Dengue fever transmission between construction site and its surrounding communities in China

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Research

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Running title: DF transmission between construction site and communities

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Abstract

Background: Due to more mosquito habitats and the lack of basic mosquito control facilities, construction sites are more likely to have secondary cases after case importation, which may increase the number of cases in the neighborhood community and the chance of community transmission. This study aims to investigate how to effectively reduce the dengue transmission in construction sites and the neighboring communities.

Methods: Susceptible-Exposed-Infectious/Asymptomatic-Recovered (SEIAR) model of human and SEI model of mosquitoes were developed to estimate the transmission of dengue virus between human and mosquitoes within the construction site and within a neighboring community, as well between them. With the calibrated model, we further estimated the effectiveness of different intervention scenarios targeting at reducing the transmissibility at different locations (i.e. construction sites and community) with the total attack rate (TAR) and the duration of the outbreak (DO).

Results: A total of 102 construction site-related and 131 community-related cases of dengue were reported in our study area. Without intervention, the cases related to the construction site and the community rose to 156 (TAR: 31.25%) and 10796 (TAR: 21.59%). When cutting off the transmission route from mosquitoes to human in the community, the community cases decreased to a minimum of 33 compared with other simulated scenarios (TAR: 0.068%, DO: 60 days). If the transmission route from infectious mosquitoes in the community, and from the construction site to susceptible people on the site, was cut off at the same time, the cases in the construction site dropped to a minimum of 74 (TAR: 14.88%, DO: 66 days).

Conclusions: To control the outbreak effectively for both the construction site and the community, interventions needed to be taken within the community and from the community to the construction site. If interventions were only taken within the construction site, this could not reduce the number of cases on the construction site. If interventions were taken within the construction site or between the construction site and the community, this could not lead to a reduction in the number of cases in the community.

Key words: Dengue; Outbreak; Mathematical model; Construction site; Community

Introduction

Dengue fever (DF) is one of the most rapidly spreading mosquito-borne diseases in the world. It is caused by four different serotypes of dengue virus (DENV 1 - 4) transmitted by female *Aedes* mosquitoes [1, 2]. The incidence rate has increased 30 times over the past 50 years. More than 100 countries are facing with the threat of DF. According to an estimation made in 2013, the total number of people infected worldwide reaches 390 million each year, which brings a heavy health burden to governments and individuals[3, 4, 5]. The incidence rate of DF in China ranges from 0.0091 to 3.4581 per 100,000 people, with a total of 52,749 new dengue cases between 2009–2014 [6]. The urbanization has been provided many opportunities for *Aedes* mosquitoes reproduction, thus it has become an important risk factor of DF. The main one is the availability of containers used as breeding sites, such as waste, tires and water storage tanks[7], population density and mobility also facilitate the propagation of the virus[2, 8]. These environmental conditions and the lack of basic mosquito control facilities have made construction sites in high-risk areas for outbreaks. Moreover, after case importation, construction sites are more likely to produce secondary cases, which will increase the number of cases entering the neighborhood community and the chance of community transmission. A study published in 2018 suggested that the overall case burden of construction site-associated clusters was significantly high through three case studies of large construction site-associated dengue clusters during 2013–2016[9].

Guangdong is a subtropical province in southern China, highlighted by urbanization and dense population. From 1949 to 1977, there were no reports of DF cases in China[10]. The first outbreak of DF was reported in 1978 in Foshan City, Guangdong Province, in which has the highest infection rate of DF in Mainland China since then[11]. Over 85% of domestic dengue cases in China occurred in the Guangdong province during 2008–2018[12]. The most serious DF outbreak in China in the past 20 years was reported in June 2014, in Guangdong Province, and , more than 45,000 people were infected [10, 13]. However, the Chinese government has not developed an effective vaccination to prevent the disease until now[14, 15]. The dengue serotypes detected in Guangzhou were mainly DENV 1 and DENV 2[16]. *Aedes albopictus* mosquitoes, which was densely distributed in Guangdong province, was considered the main vector. Due to the absence of specific treatment and effective vaccination for DF, vector control remains the only strategy to prevent the disease[17].

In 2018, a serious DF outbreak occurred in Zhanjiang Prefecture, Guangdong Province. From the first indigenous DF case reported on July 19 to the last case on October 28, Zhanjiang Prefecture reported a total of 467 cases, which was 7.9 times more compared to the number of DF cases in Zhanjiang Prefecture in 2017 (59 cases). The cases in Zhanjiang Prefecture were mainly occurred in the Community A of Chikan District, which contributed to 50% (233 cases) of the total cases. The transmission spread from the construction site A (102 cases) to the surrounding residential areas (131 cases). The distribution of DF cases in Chikan District and the remote sensing images of Community A are shown in Fig. 1. The red dot in the middle of Chikan District represents the construction site A.

Due to the scope and severity of this outbreak, the main content of our research is to investigate the transmissibility of DF on the construction site and the surrounding communities, and practical significance of implementing interventions in different regions.

Prior to this, there have been many studies on DF using mathematical models[18, 19, 20, 21]. Esteva and Vargas established a mathematical model to analyze the role of vertical transmission and mechanical transmission due to interrupted feeding in the dynamics of dengue disease[18]. Favier and Schmit established a model that underlined the critical influence of the spatial structure of population scale, and stressed that contact heterogeneity must be considered to reproduce the epidemiological curve[19]. Li *et al* presented a temperature-driven coupled entomological-epidemiological model and assessed the role of seasonal vector dynamics and infection importation in driving dengue outbreaks[20]. Hartley *et al* introduced seasonally-varying parameters into a mathematical model of the transmission dynamics of dengue viruses in a step-wise way[22]. However, there has never been a model that involves the interaction between the construction site and the community for DF transmission. Mathematical models have also been applied for other mosquito-borne diseases, Ghosh, M. *et al* developed a deterministic model governed by a system of nonlinear differential equations to assess the effects of recurrent malaria, global asymptotic dynamics of the autonomous model and the non-autonomous model with time-dependent control strategies were applied to make the best plan for malaria control[23]. Zika virus transmission model with three nonlinear forces of infection were formulated by Olaniyi, S. *et al*, and the optimal control theory of Pontryagin's maximum principle is used to figure out the best measures to control the spread of Zika virus disease[24].

In this study, we developed an Susceptible-Exposed-Infectious/Asymptomatic-Removed (SEIAR) model for the host and an Susceptible-Exposed-Infectious (SEI) model for the vector, to simulate the transmission dynamics of dengue virus and evaluate the effectiveness of different intervention measures[21]. This is the first model investigating the transmissibility in the construction site and the community and analyzing their interactions.

Methods

Study site

Zhanjiang Prefecture is one of the prefecture-level cities of Guangdong Province. Chikan District (110°20' to 110°21'E, 21°14' to 21°19'N) is the central area of Zhanjiang Prefecture. It has a subtropical maritime monsoon climate — the summer is long and the winter is short, the rainy season is accompanied by high temperature. The population is about 300,000 and the land area is 79 square kilometers, with a yearly rain-fall of 1596 mm. Our research area includes a community (Community A) and a nearby construction site A. Community A is located in the northeast-central Chikan District, with a dense population of about 50,000 people and high mobility, which facilitates the spread of DF. The construction site A is located in the center of Community A. There are about 500 permanent workers, most of whom work at the construction site during the day and stay at the surrounding communities to rest at night. *Ae. albopictus* is the only vector species in this region for DF[25].

Disease data

In this outbreak, 447 cases were locally acquired, 15 cases were imported from other provinces in mainland China, and 5 cases were imported from abroad. An indigenous case is defined as those who infected DF and did not leave the province (current address) within 14 days before the onset of disease. An imported case of DF was defined as the infected patients been to a dengue endemic region within 14 days before the onset of illness. [26].

