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A Branching Process Model of Dengue Fever Epidemics Considering Parametric and Kernel Density Estimation of Offspring Distribution

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Abstract Dengue fever is an important vector-borne disease. In this paper, a branching process model of dengue fever epidemics is presented. In this study, a retrospective analysis of a data set on reproduction numbers estimated by Chowell et al (2007) is carried out. To obtain the offspring distribution, we first fitted a Poisson distribution to the data set and subsets and secondly estimated the offspring distribution with a kernel density function. The model was simulated using both forms of the offspring distribution. The objectives are, first, to compare the solutions of the model for these two different offspring distributions and, secondly, to predict the disease spread in any population with the same scenario. The solution of the model with Poisson offspring distribution performs is the same as the solution of the same model with kernel offspring distribution to the nearest whole numbers. The results further reveal that any population with similar pattern of reproduction numbers has no guarantee of elimination of the disease at population level. However, elimination of the disease can be achieved in those localities of which their reproduction numbers are below one. Based on the findings of this study, it is therefore recommended that intervention measures such as vector killing be intensified in any supercritical area.

Keywords dengue fever, branching process, Galton-Watson process, offspring distribution, parametric estimation, kernel density estimation.

Introduction

Dengue fever viruses belong to the genus Flavivirus and family Flaviviridae [1-2]. Dengue fever is regarded as an important infectious disease threatening about 2.5 billion people all over the world, especially in tropical subtropical countries. Some 50 to 100 million new infections are estimated to occur annually worldwide [3]. Around 500,000 people are estimated to be infected by hemorrhagic dengue fever each year. Dengue fever has become a major epidemic disease in Southeast Asia. Such an epidemic arises from climate change and is made worse by the population's lack of knowledge about and awareness of dengue fever, so that dengue fever may become endemic [1-2].

Symptoms of dengue fever include headache, backache, general malaise, rash, a sharp rise in temperature, a flushed face, retro-orbital pain on eye movement or eye pressure, photophobia, pain in the muscles and joints/bones. The other common symptoms include anorexia and altered taste sensation, constipation, colicky pain and abdominal tenderness, dragging pains in the inguinal region, sore throat and general depression. These symptoms usually persist from several days to a few weeks. It is noteworthy that these symptoms and signs of dengue fever vary markedly in frequency and severity [1].

Outbreaks exert a huge burden on populations, health systems and economies in most tropical and subtropical countries of the world [3].

For the transmission of dengue virus between humans to occur, the female mosquito (*Aedes aegypti)* must, first of all, bite and ingest blood meal from an infected human. Within 8 -12 days after the female mosquito feeds on an infected human, it can transfer the virus to another human [1,4].

There is no specific treatment, neither vaccine available for dengue fever; rather the symptoms are given appropriate medical care to save the lives of the patients with more serious dengue hemorrhagic fever. The most effective way to prevent dengue virus transmission is to combat the disease-carrying mosquitoes [1].

Chowell *et al* (2007) estimated the transmissibility of dengue fever during the 2002 dengue epidemic in the Mexican state of Colima using two different methods and municipal epidemic data to investigate the impact of spatial heterogeneity. The first method employs a standard dengue epidemic model with the assumptions of fixed incubation periods in both hosts and vectors, an exponentially distributed infectious period in hosts and pure initial exponential epidemic growth to estimate the reproduction number. The second approach employs an epidemic model to estimate the reproduction number via trajectory matching to case notification data [5].
The plan of this paper is as follows. Introductory part of the work is presented in section 1. Branching processes (discrete Galton-Watson branching process in particular) are presented in section 2. Section 3 is devoted to materials and methods. Simulations are carried out in section 4. Discussion and conclusive remarks are passed in sections 5 and 6 respectively.

Branching Processes and Galton-Watson Process

Branching processes are stochastic processes describing the dynamics of a population of individuals which reproduce and die independently, according to some probability distributions. Branching processes have a wide variety of applications: electron multipliers, family names, neutron chain reactions, population growth, survival of mutant genes, changes in DNA and chromosomes, cell cycle, cancer cells, chemotherapy, network and epidemiology. There are many types of branching processes. These include discrete time (Galton-Watson) branching processes, continuous time with exponential lifetime distributions (Markovian branching process) or general lifetime distribution (age-dependent, Bellman-Haris branching process), single type or multitype (with finitely or infinitely many types), population size-dependent branching process, to mention a few [7-9].

