Vaccination : between public health policy and individual options

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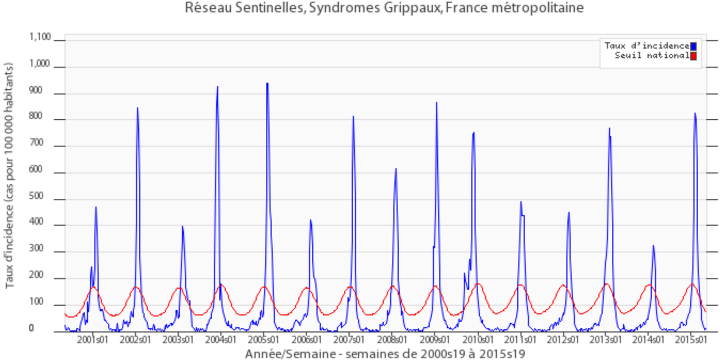
18ème Congrès de l'IUF 2015, Montpellier

Disclaimer:

What follows is a theoretical epidemiological investigation. It is not meant to be used directly for health-related decisions; if in need to take such a decision please seek professional medical advice.

Outline

Influenza incidence historical data in France



Sourse: réseau Sentinelles, INSERM/UPMC, http://www.sentiweb.fr

Influenza A (H1N1) (flu) (2009-10) : see animation.

Vaccine scares:

Influenza A (H1N1) (flu) (2009-10)

• At 15/06/2010 flu (H1N1): 18.156 deaths in 213 countries (WHO)
• France: 1334 severe forms (out of $7.7M$-$14.7M$ people infected)

Vaccination in France

• Adjuvant suspected of some neurological undesired effects; mass vaccination uncertainty (few previous studies for this size)
• Very costly campaign (500M EUR),
• Low efficiency (8% to 10% in France with respect to e.g., 24% US or 74% Canada).

Vaccine scares:

Example : Influenza A in 2009 - 2010.
Vaccination Coverage expected and realized in different countries on percentage of population: (See schedule 3 of the french parliamentary report number 2698)

Countries	Target coverage	Effective rate of vaccination
Germany	100 %	10%
Belgium	100 %	6 %
Spain	40 %	$<$ 4%
France	70 - 75 %	8.5 %
Italy	40 %	1.4 %

Vaccine scares

Previous vaccine scares (some have been disproved since):

- France: hepatitis B vaccines cause multiple sclerosis
- US: mercury additives are responsible for the rise in autism
- UK: the whooping cough (1970s), the measles-mumps-rubella (MMR) (1990s).

Vaccine Scares : "as cases of a disease decrease, people become complacent about their risk, and the threat of vaccines (imagined or real) seems greater than the threat of disease" (C. Bauch)

Further motivation: end of compulsory vaccination

• context in France: discussions on the end of general compulsory vaccination

• How is vaccination coverage evolving ? Example: nobody vaccinates then an additional individual may vaccinate; if all vaccinate an additional invididual will not vaccinate. Will the vaccination coverage become unstable or chaotic ?

• question: what are the determinants of individual vaccination

• hint: individual decisions sum up to give a global response; need a model.

Outline

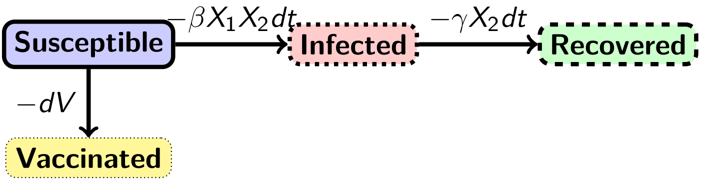


Figure: Graphical illustration of the SIR-V model. In this model all individuals are identical.

$$\begin{cases} dX_1 = -\beta X_1 X_2 dt - dV(t) \\ dX_2 = (\beta X_1 X_2 - \gamma X_2) dt \\ dX_3 = \gamma X_2 dt \\ dV = dV. \end{cases}$$

β : probability of contamination,
γ : recovery rates,
$dV(t)$: measure of vaccination

Since $X_1(t) + X_2(t) + X_3(t) + V(t) = cst = 1 \quad \forall t > 0$, the variable X_3 is dependent on the others, we denote $X = (X_1, X_2)^T$.

