The dynamical system

In order to calculate the proportion of cases and serious adverse events (including deaths) after a yellow fever (YF) outbreak, as well as the proportion of people to be vaccinated, we modelled the epidemic with a dynamical system, described by the following system of differential equations (Massad et al. 2005):

We now briefly describe some features of the system. Consider first the mosquito population, described by the first two equations of system. When a susceptible (without the infection) mosquito bites an infected person it may become (with a certain probability) infected. If it survives for a period of time, τ (the extrinsic incubation period) it

$$\pi_{yf}(p) = \frac{\int_0^\infty baM_i H_s^* / N_h dt}{(1-p)N_h}$$

$$d_{yf}(p) = \frac{\int_0^\infty (\mu_h + \alpha_h) H_i dt}{(1-p)N_h}$$

$$\pi_v(p) = \frac{\int_0^\infty \nu_h H_s^* dt}{(1-p)N_h}$$

$$d_v^*(p) = \frac{\int_0^\infty \mu_v H_v dt}{(1-p)N_h}$$

becomes infective, that is, if it bites a human it may transmit (with a certain probability) the infection. We are not interested in infected, but not yet infective mosquitoes, but rather we consider only susceptible mosquitoes, $M_{s,}$ and infective mosquitoes, M_i. The first two equations of the system above describe the dynamics of those two populations. Consider the first equation. We denote by a the biting rate of mosquitoes. So aM_s is the number of bites the susceptible mosquitoes inflict on humans per unit of time. Of those, only a proportion H_i / N_h will be on infected humans and of those only a proportion c will result in infected mosquitoes. We are aware that mosquitoes' susceptibility to infection varies geographically. However, these parameters, as well as all other shown in Table I, are estimated averages. Susceptible mosquitoes are assumed to die at a rate μ_M. The first term of the second equation describes the number of mosquitoes that became infected τ units of time earlier, survived a time interval τ and now became infective. The infective mosquitoes are assumed to die at a rate $\alpha_M + \mu_M$.

Let's now consider the human population. Humans are divided into those who were preemptively vaccinated, denoted H_s^{**} and those who did not receive the vaccine and are, therefore, truly susceptible, denoted H_s^*. The latter acquired the infection from infective mosquitoes through the bites $aM_iH_s^* / N_h$, a fraction of which, b, generates a new infection, although it is known that for *Aedes* mosquitoes this fraction is believed to be high [s]. They may be vaccinated during an outbreak, with a rate ν_h, or die by natural causes, with a rate μ_h The value of the rate ν_h was chosen in order to obtain the probability of dying by vaccination, $d_v^*(p)$ as equal to that estimated for real populations, d_v (p). The individuals preemptively vaccinated, H_s^{**}, die with rates μ_v (by the effect of the vaccine) and μ_h, the natural mortality rate of humans. Once infected, H_i, individuals can either recover from the infection, with rate γ_h, or die with rates α_h (the mortality rate of YF), or μ_h, the natural mortality rate of humans. The mortality rate quoted above, α_h, does not take into account the possible modulating effects of heterotypic flavivirus antibodies since there are no available quantitative data on this effect. Individuals vaccinated during the outbreaks, H_v, can die by natural causes or by the vaccine, with rates μ_h and μ_v, respectively. Depending on the case the rate μ_v also represent the rate of developing vaccine-induced serious adverse events. Those recovered from the infection, H_r, die only by natural causes.

Using the parameters and initial conditions described in Table I, we numerically solved the system in order to obtain the quantities necessary to estimate the optimum proportion to vaccinate, p_{gr}, that minimises the total number of serious adverse events (including deaths):

$$\pi_{yf}(p) = \frac{\int_0^\infty baM_i H_s^* / N_h dt}{(1-p)N_h}$$

$$d_{yf}(p) = \frac{\int_0^\infty (\mu_h + \alpha_h) H_i dt}{(1-p)N_h}$$

$$\pi_v(p) = \frac{\int_0^\infty \nu_h H_s^* dt}{(1-p)N_h}$$

$$d_v^*(p) = \frac{\int_0^\infty \mu_v H_v dt}{(1-p)N_h}$$

where p is the proportion of the population preemptively vaccinated, as described in the main text.

TABLE I

Delphi scores, risk of outbreak and optimum vaccination proportions for the still unvaccinated regions of the state of São Paulo, Brazil

	Delphi score	r	Vaccination (%)
Capital	9	0.16	16
Santo André	9	0.16	16
Mogi das Cruzes	10	0.18	20
Franco da Rocha	11	0.20	23
Osasco	10	0.18	20
Botucatu	22	0.40	100
Campinas	14	0.25	30
Piracicaba	15	0.27	36
Registro	18	0.33	50
Santos	14	0.25	30
São João da Boa Vista	15	0.27	36
São José dos Campos	9	0.16	16
Taubaté	12	0.22	26
Sorocaba	18	0.33	50
Caraguatatuba	15	0.27	36

TABLE II

Calculated optimum proportion for vaccination according to model (The dynamical system)

