Environmentally Transmitted Pathogens

Models – Part deux :)

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January 2023

A few models of Cvjetanović
- A tetanus model

A model of Capasso for ETP

A model for zoonotic transmission of waterborne disease

A few models of schistosomiasis
- A first model of Woolhouse
- A second model of Woolhouse – Latency
- A third model of Woolhouse – Heterogeneous contacts
- Spatial aspects – Cholera in Haiti

- Cvjetanović, Grab, Uemura & World Health Organization. Dynamics of acute bacterial diseases : epidemiological models and their application in public health. World Health Organization (1978)
- Briscoe. On the use of simple analytic mathematical models of communicable diseases. *International Journal of Epidemiology* **9**(3) (1980)

Models of (Branko) Cvjetanović are in discrete time and quite detailed on the epi side

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Tetanus

Bacterial infection caused by *Clostridium tetani*

Spores everywhere in the environment, including soil, dust, and manure

Spores develop into bacteria when they enter the body

Not spread P2P (so not a classic model)

Incubation period usually 3-21 days (average 8 days). Can range from 1 day to several months, depending on the kind of wound. Most cases occur within 14 days

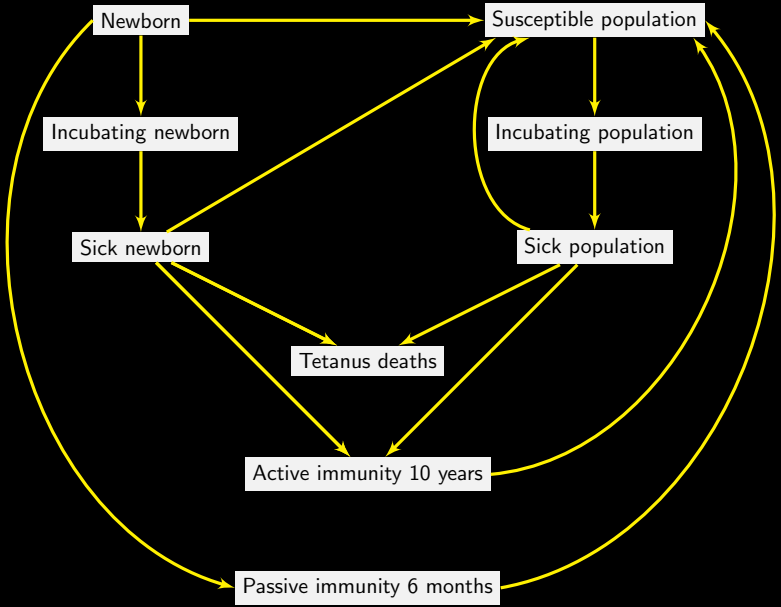
1 to 2 in 10 cases are fatal

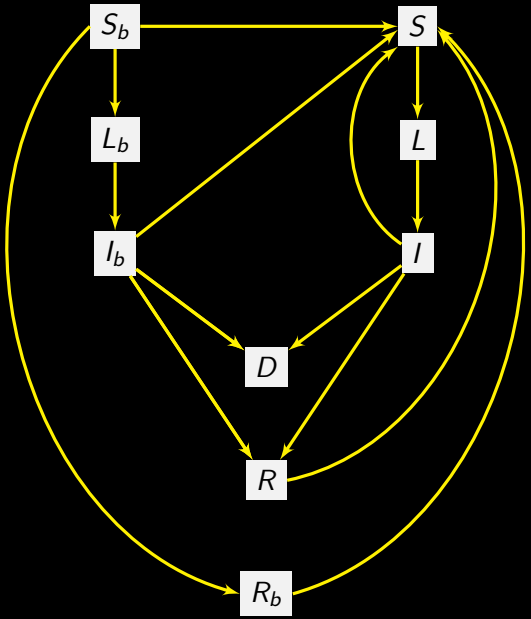
People of all ages need
TETANUS VACCINES

DTaP for young children	Tdap for preteens	Td or Tdap for adults
✓ 2, 4, and 6 months ✓ 15 through 18 months ✓ 4 through 6 years	✓ 11 through 12 years	✓ Every 10 years

www.cdc.gov/tetanus

CDC


Newborn
Susceptible population
Incubating newborn
Incubating population
Sick newborn
Sick population
Tetanus deaths
Active immunity 10 years
Passive immunity 6 months