All the DF cases were identified following the diagnostic criteria (WS216-2008) announced by the National Health Commission (formerly named as the Ministry of Health) of the People's Republic of China[27].

a) Clinically diagnosed case: a suspected case with leucopenia or thrombocytopenia; or a suspected case with IgG or IgM positive in serum detection

b) Laboratory confirmed case: a suspected case if dengue virus (DENV) Ribonucleic Acid (RNA) was detected in the serum by real-time polymerase chain reaction (PCR); or if virus was isolated from the acute infection patient's blood, tissue or cerebrospinal fluid; or if the IgG titer in recovery period was 4 times higher than that in acute period.

We obtained all clinically diagnosed and laboratory confirmed cases related to this DF outbreak from the field epidemiological investigation conducted by Guangdong Center for Disease Control and Prevention (CDC). Demographic information included age, gender, address, and occupation of the cases. The study period was defined as from August 17 — the reporting date of the putative index case — to October 2 — the reporting date of the last case in Community A. We considered the case reported on August 17 in Zhanjiang Prefecture as the index case in our study area, given the facts that first, the extrinsic incubation period of DF is about 10 days[21] and the time interval between this case and the first case in our study area on construction site A on August 27 falls into the typical range of the serial interval of dengue; second, this case lives in Community B, Chikan District, which is <1km away from the construction site A; and third, the case visited the construction site several times before August 27. The residential location and activity path of the index case were shown in Fig. 1. Local CDC started interventions, including case isolation, environmental cleaning, spraying insecticides and surveillance of Breteau Index on September 12, which may change the transmissibility of the disease. Therefore, we used the data collected before September 12 in our model to simulate the transmissibility without intervention.

Model structure

We developed a model to simulate the transmission of dengue virus within the residential areas and the construction site A in Community A, and between them. The model was based on our previous studies which was used to study the dynamic transmission of mosquito-borne diseases [21, 25]. The model structure is shown in Fig. 2. In the model, individuals on the construction site can be divided into the following five parts: S_{ps}, susceptible; E_{ps}, exposed; I_{ps}, infectious; A_{ps}, asymptomatic; R_{ps}, removed. The subscript *ps* represents people on the construction site. I_{IS} represents imported cases into the construction site. Mosquitoes on the construction site can be divided into the following three parts: S_{ms}, susceptible; E_{ms}, exposed; I_{ms}, infectious. The subscript *ms* represents mosquitoes on the construction site. N_{ms} represents the sum of three mosquito parts. Each part of the SEIAR-SEI model in the residential areas of the community represents the same meaning as the site. We simplified the residential areas of the community as community. The human in community were divided into S_{pc}, susceptible; E_{pc}, exposed; I_{pc}, infectious; A_{pc}, asymptomatic; R_{pc}, removed. The subscript *pc* represents people in the the community. Mosquitoes in the community can be divided into the following three parts: S_{mc}, susceptible; E_{mc} exposed; I_{mc}, infectious. The subscript *mc* represents mosquitoes in the community.

The model is based on the following assumptions or facts:

a) The imported case transmitted the virus to a construction worker, who further transmitted it to other construction workers and community residents. The first case occurred in the residential areas around the construction site A was on September 8, which was 13 days later than the first case of the construction site A., The initial value of the number of imported cases I_{IS} was set to 1.

b) The susceptible individuals become either asymptomatic or symptomatic after a latent period or incubation period. The parameter *q* represents the proportion of asymptomatic individuals, so the *(1-q) E* exposed individuals would eventually enter the *I* compartment, while the other *qE* exposed individuals would end up in the *A* compartment.

c) Human recover with immunity, while infected mosquitoes are infectious till death.

d) According to the investigation of the Field Epidemiology, construction workers stayed at the construction site A during the day mostly returned to their homes in Community A after work, while residents of the community that are not construction workers are not allowed to enter the construction site due to safety consideration.

e) Mosquitoes in the construction site only stay there and cannot fly to the community, and vice versa, since studies have shown that the mean flight distance of *Ae. albopictus* rarely exceed 75 meters[28, 29]. Therefore, the movement of construction workers is the only way to transmit the virus between the construction site and the community.

The mathematical model is described by the following ordinary differential equations (ODE):

$$\frac{dI_{Is}}{dt} = -\varepsilon I_{Is}$$

$$\frac{dS_{ms}}{dt} = a_s c_s (N_{ms} - n_s I_{ms}) - \beta_{Is} S_{ms} I_{Is} - \beta_{psms} S_{ms} (A_{ps} + I_{ps}) - b_s S_{ms}$$

$$\frac{dE_{ms}}{dt} = \beta_{Is} S_{ms} I_{Is} + \beta_{psms} S_{ms} (A_{ps} + I_{ps}) - (b_s + \omega_m) E_{ms}$$

$$\frac{dI_{ms}}{dt} = a_s c_s n_s I_{ms} + \omega_m E_{ms} - b_s I_{ms}$$

$$N_{ms} = S_{ms} + E_{ms} + I_{ms}$$

$$\frac{dS_{ps}}{dt} = -\beta_{msps} S_{ps} I_{ms} - \beta_{mcps} S_{ps} I_{mc}$$

$$\frac{dE_{ps}}{dt} = \beta_{msps} S_{ps} I_{ms} + \beta_{mcps} S_{ps} I_{mc} - \omega_p E_{ps}$$

$$\frac{dI_{ps}}{dt} = (1 - q)\omega_p E_{ps} - \gamma I_{ps}$$

$$\frac{dA_{ps}}{dt} = q\omega_p E_{ps} - \gamma' A_{ps}$$

$$\frac{dR_{ps}}{dt} = \gamma I_{ps} + \gamma' A_{ps}$$

$$\frac{dS_{mc}}{dt} = a_c c_c (N_{mc} - n_c I_{mc}) - \beta_{pcmc} S_{mc} (A_{pc} + I_{pc}) - \beta_{psmc} S_{mc} (A_{ps} + I_{ps}) - b_c S_{mc}$$

$$\frac{dE_{mc}}{dt} = \beta_{pcmc} S_{mc} (A_{pc} + I_{pc}) + \beta_{psmc} S_{mc} (A_{ps} + I_{ps}) - (b_c + \omega_m) E_{mc}$$

$$\frac{dI_{mc}}{dt} = a_c c_c n_c I_{mc} + \omega_m E_{mc} - b_c I_{mc}$$

$$N_{mc} = S_{mc} + E_{mc} + I_{mc}$$

$$\frac{dS_{pc}}{dt} = -\beta_{mcpc} S_{pc} I_{mc}$$

$$\frac{dE_{pc}}{dt} = \beta_{mcpc} S_{pc} I_{mc} - \omega_p E_{pc}$$

$$\frac{dI_{pc}}{dt} = (1 - q)\omega_p E_{pc} - \gamma I_{pc}$$

$$\frac{dA_{pc}}{dt} = q\omega_p E_{pc} - \gamma' A_{pc}$$

$$\frac{dR_{pc}}{dt} = \gamma I_{pc} + \gamma' A_{pc}$$

A simplified transmission process diagram was drawn to simulate the transmission of dengue virus between the construction site and the community (Fig. 3).

Parameter estimation

We set all other parameters according to literature (Table 1), while only fitted the values for β_{IS}, β_{psms}, β_{msps}, β_{mcps}, β_{psmc}, β_{pcmc}, β_{mcpc}. Since these parameters were fitted to data before the start of interventions on September 12, we named them as β_{unc}. The incubation period of the dengue virus in human spans usually from 4 to 8 days. The value of 6 days was selected as the average value, thus ω_p = 0.1667 per day [30]. The extrinsic incubation period, i.e. the time-interval between a mosquito infection and when its bites become infectious[31], is 8-12 days. Ten days were thus considered in the simulation, ω_m = 0.1000 per day. The ratio of symptomatic to asymptomatic infection of DF is 2.2: 1[32], thus q = 0.6875. The infectious period is 3-14 days[31], we assumed it to be 7 days in the model, thus $\gamma = \gamma' = \varepsilon$ = 0.1429 per day. The birth rate ad death rate of mosquitoes were set to be $a_s = a_c = b_s = b_c$ = 0.0714, according to a previous study[21]. The vertical infection rates of individual positive families of DENV-1 are ranging from 1.4% to 17.4%[33]. We assumed it to be 10.0% in our model according to a previous work[21], thus $n_s = n_c$ = 0.1000. The abundance of *Ae. albopictus* varies with seasons and regions[34], thus we introduced two seasonal parameters c_s and c_c and used a trigonometric function to simulate them according to the previous study [35]. The calculation of parameter c_s and c_c was as follows:

$$c_s = c_c = \cos\left[\frac{2\pi(t-\tau)}{T}\right]$$

where τ and T refer to simulation delay of the initial time in the whole season, and the time span of the season cycle respectively.