Materials and Methods

In this paper, we apply a discrete single type Galton-Watson branching process to predict the number of cases of dengue disease in a population on generation basis.
We denote the number of index cases in the zeroth generation by Z_o. Then $Z_1, Z_2, \dots, Z_{n-1}, Z_n$ represent the numbers of infections in the first, second,…, (n-1)th and nth generations respectively.
We make the following assumptions about the branching process.

i. Every infected individual has an independently and identically distributed stochastic random variable X representing the number of secondary cases produced in generation n,
ii. Environmental stochasticity and immigration/emigration are ignored,
iii. The pattern of secondary transmissions follows a discrete probability distribution

$p_k = \Pr(X = k), \quad k = 0, 1, 2, \dots$
Let X be a non-negative integer-valued random variable with distribution $p(x)$. Then,
$G(s) = p(0) + p(1)s + p(2)s^2 + \cdots = p(k)s^k = Es^X$ is the probability generating function of X
We should note that if $Z_0 = 1$(i.e. only one index case, the Galton-Watson process has the following identity:
$G_0(s) = s,$

$$G_1(s) = G(s) = \sum_{k=0}^{\infty} p_k s^k$$

$G_{n+1}(s) = G_n(G(s)) = G(G_n(s)).$
We employ the data in Table 1 to estimate the basic reproduction numbers. We first suppose that the offspring distribution is a Poisson distribution with a constant parameter, R so that the conditional distribution of observing Z_{n+1} cases, given Z_n cases, follows a Poisson distribution:

$Z_n\big|_{+1} Z_n \sim Poisson[Z_n, R_0]$; and secondly we suppose that the offspring distribution can be estimated by a kernel density function. Details of Poisson distribution and its applications can be obtained in Stirzaker (1999) and Chowell and Nishiura (2007) [10-11]. For details of kernel density estimation, see Shalizi (2015) [12].

Table 1: Estimates of the reproduction numbers, the number of epidemic weeks of the cumulative number of dengue notifications t^* used in the estimation, and other related parameters obtained from the two different methods from the foregoing

Municipality	Method I					Method II			
	t^*wks	$r(95\%\ CI) per\ wk$	$R_p(95\%\ CI)$	Cb_v	Cb_h	$I_v(0)$	$I_{h1}(0)$	t^*wks	$R_p(95\%\ CI)$
Whole state	12	0.25 (0.22, 0.27)	3.09(2.34,3.84)	1.46	0.04	4.68	64.60	16	2.0(1.75,2.23)
Manzanillo	13	0.24 (0.22, 0.26)	3.26(2.70,3.82)	0.81	0.08	5.89	17.66	16	2.30(2.00,2.59)
Colima	16	0.14 (0.12, 0.15)	1.84(1.62,2.06)	1.36	0.01	1.58	7.34	14	1.08(0.46,1.70)
Villade Alvarez	17	0.12 (0.09, 0.14)	1.67(1.46,1.89)	0.36	0.06	0.99	2.84	17	1.07(0.45,1.70)
Tecoman	10	0.33 (0.27, 0.39)	4.22(2.90,5.54)	0.63	0.09	1.20	0.93	13	3.30(1.63,4.97)

Cuauhtemoc	22	0.11 (0.09, 0.13)	1.64(1.44,1.83)	2.68	0.004	0.68	5.16	13	0.54 (0.0, 1.48)
Coquimatlan	21	0.05 (0.04, 0.06)	1.24(1.15,1.33)	2.64	0.003	1.64	17.14	19	0.49(0.0, 0.99)

Source: Chowell *et al* (2007)

Simulation

We performed the following simulations to determine some possible realizations.

