



The spatiotemporal transmission of dengue and its driving mechanism: A case study on the 2014 dengue outbreak in Guangdong, China

Guanghu Zhu^{a,b}, Jianpeng Xiao^a, Bing Zhang^a, Tao Liu^a, Hualiang Lin^a, Xing Li^a, Tie Song^c, Yonghui Zhang^c, Wenjun Ma^{a,*}, Yuantao Hao^{b,*}

^a Guangdong Provincial Institute of Public Health, Guangdong Provincial Center for Disease Control and Prevention, Guangzhou 511430, China

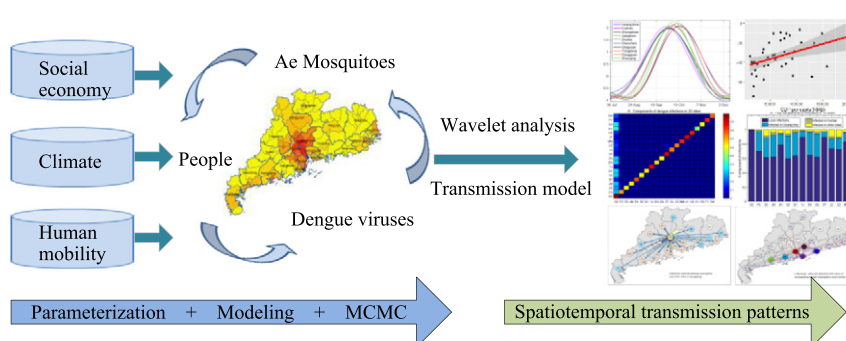
^b Department of Medical Statistics and Epidemiology, School of Public Health, Sun Yat-sen University, Guangzhou 510080, China

^c Guangdong Provincial Center for Disease Control and Prevention, Guangzhou 511430, China

HIGHLIGHTS

- Wavelet analysis and a new transmission model are used to infer dengue transmission patterns and driving mechanism.
- Temporal sequence and spatial correlation of dengue transmission are observed among cities.
- Infectivity network is proposed for clarifying dengue driving forces.
- Guangzhou and Foshan as the hubs played a significant role in driving dengue transmission intensity.

GRAPHICAL ABSTRACT



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ABSTRACT

Dengue transmission is a complex spatiotemporal process with hidden interactions between hosts, vectors, and viruses as well as environment. This study aims to identify the transmission patterns and the driving mechanism that contributed to the dengue epidemics occurred in Guangdong Province of China in 2014. Based on the city-specific epidemiological, meteorological, demographic and geographic data, we first performed wavelet analysis and then integrated the key dynamics (i.e., mosquito population dynamics, human movement, virus transmission, and parameter estimation) into a transmission model. Using these methods, we found a clear temporal sequence and correlation of dengue transmission between cities, and such relationship is associated with socioeconomic factors. We further obtained the specific component of dengue incidence data in each city, and presented the underlying infectivity networks for characterizing how dengue transmits from one location to another. The results showed that the communication of in-out infections with Guangzhou and Foshan could be responsible for the large-scale diffusion of dengue epidemics in Guangdong in 2014. Our findings can offer new insights into how to improve the predictability and risk assessment of dengue transmission.

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1. Introduction

Dengue is a mosquito-borne febrile disease caused by a flavivirus with four serotypes (Guzman et al., 2010). Over the past few decades,

dengue has been gradually spreading throughout tropical and sub-tropical regions, resulting in an increased frequency of epidemics and endemicity in Americas, South-East Asia and Western Pacific regions (Guzman et al., 2010; WHO, 2012). The worldwide incidence has increased 30-fold compared with 50 years ago (WHO, 2012), with an estimation of 390 million dengue infections per year (Bhatt et al., 2013). Now dengue is endemic in more than 120 countries and

* Corresponding authors.

E-mail addresses: mawj@gdiph.org.cn (W. Ma), haoyt@mail.sysu.edu.cn (Y. Hao).

has posed half of the world's population being at risk of infections. Current frequent emergence and rapid expansion of dengue fever probably result from urbanization, population growth, climatic variation, convenient transportation, and global trade (Guzman et al., 2010; Bhatt et al., 2013; WHO, 2009).

In 1978, a dengue outbreak in Guangdong Province signaled its reemergence in mainland China after being absent for about 30 years (Wu et al., 2010; Lai et al., 2015). Since then, dengue epidemics have shown potentially upward trends both in extent and severity in China, and Guangdong has always been the hardest-hit area with cases reported every year since 1997 (Wu et al., 2010; Sang et al., 2015a). Particularly in 2014, an unprecedented explosive outbreak of dengue occurred in Guangdong, where the number of cases was more than 3 times of the total number in previous 20 years (Xiao et al., 2016). Several studies have described the epidemiological characteristics of this outbreak and explored the possible driving factors (Lai et al., 2015; Xiao et al., 2016; Li et al., 2016; Cheng et al., 2016a; Zhu et al., 2016; Sang et al., 2015b; Tian et al., 2016; Lin et al., 2016). However, some scientific questions such as the spatiotemporal transmission process among regions and transmission dynamics behind the outbreak remain unclear.