According to the reported data, the illness onset date of the infection source was August 17, the peak of the disease spanned along September. To calculate the seasonal parameter c_s and c_c, we simulated the seasonality of the vector population dynamic with a cycle of 12 months where T =365, for accuracy and to achieve a better effect for model simulation, thus τ = 242.

Evaluating the effectiveness of different intervention strategies

We assessed the effectiveness of different intervention scenarios targeting at reducing the transmissibility of dengue virus between different population and mosquito subgroups at different places (e.g. between infected construction workers and susceptible mosquitoes at construction site, and between infected mosquitoes and susceptible community residents in the community). We examined the scenarios of setting one to all seven β_{unc} to zero by assuming that the intervention is perfect and can reduce the targeted β_{unc} to zero. We set the time of intervention is the same as the actual situation, which means that after the disease develops at the original speed for a period of time, the targeted β_{unc} will only become zero after September 12.

Scenario 1: Only one coefficient β was controlled to be zero

Firstly, we made $\beta_{IS} = 0$ or $\beta_{psms} = 0$ or $\beta_{msps} = 0$ or $\beta_{mcps} = 0$ or $\beta_{psmc} = 0$ or $\beta_{pcmc} = 0$ or $\beta_{mcpc} = 0$, respectively. At the same time, we kept the other six coefficients β unchanged.

Scenario 2: Two coefficients β were controlled to be zero

Then we combined these seven coefficients β_{unc} in pairs, so that two of them were equal to zero, we kept the other five coefficients β unchanged at the same time. There were a total of 21 combinations.

Scenario 3: Three coefficients β were controlled to be zero

Three of these seven coefficients were set to zero, while the others remained unchanged. There were a total of 35 combinations.

Scenario 4: Four coefficients β were controlled to be zero

We made four out of these seven coefficients equal to zero, while the others remained unchanged. There were a total of 35 combinations.

Scenario 5: Five coefficients β were controlled to be zero

We set five out of these seven coefficients to zero, while the others remained unchanged. There were a total of 20 combinations.

Scenario 6: Six coefficients β were controlled to be zero

We made six of these seven coefficients equal to zero, while the others remained unchanged. There were a total of 7 combinations.

Scenario 7: Seven coefficients β were controlled to be zero

We made all seven coefficients equal to zero.

The specific meaning of controlling β_{unc} to be zero is as follows:

$\beta_{IS} = 0$ means cutting off the transmission route from the imported case to susceptible mosquitoes on the construction site. $\beta_{psms} = 0$ means cutting off the transmission route from infectious and symptomatic people to susceptible mosquitoes inside the construction site. $\beta_{msps} = 0$ means cutting off the transmission route from infectious mosquitoes to susceptible people inside the construction site. $\beta_{mcps} = 0$ means cutting off the transmission route from infectious mosquitoes in the community to susceptible people on the construction site. $\beta_{psmc} = 0$ means cutting off the transmission route from infectious and symptomatic people on the construction site to susceptible mosquitoes in the community. $\beta_{pcmc} = 0$ means cutting off the transmission route from infectious and symptomatic people to susceptible mosquitoes inside the community. $\beta_{mcpc} = 0$ means cutting off the transmission route from infectious mosquitoes to susceptible people inside the community.

Indicators for assessing the effectiveness of interventions

The effectiveness of the interventions is represented by absolute effectiveness (AE) and relative effectiveness (RE), which are calculated as:

$$\boldsymbol{AE_i = TAR_i - TAR_{baseline}}$$

$$\boldsymbol{RE_i = (TAR_i - TAR_{baseline})/TAR_i \times 100\%}$$

where $\mathrm{TAR_i}$ represents the total attack rate (TAR) defined as the proportion of population being infected (only symptomatic) during the simulation period, $\mathrm{TAR_{baseline}}$ represents the TAR when β are kept at the fitted values using data before September 12.

From the simulation results, we could obtain the number of susceptible people and infected people at different times. We first considered the number of susceptible people when the number of infected persons was 1, which means the disease was effectively controlled at this time. We then subtracted the number of susceptible people at this time from the total number of people at the start in the construction site or the community to obtain the total number of infected people, considering that there were not only asymptomatic but also symptomatic individuals in this process. Finally, we obtained the TAR by dividing the total number of people infected by the proportion of symptomatic individuals. Duration of outbreak (DO) represents the number of days calculated from the beginning to the date when the number of infected people reaches the value of one.

Simulation method

We used Berkeley Madonna 8.3.18 (developed by Robert Macey and George Oster of the University of California at Berkeley) for parameter fitting and model simulation. The goodness-of-fitting was assessed by least root mean square error between simulated and observed number of new cases per day between August 17 and September 12. The coefficient of determination (R^2), was assessed using SPSS 13.0 (IBM Corp, Armonk, NY, USA) to quantify the significance of the fit.

Results

Epidemiological characteristics of the outbreak

A total of 467 cases of DF were reported in Zhanjiang Prefecture in 2018, and the first indigenous case was reported in Chikan District on August 29. The number of new cases on the construction site and the community per day were shown in Fig. 4. The first indigenous case was reported in the construction site A whithin Community A in Chikan District on August 27, then it was spread within the construction site. In early September, it began to spread to the surrounding communities and caused the outbreak. The indigenous cases began to increase on September 3, and the number of new cases reached to 13 on September 12. After that, Zhanjiang Municipal CDC began to take intervention measures. The outbreak on the construction site ended in late September with a total of 102 cases while the community outbreak continued to spread until October 2 with a cumulative number of cases of 131. The outbreak source was identified as a 30-year old woman living in the community close to the construction site who developed symptoms on August 17.

Results of curve fitting

The model fitting results are shown in Fig. 5. The values of R^2 were 0.829 ($P < 0.001$) and 0.878 ($P < 0.001$) for the construction site and the community, respectively. Therefore, the optimal values of β_{IS}, β_{psms}, β_{msps}, β_{mcps}, β_{psmc}, β_{pcmc}, β_{mcpc} are generated by curve fitting and are summarized in Table 1.

Simulation for the baseline scenario

We used the fitted β_{unc} to simulate the baseline scenario when no intervention measures were applied. The simulation results indicated that in the absence of any intervention, the number of cases in the construction site would reach 156, yielding a TAR of 31.25% (95%CI: 27.18%-35.31%) and a DO of 73 days. In the community, the number of cases would reach up to 10,796, yielding a TAR of 21.59% (95%CI: 21.23%- 21.95%) and a DO of 127 days, the results were shown in Fig. 5. The AE and RE of the outbreak control strategy implemented by Zhanjiang Municipal CDC on the construction site were 10.65% and 34.08%, respectively, and the AE and RE of the community were 21.33% and 98.79%, respectively.