Vaccination cost functional

Cost for an infected person : r_I.
Cost of the vaccine (including side-effects) : r_V.

Global cost for the society (from the initial state $X_0 = (X_1(0), X_2(0))^T$) :

$$J(X_0, V) = r_I \int_0^\infty \beta X_1 X_2 dt + r_V \int_0^\infty dV(t) \quad (1)$$

It is an optimal control problem. The value function :

$$\mathcal{V}(X) = \inf_{w \in \Omega} J(X, w)$$

Here, Ω is some set of admissible functions; e.g., measurable functions $w : [0, \infty[\to [0, u_{max}]$ and such as $0 \leq X_i(t) \leq 1, \forall t \geq 0, i \in \{1, 2\}$.

Existing literature

There has been a lot of work on this subject in the literature :

Abakuks, Andris, 1974 "*Optimal immunisation policies for epidemics*",

Behncke, Horst, 2000, "*Optimal control of deterministic epidemics*",

Piunovskiy, Alexei B. and Clancy, Damian, 2008, "*An explicit optimal intervention policy for a deterministic epidemic model*"

Funk, Sebastian and Salathé, Marcel and Jansen, Vincent A. A, "*Modelling the influence of human behaviour on the spread of infectious diseases: a review*"

C. T. Bauch, 2005, "*Imitation dynamics predict vaccinating behaviour*"

Hethcote, Herbert W. and Waltman, Paul, 1973, "*Optimal vaccination schedules in a deterministic epidemic model*"

Sethi, Suresh P. and Staats, Preston W., 1978, "*Optimal control of some simple deterministic epidemic models*",

Morton, R. and Wickwire, K. H., 1974, "*On the optimal control of a deterministic epidemic*"

Ledzewicz, Urszula and Schättler, Heinz, 2011, "*On optimal singular controls for a general SIR-model with vaccination and treatment*"

Andris Abakuks, 1972, "*Some optimal isolation and immunisation policies for epidemics*"

but none shows any regularity of the value function

HJB equation

The value function $\mathcal{V}$ must satisfy the HJB equation :

$$-\mathcal{H}(X, \nabla\mathcal{V}) = 0$$

Let $X = (x_1; x_2)^T$ and $f(X, w) = (-\beta x_1 x_2 - w; \beta x_1 x_2 - \gamma x_2)$

$$\begin{aligned}\mathcal{H}(X, p) &= \min_{w\in[0,u_{max}]} [f(X, w) \cdot p + r_I \beta x_1 x_2 + r_V w] \\ &= -u_{max}(p_1 - r_v)_+ + \beta x_1 x_2 (r_I + p_2 - p_1) - \gamma x_2 p_2.\end{aligned}$$

But there is no a priori certainty that the solutions are $\mathcal{C}^1$ (possible discontinuity introduced by V).

We use the concept of viscosity solution introduced by Pierre-Louis Lions and Michael Crandall (1992, 1997). Widely used for the optimal control problem.

Results

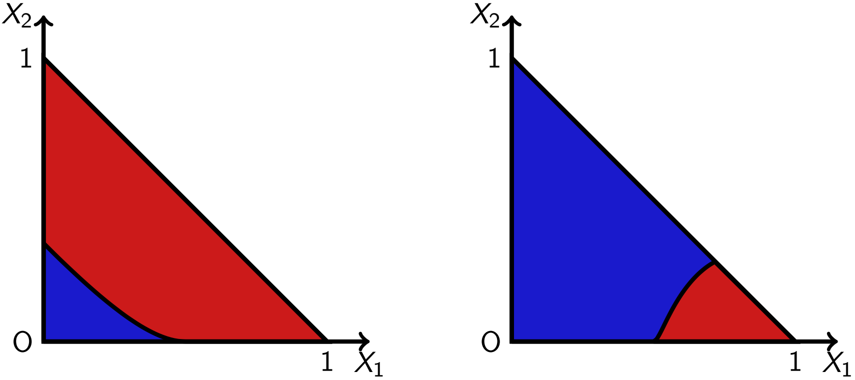
Results obtained (GT, LL 2014):