Previous studies have confirmed that a series of socioeconomic, environmental and climatic factors are closely related with dengue spatiotemporal transmission by either facilitating virus amplification/replacement or favoring vectors survival (Descoux et al., 2012; Johansson et al., 2009; Khormi and Kumar, 2011; Delmelle et al., 2016; Eastin et al., 2014). Since vector flight range is less than 400 m (WHO, 2009), human movement was recognized as an important spatiotemporal driver of transmission dynamics for dengue diffusion (Stoddard et al., 2013; Reiner et al., 2014; Sanna and Hsieh, 2017), which can introduce dengue viruses into previously low-transmission or dengue-free areas. In China, dengue is still an imported disease (Sang et al., 2015a). Recent studies suggested that imported cases, climate, urbanization, and human behaviors were the key factors leading to the dengue outbreak in Guangdong in 2014 (Li et al., 2016; Cheng et al., 2016a; Zhu et al., 2016; Sang et al., 2015b; Tian et al., 2016). Yet less attention has been devoted to explore its spatiotemporal transmission mechanism.

Epidemiological models have been widely applied for understanding dengue transmission patterns (Racloz et al., 2012; Guzman and Harris, 2015; Reiner et al., 2013). These models, either based on mapping techniques and statistical methods (Kraemer et al., 2015; Khormi and Kumar, 2011; Cheng et al., 2016b), or dynamic models and computational techniques (Zhu et al., 2016; Cheng et al., 2016a; Shi et al., 2014; Tang et al., 2016), can help to (i) determine the hot spots and cluster of dengue epidemics (Cheng et al., 2016b); (ii) evaluate the association between factors and dengue incidence (Johansson et al., 2009; Khormi and Kumar, 2011; Delmelle et al., 2016); (iii) identify the driving factors of dengue outbreak and the transmission route (Zhu et al., 2016; Shi et al., 2014; Li et al., 2016; Cheng et al., 2016a); and (iv) predict dengue epidemics (Eastin et al., 2014; Descoux et al., 2012; Sang et al., 2015b). However, some reviews indicated that existing studies have not sufficiently accounted for the spatiotemporal features of dengue transmission (Racloz et al., 2012; Reiner et al., 2013), and the concepts of networks and social distance are seldom incorporated into the mosquito-borne pathogen theory (Smith et al., 2014).

In order to fill aforementioned knowledge gap, we integrated epidemiological, meteorological, demographic and geographic data, and employed the methods of wavelet approach and mathematical models, to explore the hidden transmission patterns and the driving mechanism of dengue infections across the cities of Guangdong in 2014. First, wavelet analysis was used to decompose and reconstruct incidence data, and thus help to reveal the temporal association of dengue incidence among different cities. Second, based on the Ross-Macdonald theory (Reiner et al., 2013; Smith and McKenzie, 2004; Smith et al., 2007), a transmission model was developed to

further infer the hidden dynamics of dengue transmission. The proposed model closely coupled four key parts necessary for describing the integrated dynamics of the system, namely, those representing mosquito population dynamics, human movement, virus transmission, and parameters estimation. Thereinto, the density and activity of vectors was estimated by climatic and demographic information; human movement was estimated from a modified radiation model proposed by Yan et al. (2014); and the underlying transmission parameters was quantified by fitting the model to real-world observations by using Markov chain Monte Carlo (MCMC) method.

2. Materials and methods

2.1. Study areas

Guangdong Province (20°13'N to 25°31'N and 109°39'E to 117°19'E) is located in South China with 179,800 km². Its population size is about 10.7 million, ranking first in China. The climate in Guangdong is humid and subtropical, where the annual mean temperature is 21.8 °C and the annual accumulate precipitation is 1789 mm. There are 21 prefecture-level cities and 128 counties/districts in Guangdong Province (see Figs. S1 and 1). The Pearl River Delta (PRD) region, which includes seven cities (Guangzhou, Shenzhen, Foshan, Dongguan, Zhongshan, Zhuhai and Jiangmen), is one of the most developed and densely-populated area in China. The PRD region accounted for about 90% of the dengue cases in Guangdong in 2014.

2.2. Data collection

The information on dengue cases was extracted from the Guangdong Provincial Center for Disease Control and Prevention. The data included residence and the dates of illness onset. The economic and demographic data (i.e., GDP and resident population size) in each region was collected from the 2015 Guangdong Statistical Yearbook. Due to the short period of our study, it is supposed that the demographic data in each city is stable, but some of the inhabitants in certain city (registered as residents) may travel to other cities and then return back to the original places. The locations of these cities and their mutual distances (between the downtowns of the cities) were obtained from Baidu map using GIS technology. The migrant population (i.e., people who migrate for a limited period of time) in each city was derived from the 2010 population census of Guangdong Province. Weekly temperature was extracted from Chinese Meteorological Network (<http://data.cma.cn/>).

2.3. Analysis methods

2.3.1. Wavelet approach

We used wavelet analysis to detect the spatiotemporal association of dengue transmission among different cities and counties/districts. Wavelet analysis allows decomposition and reconstruction of multiple time series into time-frequency space, and permits analysis of the transient nature and temporal association of these series (Cazelles et al., 2007; Stewart-Ibarra et al., 2014). This method is based on the wavelet transform that decomposes a signal $x(t)$ by incorporating a dilated and translated function (called 'mother wavelets') $\psi(t)$:

$$W_x(a, \tau) = \frac{1}{\sqrt{a}} \int_{-\infty}^{\infty} x(t) \psi^* \left(\frac{t - \tau}{a} \right) dt,$$

where the asterisk denote the complex conjugate form. Parameters a and τ denote the dilation (scale factor) and translation (time shift), respectively. Here we used Morlet wavelet as the mother wavelet,

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