Effectiveness of different intervention strategies

We evaluated the effectiveness of different intervention strategies by setting each β_{unc} or the combination of multiple β_{unc} to 0. The first scenario is only one coefficient β is controlled to be zero: When we controlled $\beta_{IS} = 0$ or $\beta_{psms} = 0$ or $\beta_{msps} = 0$ or $\beta_{psmc} = 0$, we found that these measures were not efficient, the number of cases was the same as the uncontrolled data. When $\beta_{mcps} = 0$, that is, cutting off the transmission route from infectious mosquitoes in the community to susceptible people on the construction site, the number of cases in the construction site would reach 129, yielding a TAR of 25.81% (95% CI: 21.97%- 26.65%) and a DO of 85 days, and did not have any effect in the community. When $\beta_{pcmc} = 0$, that is, cutting off the transmission route from infectious and symptomatic people to susceptible mosquitoes inside the community, the number of cases in the community would reach to 2,794, yielding a TAR of 5.60% (95%CI: 5.40%- 5.80%) and a DO of 145 days with no effect on the construction site. When $\beta_{mcpc} = 0$, that is, cutting off the transmission route from infectious mosquitoes to susceptible people inside the community, the number of cases in the community would go down to 33, yielding a TAR of 0.068% (95%CI: 0.05%- 0.09%) and a DO of 60 days with no effect on the construction site.

The second scenario is that two coefficient β are controlled to be zero. When we controlled $\beta_{psms} = 0$ and $\beta_{mcps} = 0$ at the same time, the number of cases on the construction site would drop to 103. When we controlled $\beta_{msps} = 0$ and $\beta_{mcps} = 0$ at the same time, that is, cutting off the transmission route from infectious mosquitoes in the community and the construction site to susceptible people on the construction site at the same time, the number of cases on the construction site would drop to 74.

The following scenarios are three or more β_{unc} are changed to be zero. After more than one hundred simulations, it was found that even if we controlled β_{IS}, β_{psms}, β_{msps}, β_{mcps}, β_{psmc}, β_{pcmc}, β_{mcpc} to zero at the same time, the number of cases on the construction site would not be less than 74 and the number of cases in the community would not be less than 33. Detailed data of these results has been shown in Additional file 1: Table S1-S6.

Discussion

Guangdong Province has been suffering from serious DF outbreaks in mainland China. This province has a dense population, a large number of immigrants and massive mobility. In our study, the outbreak first occurred in the construction site, followed in the community. This indicates that once the transmission route is established, the virus may circulate between the construction site and the surrounding areas.

We developed an ODE model, and applied the model to examine the effectiveness of different intervention scenarios targeting at reducing the transmissibility between different human and mosquito subpopulations at different places (i.e. the construction site and the nearby community). The coefficient of determination showed a high good-of-fitness of our models to the reported data, which indicated that this model was well fitted to similar situations with urbanization, where construction sites and communities were gathered.

Our simulation results showed that after an index case was introduced to the construction site but there were no intervention measures, the epidemic started earlier on the construction site compared to the community, although the first indigenous case moved back and forth between the construction site and the community on a daily basis. Given the high mosquito abundance at the construction sites, the virus could be more easily to be spread there than in the community. As the total case counts at the construction site accumulated, the probability of local transmission in the community also increased. Detecting cases in the high-risk areas could be used as an early warning signal to apply local interventions. We found that when we only controlled the transmission inside the construction site, it would not have any impact on reducing the transmission of the epidemic on the site. However, the number of cases on the construction site would reach a minimum when we cut off the transmission route from infectious mosquitoes in the community and the construction site to susceptible people on the construction site at the same time. In other words, only by controlling mosquitoes in the community, the number of DF cases on the construction site would be reduced.

Poor hygiene, humid areas, presence of multiple water-holding containers and densely populated areas are ideal breeding places for *Aedes* mosquitoes[36]. Construction sites have these requirements. *Aedes* mosquitoes are more likely to bite during the day to spread the virus, and the biting activity increases within two hours after sunrise and a few hours after sunset, which is the time when workers are working outside so that they are easier to get infected. Also, workers are working the whole day without protective measures or wearing light clothes, which may lead to the infection of mosquito-borne diseases[37]. In addition, the factors including the densely populated construction sites, the strong labor intensity, high temperature, are significantly related to the increase in the number of DF cases[38]. Moreover, due to the high level of urbanization in China, construction sites are emerging one after another, along with a large population of construction workers and massive mobility[9]. Once external cases are imported, DF may be prevalent on the construction sites. Therefore, construction sites should be regularly inspected, and the places where mosquitoes breed and workers should be checked to detect early case. However, just controlling the β between mosquitoes and people inside the construction site was not enough. This might reflect the fact that transfer of the virus by human to naive populations of mosquitoes in the communities must also be considered. *Aedes* mosquitoes involved in dengue transmission do not fly more than 75 meters from their breeding sites, therefore the longer distance transmission of DF necessarily involves human either directly as infected source or indirectly by transporting mosquitoes.

When focusing on the community, our study demonstrated that the number of cases in the community would increase to an extremely high level in a short period of time without intervention, and controlling the transmission route within the construction site or between the construction site and the community would not decrease the dengue cases of the community. We found that the number of community cases would be significantly reduced only when we controlled the transmission routes within the community, and the outbreak in the community would be significantly controlled when we cut off the transmission route from infectious mosquitoes to susceptible people inside the community. Furthermore, controlling the transmission within the construction site alone only had marginal impact on the number of cases in the community in our study, since the population size of construction workers is much smaller compared to the community inhabitants. More attention should be paid to the interaction between people and vector inside community to control the DF in it.

Community participation is considered to be the key to control endemic diseases, especially in the case of DF, as the activity of insects is closely related to lifestyle and housing in urban areas[39]. Mosquitoes in the community will not only cause outbreaks of diseases within the community, but also affect the surrounding construction sites, causing a wider spread of DF. In the past few decades, the main method to prevent and control DF was to reduce mosquito breeding sites and control their density[8]. However, this method often fails to achieve good results due to the lack of active community participation. It is necessary for communities to plan anti-mosquito actions in an organized way. For example, communities should propagate the importance of DF prevention, regularly inspect houses, kill insects on various containers, especially in water storage containers[40], and control adult mosquito density.

Of note, our study has the following limitations. First, we did not take the death toll of the disease into account. Even though the fatality rate of the disease is extremely low, when the outbreak is more serious and lasts longer, without the fatality rate may have a slight impact on the simulated data. Second, we did not simulate multiple countermeasures in this outbreak, such as case isolation, adult vector control and larvae control, thus was not been able to explore the specific effect of different measures. Third, because of the complex model structure, and dengue is transmitted through vector rather than simply from person to person, we could not calculate R_0 (the basic reproduction number) to assess the transmissibility of this disease with or without intervention. In future work, we should further explore a feasible method to solve this problem.

Conclusions

When the infection source of dengue is introduced to the construction site, the epidemic would first break out on the site. Without intervention, DF could break out rapidly in the densely populated communities around the construction site after that. The ODE models can be useful to simulate the outbreak of DF and to predict the transmissibility of the disease. Controlling the transmission route within the construction site or between the construction site and the community could not curb the outbreak in both construction site and community. Cutting off the transmission routes and properly controlling vectors in communities should be recommended as primary measures to control this disease.

Additional files

Supplementary information

Additional file 1: Table S1. Simulated results of scenario 1**. Table S2.** Simulated results of scenario 2**. Table S3.** Simulated results of scenario 3**. Table S4.** Simulated results of scenario 4**. Table S5.** Simulated results of scenario 5**. Table S6.** Simulated results of scenario 6 and scenario 7.

Abbreviations

DF： dengue fever; R^2: the coefficient of determination; SEIAR: susceptible – exposed – symptomatic – asymptomatic – recovered/removed; TAR: the total attack rate; DO: duration of the outbreak; *CI*: confidence interval; CDC: Center for Disease Control and Prevention; ODE: ordinary differential equation; R_0: the basic reproduction number.

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Not applicable.

Ethics approval and consent to participate

This effort of disease control was part of CDC's routine responsibility in Guangdong Province, China. Therefore, institutional review and informed consent were not required for this study. All data analyzed were anonymized.

Consent for publication

Not applicable.

Availability of data and material

Data supporting the conclusions of this article are included within the article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

TMC and XCL designed research; TMC, BHZ, and XCL conceived the experiments, TMC, MZ, XCL, TS, MK, QQH, ZYZ, JR, YTZ, QC and GQY conducted the experiments and analyzed the results; TMC and XCL wrote the manuscript. All authors read and approved the final manuscript.