S_b
S
L_b
L
I_b
I
D
R
R_b

The discrete-time tetanus model (my notation)

$$\Delta S_b = bT \tag{1a}$$
$$\Delta S = b(1-\lambda_b)(T-R) + \nu R + \nu_b I + R_{5,2}\gamma_b I_b + R_{6,2}\gamma I - (\lambda + d - \delta_T)S \tag{1b}$$
$$\Delta L_b = \lambda_b b(T-R) - (\varepsilon_b + d - \delta_T)L_b \tag{1c}$$
$$\Delta L = \lambda S - (\varepsilon + d - \delta_T)L \tag{1d}$$
$$\Delta I_b = \varepsilon_b L_b - (\gamma_b + d - \delta_T)I \tag{1e}$$
$$\Delta I = \varepsilon L - (\gamma + d - \delta_T)I \tag{1f}$$
$$\Delta R = R_{5,7}\gamma_b I_b + R_{6,7}\gamma I - (\nu + d - \delta_T)R \tag{1g}$$
$$\Delta R_b = bR - (\nu_b + d - \delta_T)R_b \tag{1h}$$
$$\Delta D = R_{5,9}\gamma_b I_b + R_{6,9}\gamma I \tag{1i}$$

where

$$T = S + L_b + L + I_b + I + R + R_b \quad \text{and} \quad \delta_T = \frac{\Delta D}{T} \tag{1j}$$

PI: period of incubation. Mean duration 6 days for newborn and 8 days for general population. Corresponding daily rate of exit $\varepsilon_b = 0.1667$ and $\varepsilon = 0.125$
PS: period of sickness. Mean duration 3 days for newborn and 14 days for general population. So daily rate of exit $\gamma_b = 0.3333$ per sick newborn and $\gamma = 0.0714$ for sick general in general population.
Mortality from tetanus. Untreated tetanus cases, fatality rate 90% for newborn S_b and 40% for general population. Treated: 80% for newborn and 30% general population.
Immunity. Tetanus cases do not lead to immunity to reinfection. But as a general rule, recovered people are vaccinated. Convalescents and general population effectively immunised by complete course of vaccination go to R for average 10 years, Daily rate of exit is $\nu = 0.000274$ per person. Newborn to women vaccinated during pregnancy are temporarily protected by maternal antibodies and pass through R_b for a mean duration of 6 months. Daily rate of exit $\nu_b = 0.005479$ per immunised newborn
Live birth rate 35 per 1,000 population and annual crude death rate 15 per 1,000 population (annual rate of growth 2%). Corresponding daily birth and death rates $b = 0.00009889$ and $d = 0.0000411$ per person.

Force of infection

No H2H transmission $\Longrightarrow$ incidence proportional to number of susceptible individuals and force of infection, which quantifies combined effect of all variables involved in infection process:

- degree of soil contamination with *Clostridium tetani*
- climate
- frequency of lesions
- proportion of rural population
- socioeconomic conditions
- level of medical care for the wounded and during deliveries

Force of infection acting on newborn (λ_b) and susceptible population (λ) fixed at 3 different levels adequate for reproducing the following stable annual incidence rates of tetanus cases in the community

- For newborn, 200 cases, 400 cases and 600 cases per 100,000 newborn
- For general population (without newborn), 9, 18 and 27 cases

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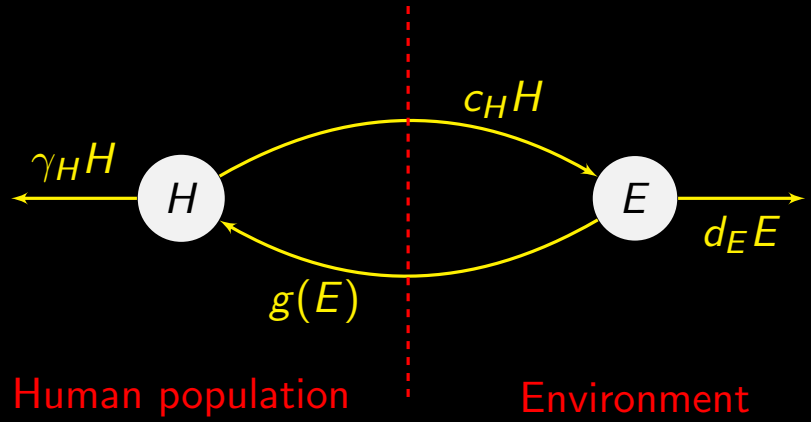
A minimal model of V. Capasso



