

# Optimal Vaccination Strategies and Rational Behavior in Seasonal Epidemics

**Fabio Chalub**

P. Rodrigues, M. C. Soares, P. Doutor

Centro de Matemática e Aplicações  
Universidade Nova de Lisboa

**DSABNS 2016**  
5/2/2016



**IF INVESTIGADOR FCT**

Partially funded by UID/MAT/00297/2013 and EXPL/MAT-CAL/0794/2013

# Vaccine wars

## How it used to be



Vaccine Rebellion - Rio de Janeiro, 10-16 November 1904

# Vaccine wars

## Prevention and sceptiks

# WARNING!



## H1N1 FLU SHOT CONTAINS:

**Beta-Propiolactone: Carcinogen**

**Neomycin Sulfate: Immunotoxin**

**Polymyxin B: Neurotoxin**

**Potassium Chloride: Neurotoxin**

**Sodium Taurodeoxycholate: Carcinogen/Immunotoxin**

**Thimerosal (Mercury Derivative) : Neurotoxin**

## VACCINES ARE LINKED TO:

**Narcolepsy**

**Guillain-Barre Syndrome**

**Autism**

**Paralysis**

**Dystonia**

**Rheumatoid Arthritis**

**Multiple Sclerosis**

**Lupus**

**Cancer**

**Death**



**THE H1N1 VACCINE IS NOW BANNED IN MULTIPLE COUNTRIES!**

**THE H1N1 VACCINE'S DEVELOPERS HAVE REFUSED TO TAKE IT!**

**PROTECT YOURSELVES WITH KNOWLEDGE!**

### I'm taking a shot

for my customers

As a barista, I'd hate to pass on the flu with the coffee. So I'm taking the flu shot—to protect my customers and me.

Get the flu vaccine.

[yukonflushot.ca](http://yukonflushot.ca)



### I'm taking a shot

for your kids

As a child care worker, I don't want to pass the flu on to my kids. So I'm taking the flu shot—to protect them and me.

Get the flu vaccine.

[yukonflushot.ca](http://yukonflushot.ca)



### I'm taking a shot

for my patients

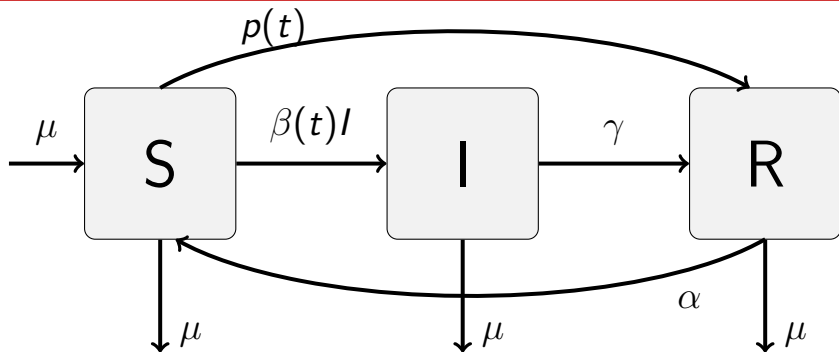
As a nurse, I'd hate for my patients to get even sicker. So I'm taking the flu shot—to protect them and me.

Get the flu vaccine.

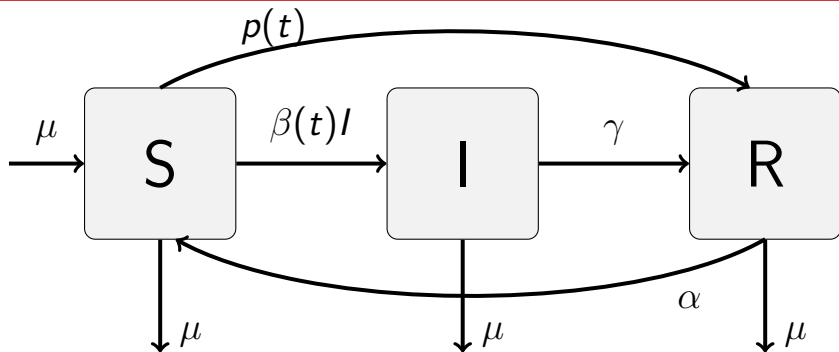
[yukonflushot.ca](http://yukonflushot.ca)