References

1. Lai S, Huang Z, Zhou H, Anders KL, Perkins TA, Yin W, et al. The changing epidemiology of dengue in China, 1990-2014: a descriptive analysis of 25 years of nationwide surveillance data. BMC Med. 2015;13:100.
2. Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. The global distribution and burden of dengue. Nature. 2013;496(7446):504-7.
3. Guzman MG, Harris E. Dengue. Lancet. 2015;385(9966):453-65.
4. Lee HS, Nguyen-Viet H, Nam VS, Lee M, Won S, Duc PP, et al. Seasonal patterns of dengue fever and associated climate factors in 4 provinces in Vietnam from 1994 to 2013. BMC Infect Dis. 2017;17(1):218.
5. Li Q, Cao W, Ren H, Ji Z, Jiang H. Spatiotemporal responses of dengue fever transmission to the road network in an urban area. Acta Trop. 2018;183:8-13.
6. Chen B, Liu QY. Dengue fever in China. Lancet. 2015;385(9978):1621-2.
7. Van Benthem BH, Vanwambeke SO, Khantikul N, Burghoorn-Maas C, Panart K, Oskam L, et al. Spatial patterns of and risk factors for seropositivity for dengue infection. Am J Trop Med Hyg. 2005;72(2):201-8.

8. Hermann LL, Gupta SB, Manoff SB, Kalayanarooj S, Gibbons RV, Coller BA. Advances in the understanding, management, and prevention of dengue. J Clin Virol. 2015;64:153-9.
9. Liang S, Hapuarachchi HC, Rajarethinam J, Koo C, Tang CS, Chong CS, et al. Construction sites as an important driver of dengue transmission: implications for disease control. BMC Infect Dis. 2018;18(1):382.
10. Wu JY, Lun ZR, James AA, Chen XG. Dengue Fever in mainland China. Am J Trop Med Hyg. 2010;83(3):664-71.
11. Fan J, Lin H, Wang C, Bai L, Yang S, Chu C, et al. Identifying the high-risk areas and associated meteorological factors of dengue transmission in Guangdong Province, China from 2005 to 2011. Epidemiol Infect. 2014;142(3):634-43.
12. Zhao S, Musa SS, Meng J, Qin J, He D. The long-term changing dynamics of dengue infectivity in Guangdong, China, from 2008-2018: a modelling analysis. Trans R Soc Trop Med Hyg. 2020;114(1):62-71.
13. Huang L, Luo X, Shao J, Yan H, Qiu Y, Ke P, et al. Epidemiology and characteristics of the dengue outbreak in Guangdong, Southern China, in 2014. Eur J Clin Microbiol Infect Dis. 2016;35(2):269-77.
14. Liu J, Tian X, Deng Y, Du Z, Liang T, Hao Y, et al. Risk Factors Associated with Dengue Virus Infection in Guangdong Province: A Community-Based Case-Control Study. Int J Environ Res Public Health. 2019;16(4).
15. Guo Y, Song Z, Luo L, Wang Q, Zhou G, Yang D, et al. Molecular evidence for new sympatric cryptic species of Aedes albopictus (Diptera: Culicidae) in China: A new threat from Aedes albopictus subgroup? Parasit Vectors. 2018;11(1):228.
16. Sang S, Chen B, Wu H, Yang Z, Di B, Wang L, et al. Dengue is still an imported disease in China: a case study in Guangzhou. Infect Genet Evol. 2015;32:178-90.
17. San Martin JL, Brathwaite O, Zambrano B, Solorzano JO, Bouckenooghe A, Dayan GH, et al. The epidemiology of dengue in the americas over the last three decades: a worrisome reality. Am J Trop Med Hyg. 2010;82(1):128-35.
18. Esteva L, Vargas C. Influence of vertical and mechanical transmission on the dynamics of dengue disease. Math Biosci. 2000;167(1):51-64.

19. Favier C, Schmit D, Muller-Graf CD, Cazelles B, Degallier N, Mondet B, et al. Influence of spatial heterogeneity on an emerging infectious disease: the case of dengue epidemics. Proc Biol Sci. 2005;272(1568):1171-7.

20. Li MT, Sun GQ, Yakob L, Zhu HP, Jin Z, Zhang WY. The Driving Force for 2014 Dengue Outbreak in Guangdong, China. PLoS One. 2016;11(11):e0166211.

21. Yi B, Chen Y, Ma X, Rui J, Cui JA, Wang H, et al. Incidence dynamics and investigation of key interventions in a dengue outbreak in Ningbo City, China. PLoS Negl Trop Dis. 2019;13(8):e0007659.

22. Bartley LM, Donnelly CA, Garnett GP. The seasonal pattern of dengue in endemic areas: mathematical models of mechanisms. Trans R Soc Trop Med Hyg. 2002;96 (4):387-97.

23. Ghosh M, Olaniyi S, Obabiyi O. Mathematical analysis of reinfection and relapse in malaria dynamics. Appl Math Comput. 2020;373.

24. Olaniyi SJAM. Dynamics of Zika virus model with nonlinear incidence and optimal control strategies. Appl. Math. Inf. Sci. 2018;12(5):969-82.

25. Cheng Q, Jing Q, Spear RC, Marshall JM, Yang Z, Gong P. Climate and the Timing of Imported Cases as Determinants of the Dengue Outbreak in Guangzhou, 2014: Evidence from a Mathematical Model. PLoS neglected tropical diseases. 2016;10 (2):e0004417.

26. Sun J, Zhang H, Tan Q, Zhou H, Guan D, Zhang X, et al. The epidemiological characteristics and molecular phylogeny of the dengue virus in Guangdong, China, 2015. Sci Rep. 2018;8(1):9976.

27. Peng HJ, Lai HB, Zhang QL, Xu BY, Zhang H, Liu WH, et al. A local outbreak of dengue caused by an imported case in Dongguan China. BMC Public Health. 2012;12:83.

28. Honorio NA, Silva Wda C, Leite PJ, Goncalves JM, Lounibos LP, Lourenco-de-Oliveira R. Dispersal of Aedes aegypti and Aedes albopictus (Diptera: Culicidae) in an urban endemic dengue area in the State of Rio de Janeiro, Brazil. Mem Inst Oswaldo Cruz. 2003;98(2):191-8.

29. Verdonschot PFM, Besse-Lototskaya AA. Flight distance of mosquitoes (Culicidae): A metadata analysis to support the management of barrier zones around rewetted and

newly constructed wetlands. Limnologica. 2014;45:69-79.

30. Chan M, Johansson MA. The incubation periods of Dengue viruses. PLoS One. 2012;7(11):e50972.

31. Andraud M, Hens N, Marais C, Beutels P. Dynamic epidemiological models for dengue transmission: a systematic review of structural approaches. PloS one. 2012;7 (11):e49085.

32. Wang T, Wang M, Shu B, Chen XQ, Luo L, Wang JY, et al. Evaluation of inapparent dengue infections during an outbreak in Southern China. PLoS Negl Trop Dis. 2015;9 (3):e0003677.

33. Grunnill M, Boots M. How Important is Vertical Transmission of Dengue Viruses by Mosquitoes (Diptera: Culicidae)? J Med Entomol. 2016;53(1):1-19.

34. Torres C, Barguil S, Melgarejo M, Olarte A. Fuzzy model identification of dengue epidemic in Colombia based on multiresolution analysis. Artif Intell Med. 2014;60 (1):41-51.

35. Yang HM, Macoris ML, Galvani KC, Andrighetti MT, Wanderley DM. Assessing the effects of temperature on the population of Aedes aegypti, the vector of dengue. Epidemiol Infect. 2009;137(8):1188-202.

36. Atique S, Chan TC, Chen CC, Hsu CY, Iqtidar S, Louis VR, et al. Investigating spatio-temporal distribution and diffusion patterns of the dengue outbreak in Swat, Pakistan. J Infect Public Health. 2018;11(4):550-7.