$1/\gamma_H$ mean infectious period, $1/d_E$ mean lifetime of the agent in the environment, c_H growth rate of the agent due to the human population, $g(E)$ "force of infection" (I would say "incidence") of the agent on human population

Incidence function

$$g(E) = h(E)N\beta p \tag{2}$$

where

- $h(E)$ probability for an exposed susceptible to get the infection
- N total human population
- β fraction of susceptible individuals in N
- p fraction exposed to contaminated environment per unit time ("probability per unit time to have a "snack" of contaminated food")

Typically, we would assume p and β independent of E and H and h to be saturating

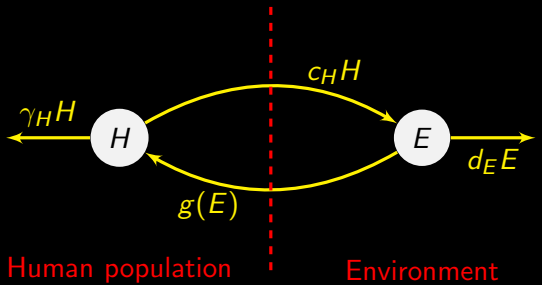
To ensure (2) satisfies these conditions, we can assume

- $0 < g(e_1) < g(e_2)$ for $0 < e_1 < e_2$
- $g(0) = 0$
- $g''(z) < 0$ for all $z > 0$
- $0 < g'_+(0) < \infty$ (right derivative)
- $\lim_{z\to\infty} \frac{g(z)}{z} < \frac{d_E \gamma_H}{c_H}$

Of course, we also assume $d_E, c_H, \gamma_H > 0$

The model

$$E' = c_H H - d_E E \tag{3a}$$
$$H' = g(E) - \gamma_H H \tag{3b}$$



Pay attention to the flows..! E' does not have a $-g(E)$ and H' does not have $-c_H H$. Why?

Let

$$\mathcal{R}_0 = \frac{g'_+(0)c_H}{d_E\gamma_H} \tag{4}$$

Theorem 1

- *If* $0 < \mathcal{R}_0 < 1$, *then* (3) *admits only the trivial equilibrium in the positive orthant, which is GAS*
- *If* $\mathcal{R}_0 > 1$, *then two EP exist:* $(0,0)$, *which is unstable, and* $z^\star = (E^\star, H^\star)$ *with* $E^\star, H^\star > 0$, *GAS in* $\mathbb{R}^2_+ \setminus \{0,0\}$

Adding a periodic component

Assume p in (2) takes the form

$$p(t) = p(t+\omega) > 0, \quad t \in \mathbb{R} \tag{5}$$

i.e., p has period ω. So we now consider the incidence

$$g(t, E) = p(t)h(E) \tag{6}$$

with h having the properties prescribed earlier. Letting

$$p_{min} := \min_{0 \le t \le \omega} p(t), \quad p_{max} := \max_{0 \le t \le \omega} p(t) \tag{7}$$

then we require that

$$\lim_{z \to \infty} \frac{g(z)}{z} < \frac{d_E \gamma_H}{c_H p_{max}} \tag{8}$$

Let

$$\mathcal{R}_0^{min} = \frac{c_H p_{min} h'_+(0)}{d_E \gamma_H}, \quad \mathcal{R}_0^{max} = \frac{c_H p_{max} h'_+(0)}{d_E \gamma_H} \tag{9}$$

Theorem 2

- *If* $0 < \mathcal{R}_0^{max} < 1$, *then* (3) *with incidence* (6) *always goes to extinction*
- *If* $\mathcal{R}_0^{min} > 1$, *then a unique nontrivial periodic endemic state exists for* (3) *with incidence* (6)