- ⋆ the HJB equation admits a unique solution; furthermore the solution is $\mathcal{C}^1$ for $r_V < r_v^{crit}$, otherwise it is Lipschitz.
- ⋆ explicit construction for the solution and the optimal vaccination strategy;
- ⋆ rigorous justification of the limit $u_{max} \to \infty$;

Global optimal vaccination strategy : decomposition in vaccination and non-vaccination region.

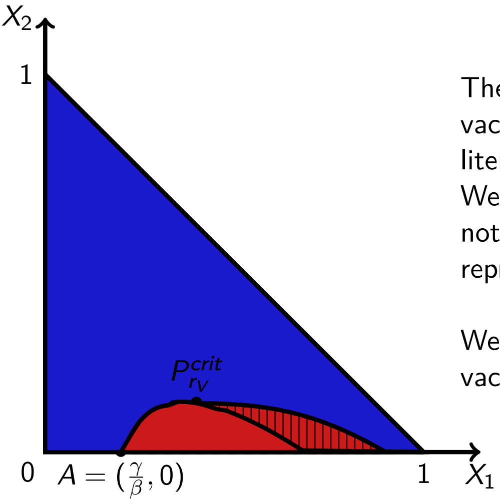
Results for $\gamma/\beta = 0.5$

Optimal strategy for $r_V = 0.5 r_I$. Optimal strategy for $r_V = 1.1 r_I$



Red region = vaccination, blue = no vaccination.
This calls for asking the nature of optimality: how can be optimal to vaccinate someone when $r_V > r_I$?

If $r_V \geq r_V^{crit}$



The red region without lines is the vaccination region present in the literature.
We find an other region vaccination not documented in the literature, represented with vertical lines.

We prove that the red domain is the vaccination region.

Outline

Taking into account the individual decisions: previous literature

Bauch & Earn (PNAS 2004) consider the SIR-V model with births and deaths :

$$\begin{cases} dS = \mu(1-p) - \beta SIdt - \mu S \\ dI = (\beta SI - \gamma I)dt - \mu I \\ dR = \gamma Idt - \mu R \\ dV = \mu p \end{cases}$$

β : probability of contamination,
γ : recovery rates,
$dV(t)$: measure of vaccination
μ : the birth / death rate
p the probability to vaccinate at birth

- ⋆ the vaccination is at birth only (probability p) ; at equilibrium vaccination occurs when the probability to be infected $\geq r_V / r_I$.
- ⋆ no time dependence; final state stationary.
- ⋆ equilibrium ok if everybody does the same
- ⋆ no eradication possible through voluntary vaccination, endemic state (coherent with literature)
- ⋆ "vaccine scare behavior" : let other vaccinate (when perceived risk differs from that of majority)

Taking into account the individual decisions: previous literature

Francis (2004) : uses a SIR-V model to find an equilibrium.
Results: They identify the vaccination region although the problem is not formulated as an optimization at the individual level.

Galvani, Reluga & Chapman (PNAS 2006) consider a double SIR-V periodic model of flu with two age groups (break at 65yrs). Vaccination is separated from dynamics, once at the beginning of each season.
Results : show that actual vaccine coverage is consistent with individual optimum; explain impact of age-targetted campaigns (children).