# The model



# The model

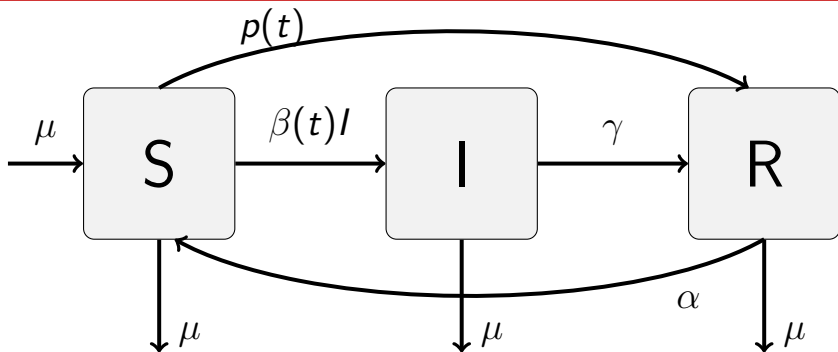


$$S' = \mu + \alpha R - \beta(t)IS - p(t)S - \mu S$$

$$I' = \beta(t)IS - \gamma I - \mu I$$

$$R' = \gamma I + p(t)S - \mu R - \alpha R$$

# The model



$$S' = \mu + \alpha R - \beta(t)IS - p(t)S - \mu S$$

$$I' = \beta(t)IS - \gamma I - \mu I$$

$$R' = \gamma I + p(t)S - \mu R - \alpha R$$

$$\begin{aligned} \beta(t+T) &= \beta(t), \quad p(t+T) = p(t). \\ \beta &\in \text{BV}([0, T]), \quad p \in \text{Radon}([0, T]) \\ \int_0^T p dt &\leq (\alpha + \mu)T \sup_{[0, T]} \beta / (\gamma + \mu) \end{aligned}$$

# Disease-free solution

## Uniqueness and a lemma

---

### Lemma

*Assume  $\beta(t + T) = \beta(t)$ ,  $p(t + T) = p(t)$ . Then, there is a unique disease-free solution  $S_0(t)$  such that  $S_0(t + T) = S_0(t)$ . All initial conditions such that  $I(0) = 0$  are attracted to this solution.*

# Disease-free solution

## Uniqueness and a lemma

### Lemma

Assume  $\beta(t + T) = \beta(t)$ ,  $p(t + T) = p(t)$ . Then, there is a unique disease-free solution  $S_0(t)$  such that  $S_0(t + T) = S_0(t)$ . All initial conditions such that  $I(0) = 0$  are attracted to this solution.

### Lemma

Consider that  $\beta(t) = \beta_0 > 0$  and  $p(t) = p_0 \geq 0$ . Then the three conditions below are equivalent:

- 1 The disease free solution  $(\hat{S}_0, 0)$  is asymptotically stable.
- 2  $\frac{\beta_0 \hat{S}_0}{\gamma + \mu} \leq 1$ .
- 3  $I' < 0$  for all  $I > 0$  and all  $S < \hat{S}_0$ .



---

Let  $\chi_p$  be the set of **preventive strategies**, i.e.,

$$\chi_p = \{p \mid I' < 0 \text{ for all } I > 0 \text{ and } S(0) < \min \hat{S}_0(t)\}.$$

We define the vaccination effort:  $\mathbb{E}[p] = T^{-1} \int_0^T p S_0[p] dt$ .

We say that a strategy  $p_{\text{opt}}$  is **optimal** if

- 1 There is a sequence  $p_n \in \chi_p$  such that  $p_n \rightarrow p_{\text{opt}}$ ;
- 2 For any strategy  $p \in \chi_p$ ,  $\mathbb{E}[p] \geq \mathbb{E}[p_{\text{opt}}]$ .

---

## Theorem

*For any  $\beta$ , there exists at least one optimal solution.*

---

## Theorem

*For any  $\beta$ , there exists at least one optimal solution.*

## Theorem

*Assume that  $\beta'(t) \geq -(\mu + \alpha)\beta(t) \left( \frac{\beta(t)}{\gamma + \mu} - 1 \right)$ . Then*

$$p_{\text{opt}}(t) = (\mu + \alpha) \left( \frac{\beta(t)}{\gamma + \mu} - 1 \right) + \frac{\beta'(t)}{\beta(t)}$$

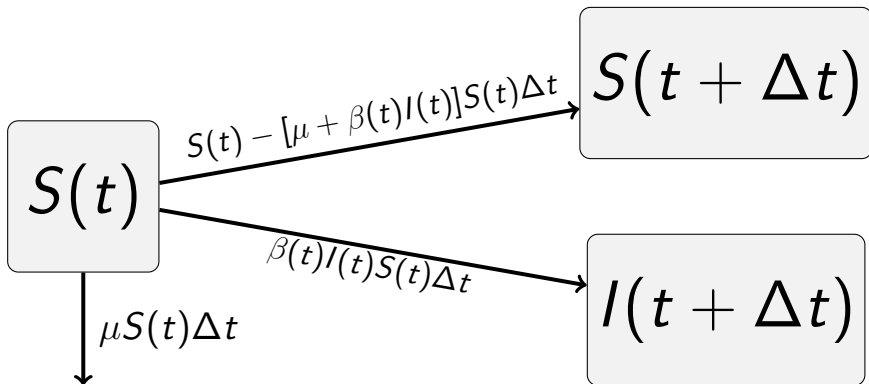
*is the optimal strategy.*

## Lemma

*At a given time  $t$  the probability that a non-vaccinated individual get the disease is given by  $\beta(t)I(t)\Delta t$ .*

## Lemma

At a given time  $t$  the probability that a non-vaccinated individual get the disease is given by  $\beta(t)I(t)\Delta t$ .