Simulation 1: kernel

Table 2: The following table shows the results of 10 simulations of the branching process

simulation	Z_0	Z_1	Z_2	Z_3	Z_4	Z_5	Z_6	Z_7	Z_8	Z_9	Z_{10}
1	1	3	4	3	8	10	15	28	52	101	195
2	1	2	6	13	16	28	44	83	153	291	584
3	1	2	5	12	20	39	67	139	270	502	944
4	1	2	4	3	5	10	26	64	118	259	497
5	1	1	3	9	18	34	67	125	253	453	891
6	1	3	4	12	24	50	105	230	294	696	1334
7	1	4	13	36	74	148	268	536	998	1925	3593
8	1	1	3	6	9	17	42	82	150	306	608
9	1	4	9	13	27	41	60	114	224	425	812
10	1	2	6	13	22	33	63	115	231	473	901

Simulation 2: Poisson

Table 3: The following table shows the results of 10 simulations of the branching process

simulation	Z_0	Z_1	Z_2	Z_3	Z_4	Z_5	Z_6	Z_7	Z_8	Z_9	Z_{10}
1	1	3	9	13	27	56	98	165	311	569	1067
2	1	0	0	0	0	0	0	0	0	0	0
3	1	0	0	0	0	0	0	0	0	0	0
4	1	1	2	5	15	27	48	103	191	348	671
5	1	2	3	5	14	27	48	95	169	311	582
6	1	1	4	5	11	31	59	108	209	388	734
7	1	2	6	8	13	19	37	77	164	318	564
8	1	4	7	9	18	30	50	72	133	252	481
9	1	1	3	5	10	17	29	56	91	177	328
10	1	2	6	14	23	43	82	157	297	516	960

Simulation 3: kernel

Table 4: The following table shows the results of 10 simulations of the branching process

simulation	Z_0	Z_1	Z_2	Z_3	Z_4	Z_5	Z_6	Z_7	Z_8	Z_9	Z_{10}
1	1	2	2	4	7	6	10	21	27	46	61
2	1	1	1	4	2	3	6	9	10	14	31
3	1	1	0	0	0	0	0	0	0	0	0
4	1	3	4	3	2	3	4	5	6	10	9
5	1	3	3	6	10	12	13	18	32	42	70
6	1	0	0	0	0	0	0	0	0	0	0
7	1	2	1	2	2	4	6	12	19	26	37
8	1	4	6	12	16	23	34	49	65	83	129
9	1	2	6	13	20	36	51	78	123	181	287
10	1	2	4	5	12	25	28	41	54	74	115

Simulation 4: Poisson

Table 5: The following table shows the results of 10 simulations of the branching process

simulation	Z_0	Z_1	Z_2	Z_3	Z_4	Z_5	Z_6	Z_7	Z_8	Z_9	Z_{10}
1	1	0	0	0	0	0	0	0	0	0	0
2	1	0	0	0	0	0	0	0	0	0	0
3	1	1	1	1	3	5	4	6	6	4	5
4	1	2	7	12	15	15	20	27	39	45	56
5	1	2	4	2	2	2	1	2	0	0	0
6	1	3	7	9	11	22	21	36	55	81	122
7	1	3	5	9	12	20	34	52	80	114	183

8	1	1	3	8	14	24	28	40	59	94	160
9	1	0	0	0	0	0	0	0	0	0	0
10	1	2	5	4	7	9	12	16	16	12	16

Simulation 5 : kernel

Table 6: The following table shows the results of 10 simulations of the branching process

simulation	Z_0	Z_1	Z_2	Z_3	Z_4	Z_5	Z_6	Z_7	Z_8	Z_9	Z_{10}
1	1	4	9	20	51	121	266	594	1331	3039	6999
2	1	3	7	17	44	108	239	568	1315	3076	7061
3	1	3	12	29	67	147	343	783	1791	4112	9585
4	1	1	4	6	14	31	73	185	422	965	2230
5	1	1	1	2	4	9	23	46	111	256	589
6	1	3	8	16	34	72	170	399	903	2089	4863
7	1	1	1	1	3	7	14	34	85	181	417
8	1	2	3	9	18	43	110	258	608	1425	3355
9	1	2	3	7	17	33	73	182	442	1038	2389
10	1	1	2	5	11	28	74	175	414	936	2225