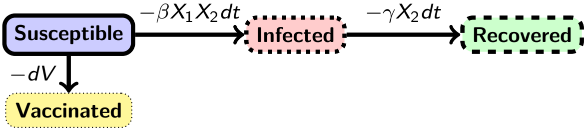
Taking into account the individual decisions: previous literature

Bauch (2005) :

- time dependent vaccination rate $p(t)$;
- probability to be infected is approximated by a "rule of thumb" (proportional to $I(t)$);
- the corresponding dynamics is a phenomenological proposal (m a parameter) :

$$\frac{dp(t)}{dt} = kp(1-p)(mr_I I(t) - r_V)$$

Individual dynamics

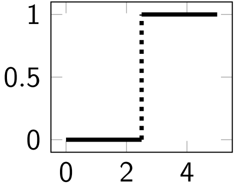


Global dynamics : continuous time deterministic ODE; is the master equation of the individual dynamics.

Individual dynamics: continuous time Markov jumps between 'Susceptible', 'Infected', 'Recovered' and 'Vaccinated' classes.

Taking into account the individual decisions : individual strategy

- the simplest one, the pure strategy : vaccinate with certainty at some given instant $\tau \in [0, \infty]$ ($\tau = \infty$ means no vaccination).

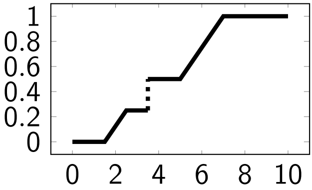


In terms of probability to vaccinate a pure strategy is $H(\cdot - \tau)$ with $H(\cdot)$ the Heaviside function. Here $\tau = 2.5$.

- is it always optimal ? NO does it give a stable equilibrium ? NO

Taking into account the individual decisions : individual strategy

- more realistic mixed strategies (related game theory concepts in "timing games" cf. Drew & Tirole): the individual chooses a probability measure $d\varphi_V$ over the space of all pure strategies.



The CDF function $\varphi_V(t)$ is increasing, right continuous with left limits (càdlàg) with $\varphi_V(0) = 0$, $\varphi_V(\infty) \leq 1$. In particular $\varphi_V(t)$ = probability to choose vaccination in the interval $[0, t]$.

Constraints : if global vaccination is at maximal rate u_{max} : $U(t + \Delta t) - U(t) \leq u_{max}\Delta t$. If everybody has the same φ_V then $dU(t) = \frac{d\varphi_V(t)}{1-\varphi_V(t)} X_1(t)$ (when this operation makes sense).
Individual constraint $d\varphi_V(t) \leq \frac{u_{max}}{X_1(t)}(1 - \varphi_V(t))dt$.

Outline

Individual cost functional

$$\begin{cases} dX_1 = -\beta X_1 X_2 dt - dU(t) \\ dX_2 = (\beta X_1 X_2 - \gamma X_2) dt \\ dX_3 = \gamma X_2 dt \\ dV = dU(t). \end{cases}$$

vaccination at the society level with $dU(t)$; it can have the form $dU(t) = u_G(t)dt$.

- Society dynamics induces a cumulative probability of infection on $[0,t]$: $\varphi_I(t)$ solution of $d\varphi_I(t) = \beta X_2(t)(1-\varphi_I(t))dt$, $\varphi_I(0) = 0$.
- Individual decision: φ_V (with constraints cf. above).
- Individual cost functional
  $J_I(\varphi_V) = \int_0^\infty [r_I(1-\varphi_V(t))d\varphi_I(t) + r_V(1-\varphi_I(t))d\varphi_V(t)]$
- Individual - global equilibrium condition (global strategy arise from individual decisions): $dU(t) = \frac{X_1(t)}{1-\varphi_V(t)} d\varphi_V(t)$ (when this operation makes sense) (Mean Field Games, cf. Lasry, Lions).

Theoretical results

Theoretical results (GT, LL 2014): fixed global (societal) policy

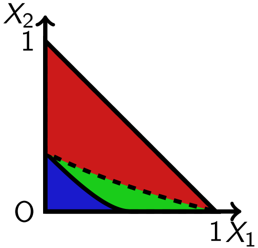
Optimal individual solution : vaccination untill the overall infection risk $\frac{\int_t^\infty \beta X_1(\tau) X_2(\tau) d\tau}{X_1(t)}$ (depending on dV) falls below $\frac{r_V}{r_I}$.