37. Sang S, Yin W, Bi P, Zhang H, Wang C, Liu X, et al. Predicting local dengue transmission in Guangzhou, China, through the influence of imported cases, mosquito density and climate variability. PLoS One. 2014;9(7):e102755.

38. Burattini MN, Chen M, Chow A, Coutinho FA, Goh KT, Lopez LF, et al. Modelling the control strategies against dengue in Singapore. Epidemiol Infect. 2008;136 (3):309-19.

39. Caprara A, Lima JW, Peixoto AC, Motta CM, Nobre JM, Sommerfeld J, et al. Entomological impact and social participation in dengue control: a cluster randomized trial in Fortaleza, Brazil. Trans R Soc Trop Med Hyg. 2015;109(2):99-105.

40. Wai KT, Htun PT, Oo T, Myint H, Lin Z, Kroeger A, et al. Community-centred eco-bio-social approach to control dengue vectors: an intervention study from Myanmar. Pathog

Glob Health. 2012;106(8):461-8.

Figure legends

Fig. 1 Distribution of dengue cases in Chikan District in 2018 and the remote sensing images of Community A and the index case

Fig. 2 Flowchart of development of the dengue transmission model. (The red parts represent two ways to control the number of dengue cases in the construction site to a minimum, the blue part represents the way to control the number of dengue cases in the community to a minimum.)

Fig. 3 The transmission process of dengue between the construction site and the community.

Fig. 4 Reported dengue cases on the construction site A and in the surrounding communities in Zhanjiang Prefecture, China in 2018.

Fig. 5 Curve fitting of reported data and SEIAR models without intervention and simulated epidemic curve with no intervention

Table legends

Table 1. Parameter definitions and values

Parameter	Description	Unit	Value	Range	Method
β_{IS}	Transmission relative rate from imported human to mosquitos on the construction site	1	1.67742×10^{-5}	$\geqslant 0$	Curve fitting
β_{psms}	Transmission relative rate from people on the construction site to mosquitos on the construction site	1	0.00200626	$\geqslant 0$	Curve fitting
β_{msps}	Transmission relative rate from mosquitos on the construction site to human on the construction site	1	0.00101487	$\geqslant 0$	Curve fitting
β_{mcps}	Transmission relative rate from mosquitos in the community to people on the construction site	1	0.00301141	$\geqslant 0$	Curve fitting
β_{psmc}	Transmission relative rate from people on the construction site to mosquitos in the community	1	3.3702×10^{-15}	$\geqslant 0$	Curve fitting
β_{pcmc}	Transmission relative rate from people in the community to mosquitos in the community	1	0.00523777	$\geqslant 0$	Curve fitting
β_{mcpc}	Transmission relative rate from mosquitos in the community to people in the community	1	1.12805×10^{-5}	$\geqslant 0$	Curve fitting
ω_m	Incubation relative rate of mosquitos infection	day^{-1}	0.1000	0.0833-0.1250	Reference [31]
ω_p	Incubation relative rate of human infection	day^{-1}	0.1667	0.1250-0.2500	Reference [30]

$\boldsymbol{q}$	Proportion of human asymptomatic infection	1	0.6875	0-1	Reference [32]
γ	Removed relative rate of infectious individuals	day^{-1}	0.1429	0.0714-0.3333	Reference [31]
γ'	Removed relative rate of asymptomatic individuals	day^{-1}	0.1429	0.0714-0.3333	Reference [31]
ε	Removed relative rate of imported individuals	day^{-1}	0.1429	0.0714-0.3333	Reference [31]
$\boldsymbol{a_s}$	Daily birth rate of mosquitos on the construction site	day^{-1}	0.0714	0.0200-0.2500	Reference [21]
$\boldsymbol{a_c}$	Daily birth rate of mosquitos in the community	day^{-1}	0.0714	0.0200-0.2500	Reference [21]
$\boldsymbol{b_s}$	Daily death rate of mosquitos on the construction site	day^{-1}	0.0714	0.0200-0.2500	Reference [21]
$\boldsymbol{b_c}$	Daily death rate of mosquitos in the community	day^{-1}	0.0714	0.0200-0.2500	Reference [21]
τ	Simulation delay of the initial time in the whole season day	day	242	$\geqslant$ 0	Analysis on the reported data
$\boldsymbol{T}$	Duration of the cycle day	day	365	$\geqslant$ 0	Analysis on the reported data
$\boldsymbol{c_s}$, $\boldsymbol{c_c}$	Seasonality parameter of the mosquitos population	1	See text	0-1	Curve fitting
$\boldsymbol{n_s}$, $\boldsymbol{n_c}$	Proportion of transovarial transmission	1	0.1000	0.0140-0.1740	Reference [21]

Figures

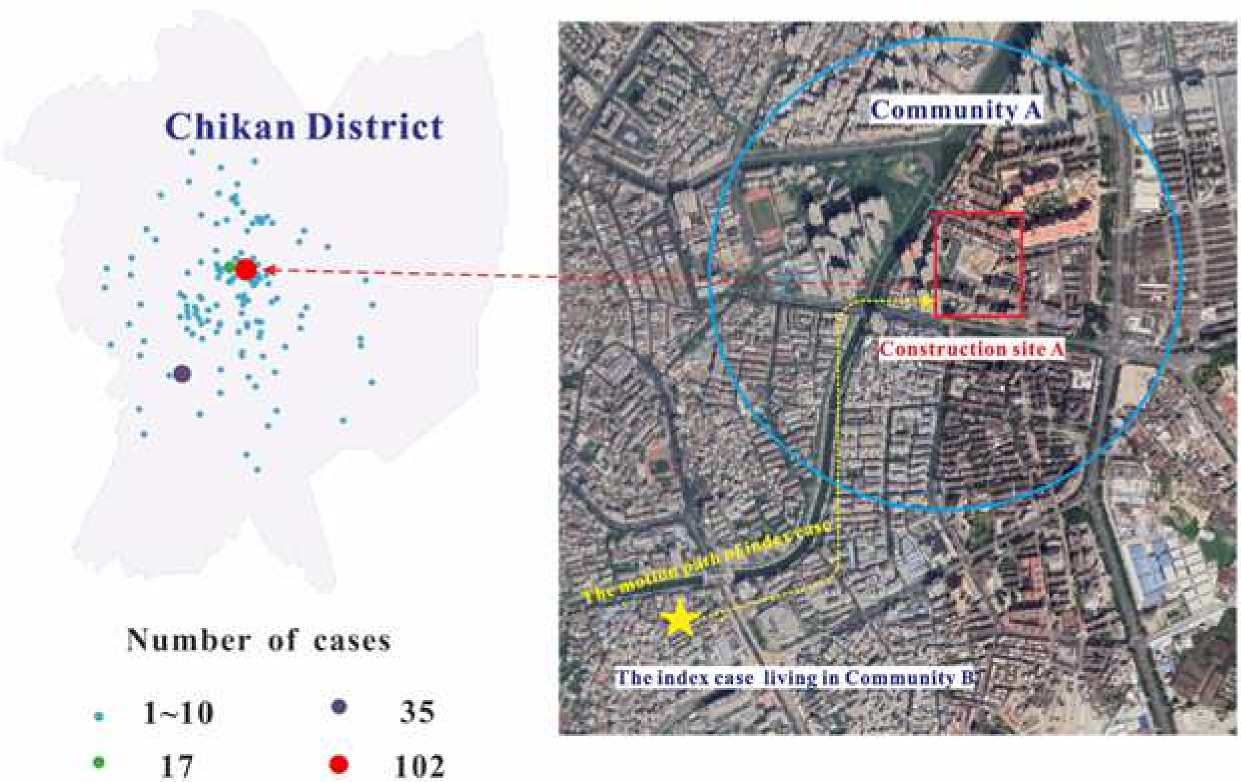

Figure 1

Distribution of dengue cases in Chikan District in 2018 and the remote sensing images of Community A and the index case