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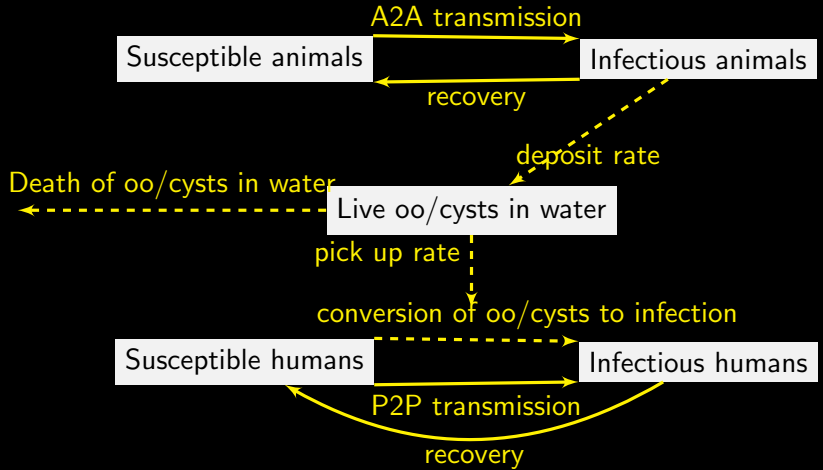
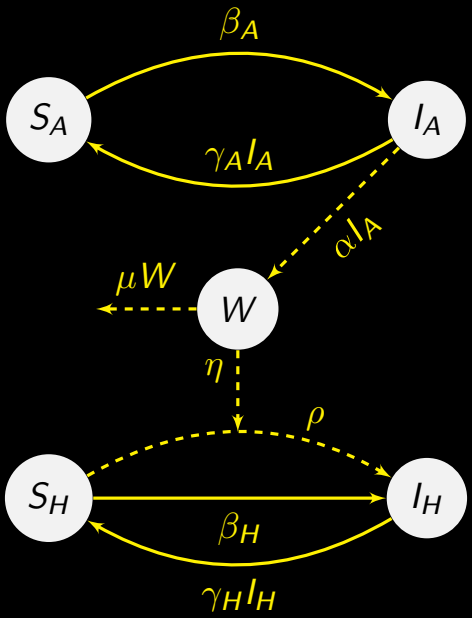
Zoonotic transmission of waterborne disease

Waters, Hamilton, Sidhu, Sidhu, Dunbar. Zoonotic transmission of waterborne disease: a mathematical model. *Bull Math Biol* (2016)
Used for instance to model Giardia transmission from possums to humans


A2A transmission
Susceptible animals
Infectious animals
recovery
deposit rate
Death of oo/cysts in water
Live oo/cysts in water
pick up rate
conversion of oo/cysts to infection
Susceptible humans
Infectious humans
P2P transmission
recovery


β_A
S_A
I_A
$\gamma_A I_A$
αI_A
μW
W
η
ρ
S_H
I_H
β_H
$\gamma_H I_H$

The full model

$$S_A' = -\beta_A S_A I_A + \gamma_A I_A \tag{10a}$$
$$I_A' = \beta_A S_A I_A - \gamma_A I_A \tag{10b}$$
$$W' = \alpha I_A - \eta W(S_H + I_H) - \mu W \tag{10c}$$
$$S_H' = -\rho\eta W S_H - \beta_H S_H I_H + \gamma_H I_H \tag{10d}$$
$$I_H' = \rho\eta W S_H + \beta_H S_H I_H - \gamma_H I_H \tag{10e}$$

Considered with $N_A = S_A + I_A$ and $N_H = S_H + I_H$ constant

Simplified model

Because N_A and N_H are constant, (10) can be simplified:

$$I_A' = \beta_A N_A I_A - \gamma_A I_A - \beta_A I_A^2 \tag{11a}$$
$$W' = \alpha I_A - \eta W N_H - \mu W \tag{11b}$$
$$I_H' = \rho\eta W(N_H - I_H) + \beta_H N_H I_H - \gamma_H I_H - \beta_H I_H^2 \tag{11c}$$

Three EP: DFE $(0, 0, 0)$; endemic disease in humans because of H2H transmission; endemic in both H and A because of W

Three EP: DFE $(0, 0, 0)$; endemic disease in humans because of H2H transmission; endemic in both H and A because of W

Let

$$\mathcal{R}_{0A} = \frac{\beta_A}{\gamma_A} N_A \quad \text{and} \quad \mathcal{R}_{0H} = \frac{\beta_H}{\gamma_H} N_H \tag{12}$$

- DFE LAS if $\mathcal{R}_{0A} < 1$ and $\mathcal{R}_{0H} < 1$, unstable if $\mathcal{R}_{0A} > 1$ or $\mathcal{R}_{0H} > 1$
- If $\mathcal{R}_{0H} > 1$ and $\mathcal{R}_{0A} < 1$, (11) goes to EP with endemicity only in humans
- Endemic EP with both A and H requires $\mathcal{R}_{0A} > 1$ and $\mathcal{R}_{0H} < 1$