Simulation 6 : Poisson

Table 7: The following table shows the results of 10 simulations of the branching process

simulation	Z_0	Z_1	Z_2	Z_3	Z_4	Z_5	Z_6	Z_7	Z_8	Z_9	Z_{10}
1	1	4	9	23	54	132	295	689	1574	3578	8229
2	1	4	5	9	19	49	127	290	650	1511	3473
3	1	1	2	5	12	30	57	133	313	736	1684
4	1	1	4	13	29	72	171	419	992	2257	5242
5	1	0	0	0	0	0	0	0	0	0	0
6	1	2	3	7	15	38	95	211	490	1148	2669
7	1	4	12	25	52	118	268	593	1378	3113	7253
8	1	1	2	4	8	16	36	83	202	521	1181
9	1	2	6	17	49	116	266	616	1446	3379	7854
10	1	3	7	13	24	56	119	287	659	1488	3406

Simulation 7 : kernel

Table 8: The following table shows the results of 10 simulations of the branching process

simulation	Z_0	Z_1	Z_2	Z_3	Z_4	Z_5	Z_6	Z_7	Z_8	Z_9	Z_{10}
1	1	1	0	0	0	0	0	0	0	0	0
2	1	1	1	1	1	1	1	0	0	0	0
3	1	0	0	0	0	0	0	0	0	0	0
4	1	1	1	1	0	0	0	0	0	0	0
5	1	0	0	0	0	0	0	0	0	0	0
6	1	0	0	0	0	0	0	0	0	0	0
7	1	1	0	0	0	0	0	0	0	0	0
8	1	1	1	0	0	0	0	0	0	0	0
9	1	1	1	0	0	0	0	0	0	0	0
10	1	0	0	0	0	0	0	0	0	0	0

Simulation 8 : Poisson

Table 9: The following table shows the results of 10 simulations of the branching process

simulation	Z_0	Z_1	Z_2	Z_3	Z_4	Z_5	Z_6	Z_7	Z_8	Z_9	Z_{10}
1	1	1	1	0	0	0	0	0	0	0	0
2	1	1	1	0	0	0	0	0	0	0	0
3	1	1	1	0	0	0	0	0	0	0	0
4	1	1	0	0	0	0	0	0	0	0	0
5	1	0	0	0	0	0	0	0	0	0	0
6	1	1	1	0	0	0	0	0	0	0	0
7	1	0	0	0	0	0	0	0	0	0	0

8	1	0	0	0	0	0	0	0	0	0
9	1	0	0	0	0	0	0	0	0	0
10	1	1	1	1	1	1	1	1	0	0

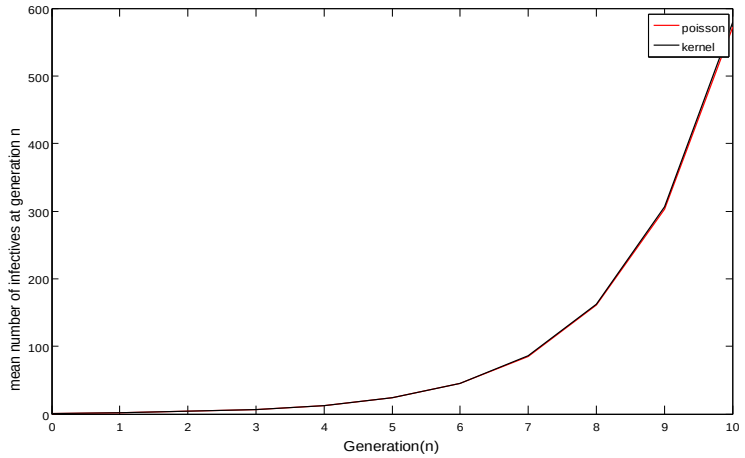

Figure 1: Graph showing the mean numbers of secondary transmissions up to the 10th generation for all Rs in methods I and II

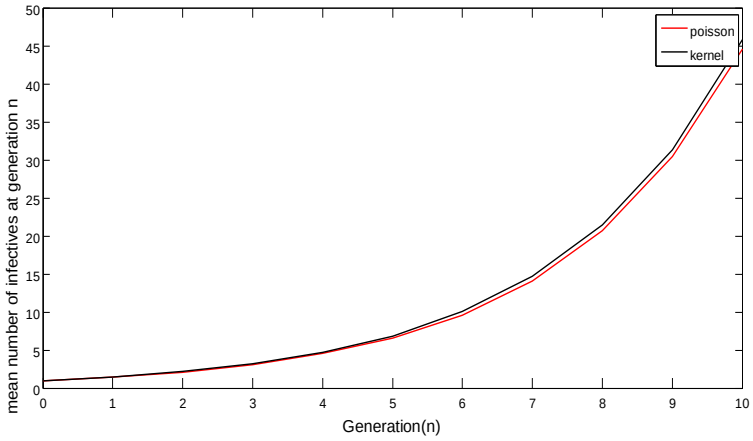

Figure 2: Graph showing the mean numbers of secondary transmissions up to the 10th generation for all Rs in method I