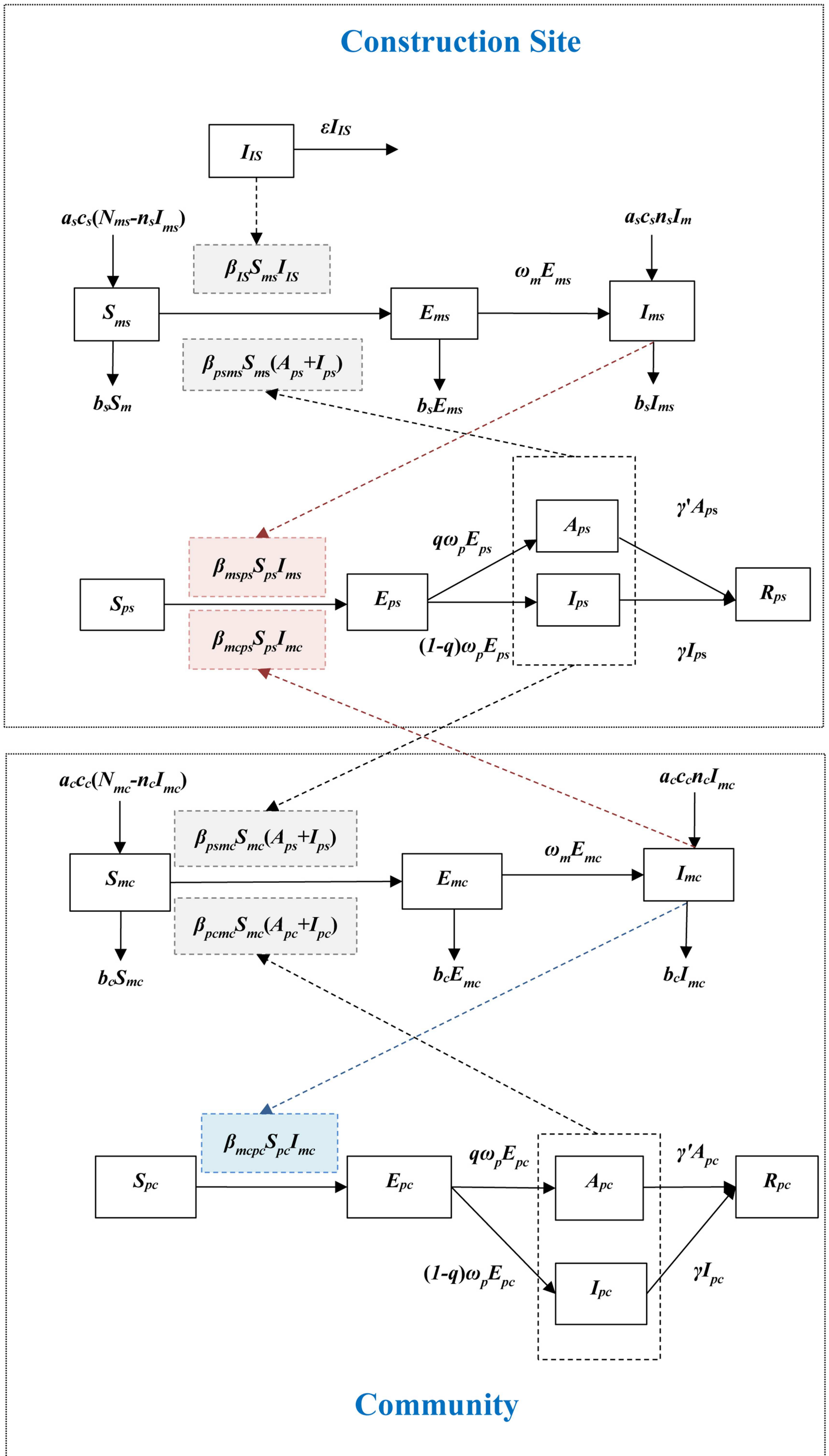

Figure 2

Flowchart of development of the dengue transmission model. (The red parts represent two ways to control the number of dengue cases in the construction site to a minimum, the blue part represents the way to control the number of dengue cases in the community to a minimum.)

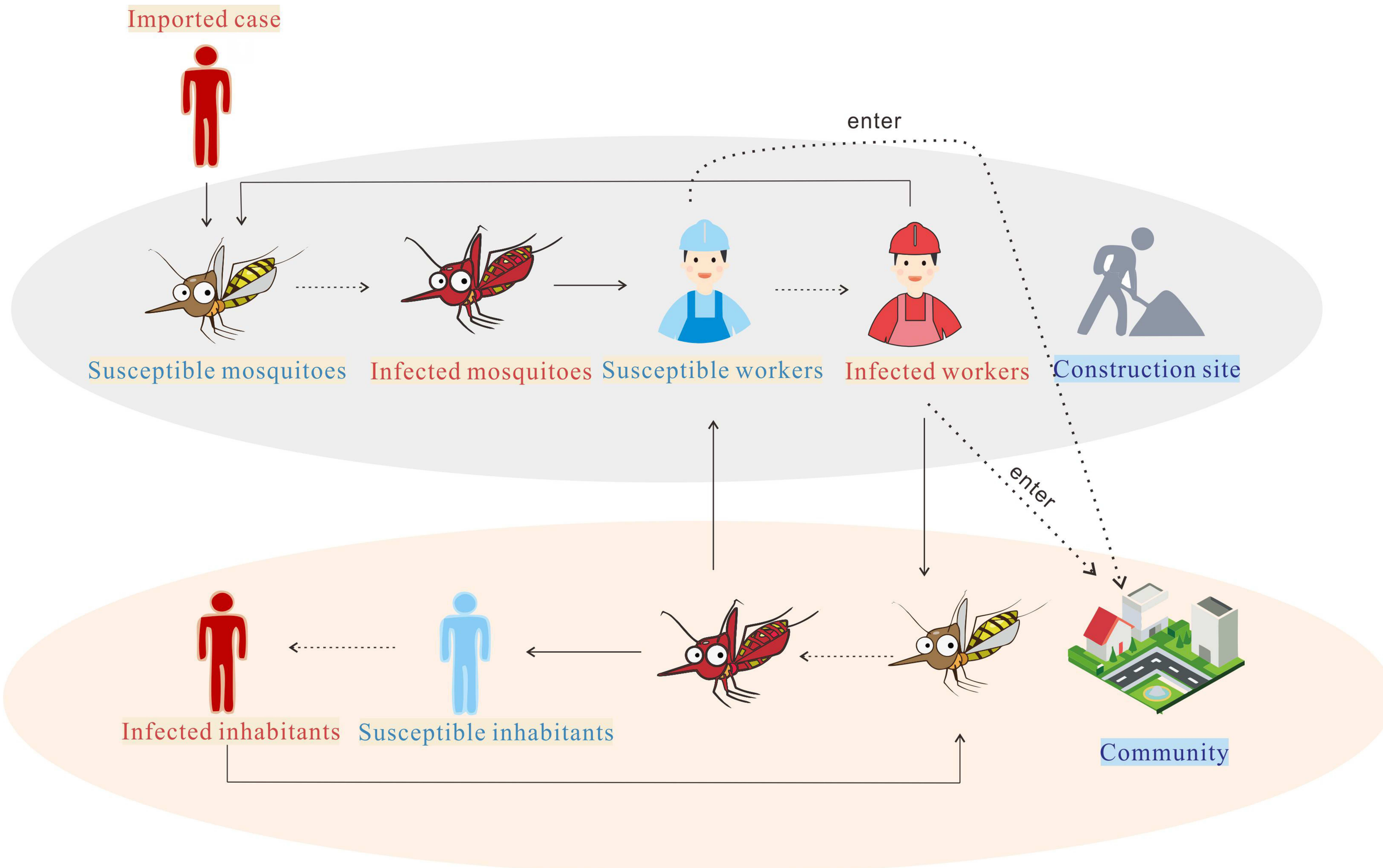

Figure 3

The transmission process of dengue between the construction site and the community.