Note that proof is **not** global

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A model of Woolhouse

Woolhouse. On the application of mathematical models of schistosome transmission dynamics. I. Natural transmission. *Acta Tropica* **49**:241-270 (1991)

The model

Population of H individuals using a body of water containing N snails

i_H mean number of schistosomes per person and i_S the proportion of patent infections in snails (prevalence)

$$i'_H = \alpha N i_S - \gamma i_H \tag{13a}$$
$$i'_S = \beta H i_H (1 - i_S) - \mu_2 i_S \tag{13b}$$

- α number of schistosomes produced per person per infected snail per unit time
- $1/\gamma$ average life expectancy of a schistosome
- $1/\mu_2$ average life expectancy of an infected snail
- β transmission parameter

Let the basic reproductive rate for schistosomes be

$$\mathcal{R}_0 = \frac{\alpha N \beta H}{\gamma \mu_2} \tag{14}$$

(13) has two EP

- $(i_H^\star, i_S^\star) = (0, 0)$, LAS when $\mathcal{R}_0 < 1$ and unstable when $\mathcal{R}_0 > 1$
- $(i_H^\star, i_S^\star) = \left(\frac{\alpha N}{\gamma} - \frac{\mu_2}{\beta H}, 1 - \frac{1}{\mathcal{R}_0} \right)$, which only "exists" when $\mathcal{R}_0 > 1$ (and is LAS then)

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Extending the model

Interval between infection of a snail and onset of patency (release of cercariae) is *prepatent* or *latent* period

$$i'_H = \alpha N i_S - \gamma i_H \tag{15a}$$
$$\ell'_S = \beta H i_H (1 - \ell_S - i_S) - \sigma \ell_S - \mu_1 \ell_S \tag{15b}$$
$$i'_S = \sigma \ell_S - \mu_2 i_S \tag{15c}$$

- $1/\sigma$ average duration of prepatent period
- $f = \sigma/(\sigma + \mu_1)$ fraction of infected snails surviving prepatent period

The basic reproductive rate for schistosomes is now

$$\mathcal{R}_0 = f\frac{\alpha N \beta H}{\gamma \mu_2} \tag{16}$$

(15) has endemic EP

$$(i_H^\star, i_S^\star) = \left(\frac{\alpha N \sigma}{\gamma(\sigma+\mu_2)} - \frac{\mu_2(\sigma+\mu_1)}{\beta H(\sigma+\mu_2)}, \frac{\sigma}{\sigma+\mu_2}\left(1-\frac{1}{\mathcal{R}_0}\right)\right)$$

Also has models

- where snails lose infectiousness (assumed to happen sometimes)
- with larval population dynamics
- single variable models
- human immigration and emigration
- reservoir hosts

Really worth a read

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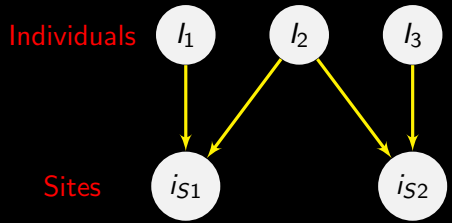
Heterogeneities in contact rates

I_i the number of schistosomes in person $i = 1, \ldots, H$ and i_{Sj} the proportion of patent infected snails in site $j = 1, \ldots, L$ (L sites each supporting N snails)



I_i the number of schistosomes in person $i = 1, \ldots, H$ and i_{Sj} the proportion of patent infected snails in site $j = 1, \ldots, L$ (L sites each supporting N snails)

$$I_i' = \alpha \left(\sum_j \eta_{ij} N i_{Sj} \right) - \gamma I_i \tag{17a}$$

$$i_{Sj}' = \beta \left(\sum_i \eta_{ij} I_i \right) (1 - i_{Sj}) - \mu_2 i_{Sj} \tag{17b}$$