Vaccination proportion	Risk of outbreak							
p	0.4	0.32	0.27	0.25	0.22	0.20	0.18	0.16
0	9.5583E-06	7.6466E-06	6.4518E-06	5.9739E-06	5.2571E-06	4.7791E-06	4.3012E-06	3.8233E-06
0.033	8.3132E-06	6.6830E-06	5.6642E-06	5.2566E-06	4.6453E-06	4.2377E-06	3.8302E-06	3.4226E-06
0.066	7.5582E-06	6.1114E-06	5.2072E-06	4.8455E-06	4.3030E-06	3.9413E-06	3.5796E-06	3.2180E-06
0.099	7.0534E-06	5.7401E-06	4.9192E-06	4.5909E-06	4.0984E-06	3.7701E-06	3.4417E-06	3.1134E-06
0.132	6.6931E-06	5.4843E-06	4.7288E-06	4.4266E-06	3.9733E-06	3.6710E-06	3.3688E-06	3.0666E-06
0.165	6.4237E-06	5.3012E-06	4.5996E-06	4.3190E-06	3.8981E-06	3.6174E-06	3.3368E-06	**3.0562E-06**
0.198	6.2149E-06	5.1666E-06	4.5114E-06	4.2494E-06	3.8562E-06	3.5942E-06	**3.3321E-06**	3.0700E-06
0.231	6.0487E-06	5.0661E-06	4.4520E-06	4.2063E-06	3.8379E-06	**3.5922E-06**	3.3466E-06	3.1009E-06
0.264	5.9136E-06	4.9905E-06	4.4135E-06	4.1827E-06	**3.8365E-06**	3.6057E-06	3.3750E-06	3.1442E-06
0.297	5.8017E-06	4.9334E-06	4.3907E-06	**4.1736E-06**	3.8480E-06	3.6309E-06	3.4138E-06	3.1968E-06
0.33	5.7077E-06	4.8907E-06	4.3800E-06	4.1757E-06	3.8693E-06	3.6651E-06	3.4608E-06	3.2565E-06
0.363	5.6278E-06	4.8592E-06	**4.3788E-06**	4.1866E-06	3.8984E-06	3.7062E-06	3.5141E-06	3.3219E-06
0.396	5.5592E-06	4.8367E-06	4.3852E-06	4.2046E-06	3.9336E-06	3.7530E-06	3.5724E-06	3.3918E-06
0.429	5.4997E-06	4.8216E-06	4.3977E-06	4.2282E-06	3.9739E-06	3.8044E-06	3.6349E-06	3.4653E-06
0.462	5.4477E-06	4.8124E-06	4.4154E-06	4.2566E-06	4.0183E-06	3.8595E-06	3.7007E-06	3.5419E-06
0.495	5.4020E-06	**4.8083E-06**	4.4373E-06	4.2889E-06	4.0662E-06	3.9178E-06	3.7694E-06	3.6210E-06
0.528	5.3616E-06	4.8085E-06	4.4627E-06	4.3244E-06	4.1170E-06	3.9787E-06	3.8404E-06	3.7021E-06
0.561	5.3257E-06	4.8122E-06	4.4912E-06	4.3628E-06	4.1703E-06	4.0419E-06	3.9135E-06	3.7851E-06
0.594	5.2937E-06	4.8190E-06	4.5223E-06	4.4036E-06	4.2256E-06	4.1070E-06	3.9883E-06	3.8696E-06
0.627	5.2649E-06	4.8284E-06	4.5556E-06	4.4465E-06	4.2828E-06	4.1737E-06	4.0646E-06	3.9555E-06
0.66	5.2391E-06	4.8402E-06	4.5909E-06	4.4912E-06	4.3416E-06	4.2419E-06	4.1422E-06	4.0425E-06
0.693	5.2158E-06	4.8540E-06	4.6279E-06	4.5375E-06	4.4018E-06	4.3114E-06	4.2209E-06	4.1305E-06
0.726	5.1947E-06	4.8696E-06	4.6664E-06	4.5851E-06	4.4632E-06	4.3820E-06	4.3007E-06	4.2194E-06
0.759	5.1756E-06	4.8868E-06	4.7062E-06	4.6340E-06	4.5257E-06	4.4535E-06	4.3813E-06	4.3091E-06
0.792	5.1582E-06	4.9053E-06	4.7472E-06	4.6840E-06	4.5892E-06	4.5260E-06	4.4627E-06	4.3995E-06
0.825	5.1424E-06	4.9251E-06	4.7893E-06	4.7350E-06	4.6535E-06	4.5992E-06	4.5449E-06	4.4905E-06
0.858	5.1280E-06	4.9460E-06	4.8323E-06	4.7868E-06	4.7186E-06	4.6731E-06	4.6276E-06	4.5821E-06
0.891	5.1148E-06	4.9680E-06	4.8762E-06	4.8394E-06	4.7844E-06	4.7476E-06	4.7109E-06	4.6742E-06
0.924	5.1028E-06	4.9908E-06	4.9208E-06	4.8928E-06	4.8508E-06	4.8228E-06	4.7947E-06	4.7667E-06
0.957	5.0919E-06	5.0145E-06	4.9661E-06	4.9468E-06	4.9177E-06	4.8984E-06	4.8790E-06	4.8597E-06
0.99	**5.0818E-06**	5.0389E-06	5.0121E-06	5.0013E-06	4.9852E-06	4.9745E-06	4.9638E-06	4.9530E-06

values in bold mean optimum vaccination ratio which minimizes the risk of death.