou. *Acta Geogr. Sin.* **2006**, *61*, 179–189.
- 34. Zhilin, L.; Maojun, W. Job accessibility and its impacts on commuting time of urban residents in Beijing: From a spatial mismatch perspective. *Acta Geogr. Sin.* **2011**, *66*, 457–467.
- 35. Wesolowski, A.; Qureshi, T.; Boni, M.F.; Sundsøy, P.R.; Johansson, M.A.; Rasheed, S.B.; Engø-Monsen, K.; Buckee, C.O.; Singer, B.H. Impact of human mobility on the emergence of dengue epidemics in Pakistan. *Proc. Natl. Acad. Sci. USA* **2015**, *112*, 11887–11892. [CrossRef] [PubMed]
- 36. Bengtsson, L.; Lu, X.; Thorson, A.; Garfield, R.; Von Schreeb, J. Improved response to disasters and outbreaks by tracking population movements with mobile phone network data: A post-earthquake geospatial study in Haiti. *PLoS Med.* **2011**, *8*, e1001083. [CrossRef] [PubMed]
- 37. Mao, L.; Yin, L.; Song, X.; Mei, S. Mapping intra-urban transmission risk of dengue fever with big hourly cellphone data. *Acta Trop.* **2016**, *162*, 188–195. [CrossRef] [PubMed]
- 38. Wen, T.-H.; Tsai, C.-T. Evaluating the role of disease importation in the spatiotemporal transmission of indigenous dengue outbreak. *Appl. Geogr.* **2016**, *76*, 137–146. [CrossRef]

- 39. Chuang, T.W.; Ng, K.C.; Nguyen, T.L.; Chaves, L.F. Epidemiological characteristics and space-time analysis of the 2015 dengue outbreak in the metropolitan region of Tainan city, Taiwan. *Int. J. Environ. Res. Public Health* **2018**, *15*, 396. [CrossRef] [PubMed]
- 40. Teurlai, M.; Menkès, C.E.; Cavarero, V.; Degallier, N.; Descloux, E.; Grangeon, J.P.; Guillaumot, L.; Libourel, T.; Lucio, P.S.; Mathieu-Daudé, F.; et al. Socio-economic and Climate Factors Associated with Dengue Fever Spatial Heterogeneity: A Worked Example in New Caledonia. *PLoS Negl. Trop. Dis.* **2015**, 9. [CrossRef] [PubMed]
- Zellweger, R.M.; Cano, J.; Mangeas, M.; Taglioni, F.; Mercier, A.; Despinoy, M.; Menkès, C.E.; Dupont-Rouzeyrol, M.; Nikolay, B.; Teurlai, M. Socioeconomic and environmental determinants of dengue transmission in an urban setting: An ecological study in Nouméa, New Caledonia. *PLoS Negl. Trop. Dis.* 2017, 11. [CrossRef]
- Xiao, J.-P.; He, J.-F.; Deng, A.-P.; Lin, H.-L.; Song, T.; Peng, Z.-Q.; Wu, X.-C.; Liu, T.; Li, Z.-H.; Rutherford, S. Characterizing a large outbreak of dengue fever in Guangdong Province, China. *Infect. Dis. Poverty* 2016, *5*, 44. [CrossRef]
- 43. *Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control: New Edition;* World Health Organization: Geneva, Switzerland, 2009; p. 990.
- 44. Chong, S.C.; Teoh, W.M.Y.; Qi, Y. Comparing customer satisfaction with China mobile and China telecom services: An empirical study. *J. Dev. Areas* **2015**, *49*, 247–262. [CrossRef]
- 45. Song, G.; Bernasco, W.; Liu, L.; Xiao, L.; Zhou, S.; Liao, W. Crime Feeds on Legal Activities: Daily Mobility Flows Help to Explain Thieves' Target Location Choices. *J. Quant. Criminol.* **2019**, *35*, 831–854. [CrossRef]
- 46. Lin, C.H.; Wen, T.H. Using Geographically Weighted Regression (GWR) to Explore Spatial Varying Relationships of Immature Mosquitoes and Human Densities with the Incidence of Dengue. *Int. J. Environ. Res. Public Health* **2011**, *8*, 2798–2815. [CrossRef] [PubMed]
- Tian, H.; Huang, S.; Zhou, S.; Bi, P.; Yang, Z.; Li, X.; Chen, L.; Cazelles, B.; Yang, J.; Luo, L.; et al. Surface water areas significantly impacted 2014 dengue outbreaks in Guangzhou, China. *Environ. Res.* 2016, 150, 299–305. [CrossRef] [PubMed]
- 48. Anselin, L. Local indicators of spatial association-LISA. Geogr. Anal. 1995, 27, 93-115. [CrossRef]
- 49. Brunsdon, C.; Fotheringham, A.S.; Charlton, M.E. Geographically weighted regression: A method for exploring spatial nonstationarity. *Geogr. Anal.* **1996**, *28*, 281–298. [CrossRef]
- 50. Fotheringham, A.S.; Brunsdon, C.; Charlton, M. *Geographically Weighted Regression: The Analysis of Spatially Varying Relationships*; John Wiley & Sons: Hoboken, NJ, USA, 2003.
- 51. Fotheringham, A.S.; Charlton, M.E.; Brunsdon, C. Geographically weighted regression: A natural evolution of the expansion method for spatial data analysis. *Environ. Plan. A* **1998**, *30*, 1905–1927. [CrossRef]
- 52. Chan, T.-C.; Chiang, P.-H.; Su, M.-D.; Wang, H.-W.; Liu, M.S.-Y. Geographic disparity in chronic obstructive pulmonary disease (COPD) mortality rates among the Taiwan population. *PLoS ONE* **2014**, *9*, e98170. [CrossRef] [PubMed]
- Goovaerts, P.; Xiao, H.; Adunlin, G.; Ali, A.; Tan, F.; Gwede, C.K.; Huang, Y. Geographically-weighted regression analysis of percentage of late-stage prostate cancer diagnosis in Florida. *Appl. Geogr.* 2015, 62, 191–200. [CrossRef]
- 54. Soljak, M.; Samarasundera, E.; Indulkar, T.; Walford, H.; Majeed, A. Variations in cardiovascular disease under-diagnosis in England: National cross-sectional spatial analysis. *BMC Cardiovasc. Disord.* **2011**, *11*, 12. [CrossRef]
- 55. Lovett, A.; Flowerdew, R. Analysis of count data using Poisson regression. *Prof. Geogr.* **1989**, *41*, 190–198. [CrossRef]
- 56. Nakaya, T.; Fotheringham, A.S.; Brunsdon, C.; Charlton, M. Geographically weighted Poisson regression for disease association mapping. *Stat. Med.* **2005**, *24*, 2695–2717. [CrossRef]
- 57. Huang, C.-Y.; Wen, T.-H.; Fu, Y.-H.; Tsai, Y.-S. EpiRank: Modeling Bidirectional Disease Spread in Asymmetric Commuting Networks. *Sci. Rep.* **2019**, *9*, 5415. [CrossRef] [PubMed]
- 58. Prem, K.; Lau, M.S.Y.; Tam, C.C.; Ho, M.Z.J.; Ng, L.C.; Cook, A.R. Inferring who-infected-whom-where in the 2016 Zika outbreak in Singapore-A spatio-temporal model. *J. R. Soc. Interface* **2019**, 16. [CrossRef] [PubMed]



© 2019 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).