η_{ij} rate of water contact by individual i at site j

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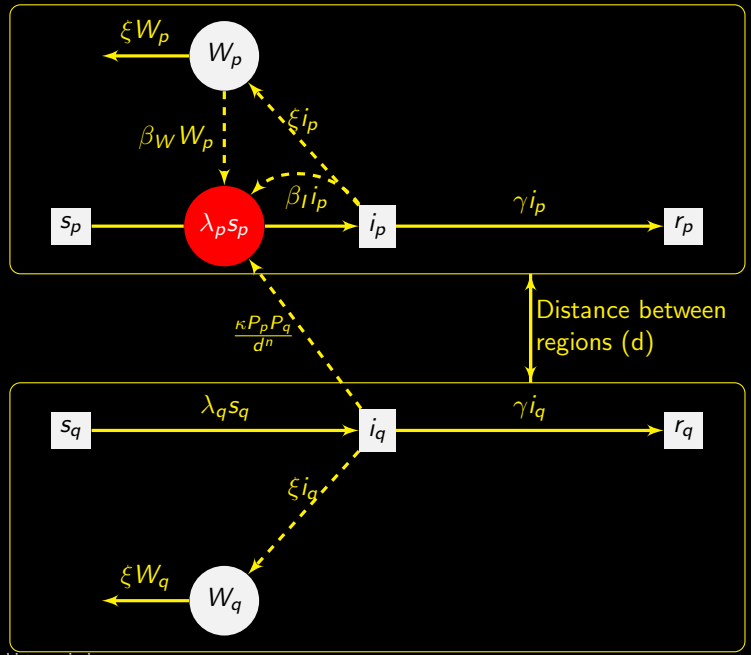
Spatial aspects – Cholera in Haiti

Tuite, Tien, Eisenberg, Earn, Ma & Fisman. Cholera Epidemic in Haiti, 2010: Using a Transmission Model to Explain Spatial Spread of Disease and Identify Optimal Control Interventions. *Annals of Internal Medicine* **154**(9) (2011)


ξW_p
W_p
ξi_p
$\beta_W W_p$
$\beta_I i_p$
s_p
$\lambda_p s_p$
i_p
γi_p
r_p
$\frac{\kappa P_p P_q}{d^n}$
Distance between regions (d)
s_q
$\lambda_q s_q$
i_q
γi_q
r_q
ξi_q
ξW_q
W_q

Metapopulation model with **implicit** movement

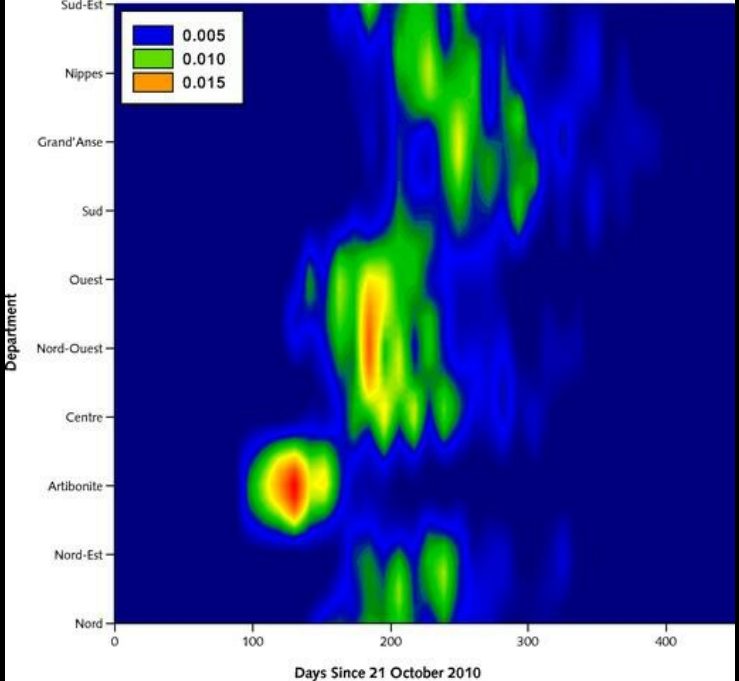
$$s_p' = \mu - \lambda_p s_p - \mu s_p \tag{18a}$$
$$i_p' = -\gamma i_p + \lambda_p s_p - \mu i_p \tag{18b}$$
$$r_p' = \gamma r_p - \mu r_p \tag{18c}$$
$$w_p' = \xi(i_p - w_p) \tag{18d}$$

with force of infection

$$\lambda_p = \beta_{i_p} i_p + \beta_{W_p} w_p + \sum_{q=1}^{10} \theta_{pq} i_q \tag{18e}$$

Influence of infection prevalence in q on incidence in p is gravity-type

$$\theta_{pq} = \kappa \frac{P_p P_q}{d^n}$$


0.005
0.010
0.015
Sud-Est
Nippes
Grand'Anse
Sud
Ouest
Nord-Ouest
Centre
Artibonite
Nord-Est
Nord
Department
0
100
200
300
400
Days Since 21 October 2010