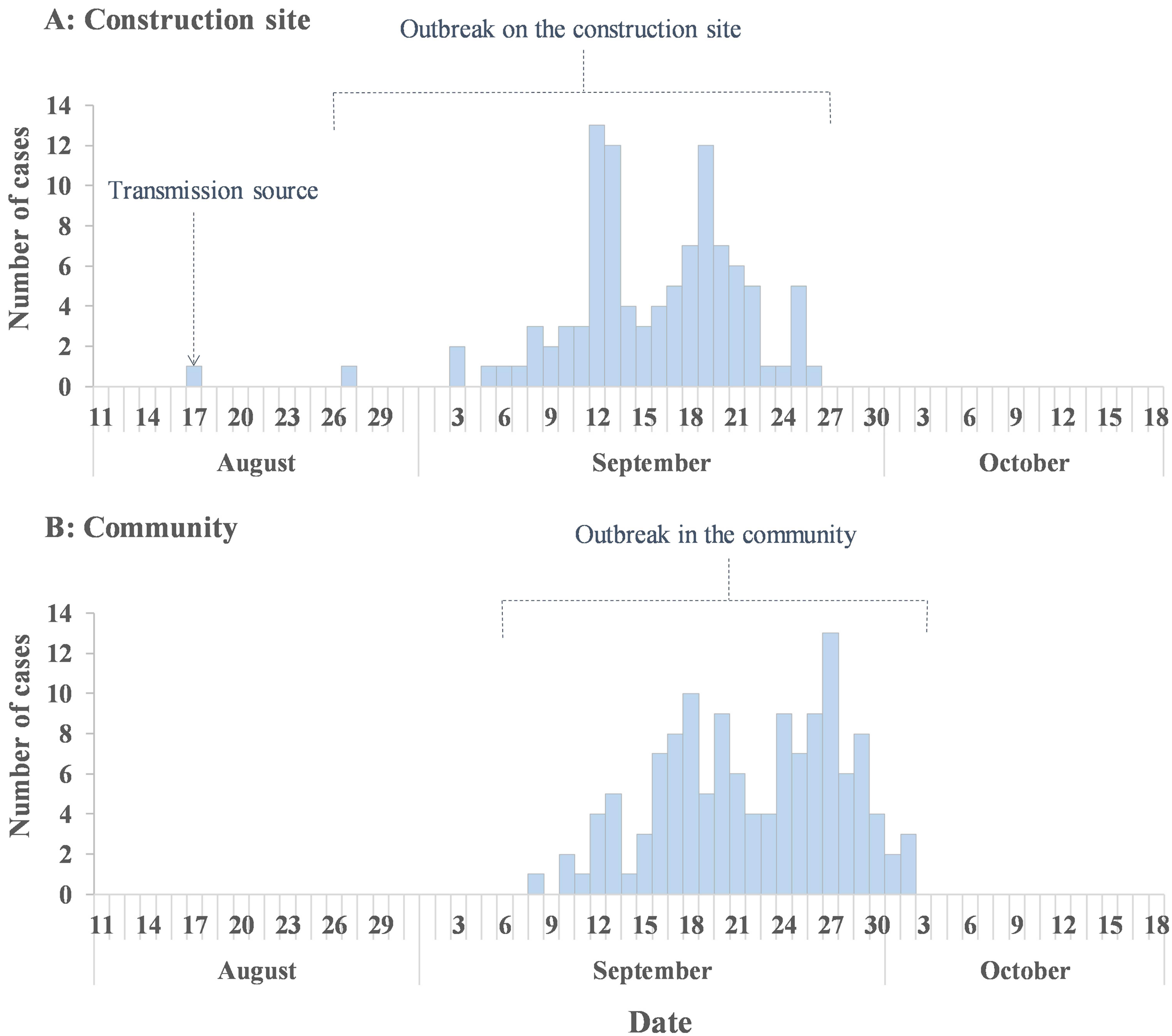

Figure 4

Reported dengue cases on the construction site A and in the surrounding communities in Zhanjiang Prefecture, China in 2018.

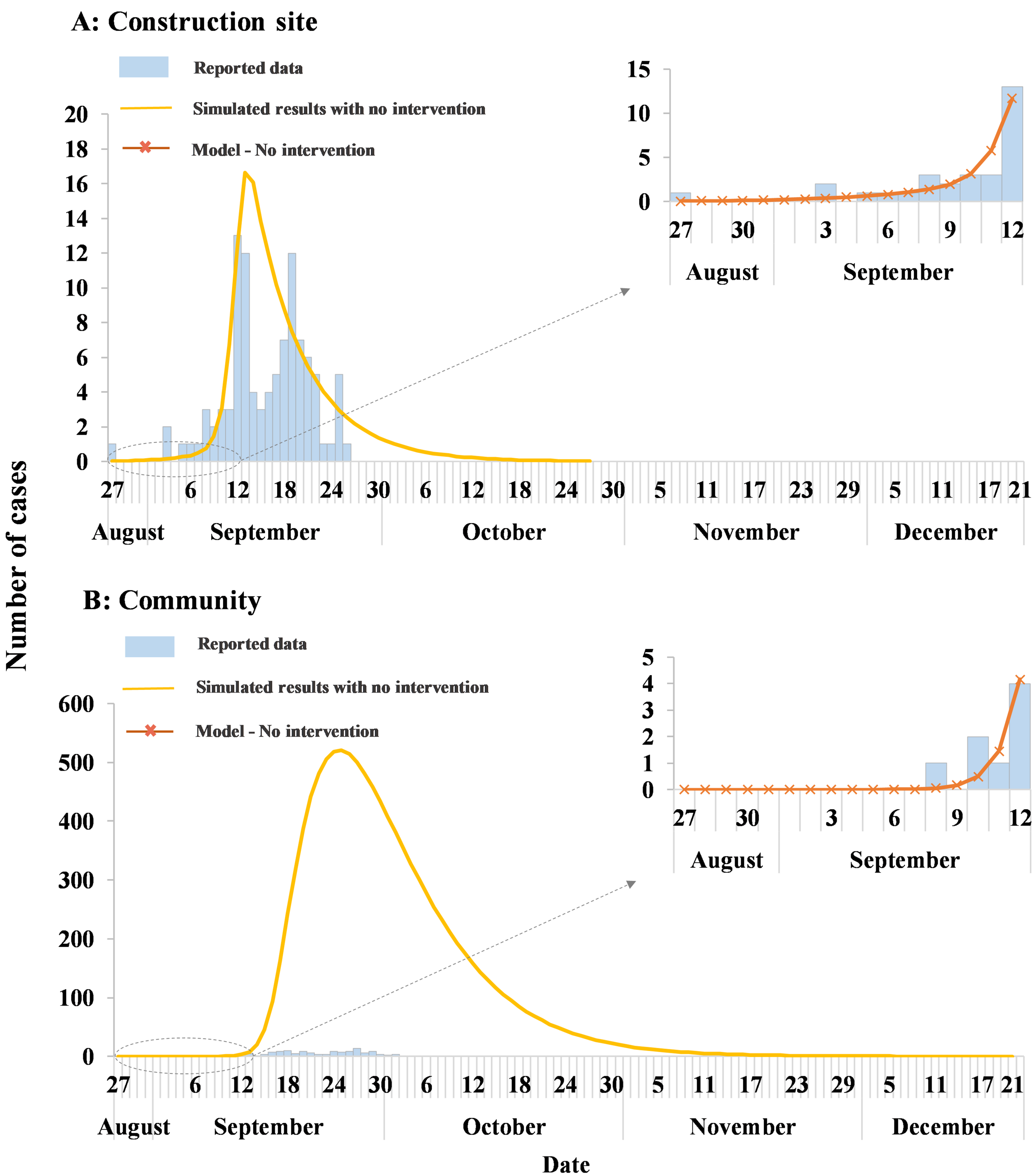

Figure 5

Curve fitting of reported data and SEIAR models without intervention and simulated epidemic curve with no intervention

Supplementary Files

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