Theoretical results (GT, LL 2014): equilibrium

- ⋆ a stable (mixed, Nash) equilibrium exists
- ⋆ the domain is divided into a vaccination region and a non-vaccination region.
- ⋆ the frontier of the vaccination region is the line: infection risk $= \frac{r_V}{r_I}$

  Formula $\frac{\zeta(X_1, X_2)}{X_1} = \frac{r_V}{r_I}$; $\zeta(X)$ = size of a non-controlled epidemic from X.

Theoretical results

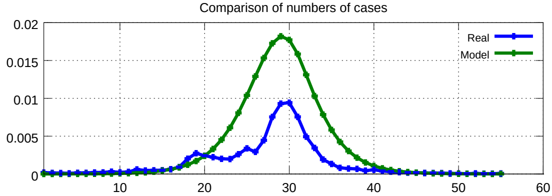


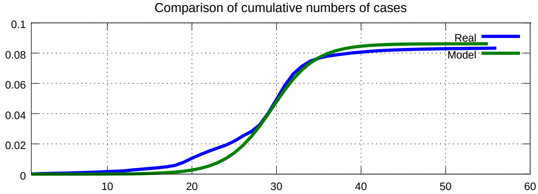
Red region: vaccination in the societal model and in the individual model, green region : vaccination for the societal model but not for the individual, blue region: no vaccination in both models.

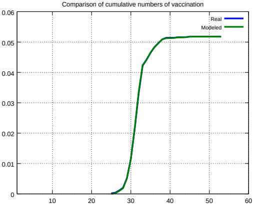
- ⋆ Mean cost for an individual in the stable individual-global equilibrium is larger than the cost for the, non equilibrium, societal (non-individual) optimum state
- ⋆ this is because in the green region, it is optimal for individuals to let other vaccinate.
- ⋆ Conclusion: the stable strategy will be obtained even if it is more costly for everyone; the "cost of anarchy" in the model is non-null.

Application to Influenza A 2009/2010 vaccination

The SIR model was fit to the observed vaccination coverage (J.P. Guthman et al. BEH 2010); the other parameters were chosen consistent with ranges from the literature (large CIs !).
Time axis = weeks starting from W19Y2009; peak = W49Y2009 (30), vaccination peak = W51Y2009 (31-32), vaccination end W05Y2010 (40).







Application to Influenza A 2009/2010 vaccination

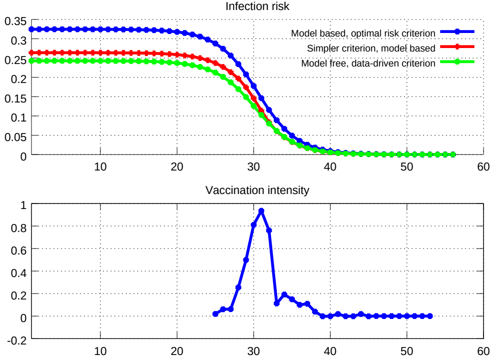


Figure: Time axis = weeks starting from W19Y2009; peak = W49Y2009 (30), vaccination peak = W51Y2009 (31-32), vaccination end W05Y2010 (40).

The results indicate that the risk perception was inhomogeneous; first group to stop vaccination perceived relative risk $r_V/r_I \simeq 5\% - 10\%$!! (week 32). The last group corresponds to $r_V/r_I < 1\%$ (week 40; model cannot be more precise with available data).

Work in progress: age-dependent coverage

In collaboration with Daniel Lévy-Bruhl and Jean-Paul Guthmann (InVS): refine vaccination dynamics by age class.

- Input: time evolution of the coverage by age class
- Output: the perception of r_V by age.
- Preliminary results: the perceived r_V decreases with age.

Perspectives

- Birth / deaths taken into account,
- Further structured population models: age (dynamics), geographical location,
- Model vaccine efficiency,
- Stochastic dynamics,
- impact of the societal penalty for non-vaccination; do we obtain convergence to the (societal, non individual) solution ? Still ok even for $r_V \geq r_I$?
- ...