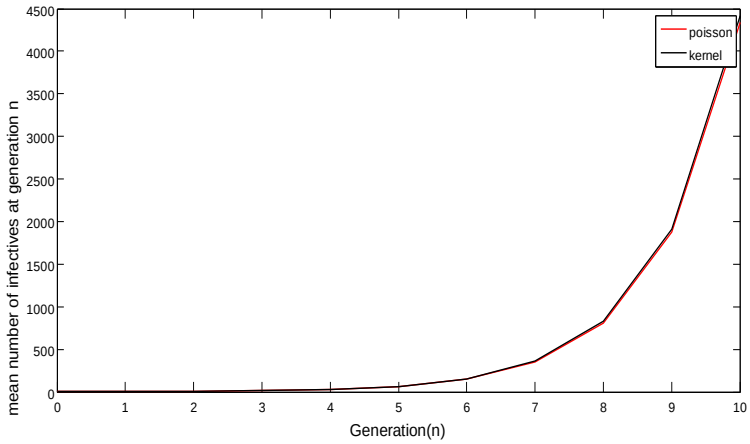

Figure 3: Graph showing the mean numbers of secondary transmissions up to the 10th generation for all Rs in methods II

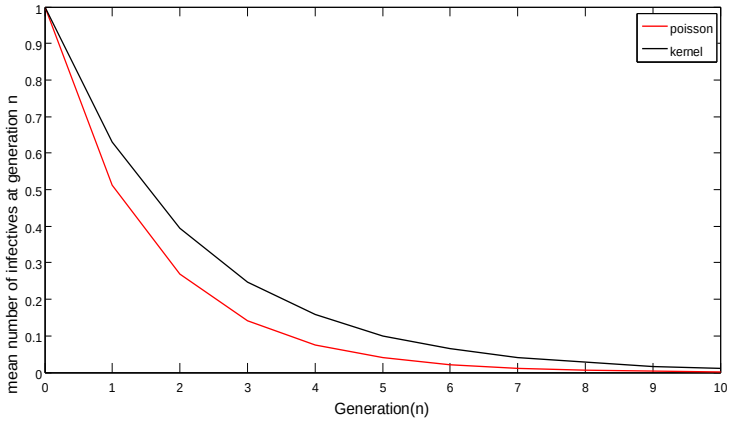

Figure 4: Graph showing the mean numbers of secondary transmissions up to the 10th generation for all Rs<1

Discussion

In this paper, a branching process model of dengue fever epidemics is studied. A data set on the estimated reproduction numbers by Chowell *et al* (2007) was used [5]. The essence is to predict the spread of the disease in any population or subpopulation with the same scenario. The results of this study are shown in Tables 2 through 9 and Figures 1 through 4. The numbers of infectives for ten generations for the dataset and subsets are shown in Tables 2 through 9. The sample paths for the mean numbers of infectives can be seen in Figures 1 through 4. The results show that the mean sample path for the branching process model with a kernel estimated offspring distribution is almost the same as the mean sample path for the same model with a Poisson estimated offspring distribution. The results further reveal that the number of new cases increases generation by generation in any population or subpopulation where the reproduction number is greater than one. However, elimination of the disease can be achieved in a population or subpopulation where the reproduction number is less than one.

Conclusion

In this paper dengue fever epidemic process is modeled as a discrete Galton-Watson branching process. This branching process is presented in section 2. We simulated the branching process to determine the number of cases in the chain up to the 10^{th} generation. The findings of the study show that in any population or subpopulation where the reproduction number is above one, there can be a major dengue fever outbreak. It is further stressed that efforts be intensified to kill the disease carrying mosquitoes, thereby reducing the reproduction number below one and stopping outbreaks.

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