---

Let  $r := r_v/r_d$  be the ratio between the risk of the vaccination and the risk of the disease.

$p$  is a *herd immunity provider strategy* if  $\beta(t)I_1[p](t) < r$  for all  $t$ . We call  $\chi_h$  the set of herd immunity provider strategies.

A rational individual minimizes the **joint risk** of the disease and the vaccination: if  $p \in \chi_h$ , a rational individual will not be vaccinated.

---

Let  $r := r_v/r_d$  be the ratio between the risk of the vaccination and the risk of the disease.

$p$  is a *herd immunity provider strategy* if  $\beta(t)I_1[p](t) < r$  for all  $t$ . We call  $\chi_h$  the set of herd immunity provider strategies.

A rational individual minimizes the **joint risk** of the disease and the vaccination: if  $p \in \chi_h$ , a rational individual will not be vaccinated.

$$\begin{aligned}\rho[p_*, p] &= r_d \int_0^T \beta(t)I[p](t)e^{-\int_0^t(p_*+\mu)dt} dt + r_v \int_0^T \left(1 - e^{-\int_0^t(p_*+\mu)dt}\right) dt \\ &= -r_d \int_0^T (r - \beta(t)I[p](t)) e^{-\int_0^t(p_*+\mu)dt} dt + r_v T ,\end{aligned}$$

where  $p$  is the population strategy, while  $p_*$  is the strategy of the focal individual.

---

Let  $r := r_v/r_d$  be the ratio between the risk of the vaccination and the risk of the disease.

$p$  is a *herd immunity provider strategy* if  $\beta(t)I_1[p](t) < r$  for all  $t$ . We call  $\chi_h$  the set of herd immunity provider strategies.

A rational individual minimizes the **joint risk** of the disease and the vaccination: if  $p \in \chi_h$ , a rational individual will not be vaccinated.

$$\begin{aligned}\rho[p_*, p] &= r_d \int_0^T \beta(t)I[p](t)e^{-\int_0^t(p_*+\mu)dt} dt + r_v \int_0^T \left(1 - e^{-\int_0^t(p_*+\mu)dt}\right) dt \\ &= -r_d \int_0^T (r - \beta(t)I[p](t)) e^{-\int_0^t(p_*+\mu)dt} dt + r_v T ,\end{aligned}$$

where  $p$  is the population strategy, while  $p_*$  is the strategy of the focal individual. We say that  $p_{\text{Nash}}$  is a Nash-strategy if all individuals behave rationally.



---

## Theorem

*For any  $\beta$  there is a Nash strategy  $p_{\text{Nash}}$ .*

## Theorem

For any  $\beta$  there is a Nash strategy  $p_{\text{Nash}}$ .

## Theorem

Assume

$$\frac{\beta'(t)}{\beta(t)} \leq \gamma + \mu \leq \frac{\beta'(t)}{\beta(t)} + \beta(t) \quad \text{and}$$
$$\frac{d}{dt} \left[ e^{(r+\alpha-\gamma)t} \frac{d}{dt} \left( \frac{e^{(\gamma+\mu)t}}{\beta(t)} \right) \right] \leq e^{(r+\mu+\alpha)t} \left( \mu + \alpha - \frac{\alpha r}{\beta(t)} \right).$$

Then, the strategy given by

$$p_{\text{Nash}}(t) = \frac{\beta(t)^2}{(\gamma + \mu)\beta(t) - \beta'(t)} \left[ \mu + \alpha + (\gamma + \mu) \frac{\beta'(t)}{\beta(t)^2} - 2 \frac{\beta'(t)^2}{\beta(t)^3} + \frac{\beta''(t)}{\beta(t)^2} - \frac{\alpha r}{\beta(t)} \right] - [(1 - \mu)r + \mu + \alpha]$$

is one Nash-equilibrium strategy.

# Facts and comparisons

---

1  $\mathbb{E}[\rho_{\text{opt}}[\beta]] < \mathbb{E}[\rho_{\text{opt}}[\langle\beta\rangle]]$ .

# Facts and comparisons

---

- 1  $\mathbb{E}[\rho_{\text{opt}}[\beta]] < \mathbb{E}[\rho_{\text{opt}}[\langle\beta\rangle]]$ .
- 2  $\mathcal{R}_0[\rho_{\text{opt}}] \leq 1$ .

# Facts and comparisons

---

- 1  $\mathbb{E}[\rho_{\text{opt}}[\beta]] < \mathbb{E}[\rho_{\text{opt}}[\langle\beta\rangle]]$ .
- 2  $\mathcal{R}_0[\rho_{\text{opt}}] \leq 1$ .
- 3  $\mathbb{E}[\rho_{\text{opt}}] < \mu + \alpha$ .

# Facts and comparisons

---

- 1  $\mathbb{E}[\rho_{\text{opt}}[\beta]] < \mathbb{E}[\rho_{\text{opt}}[\langle\beta\rangle]]$ .
- 2  $\mathcal{R}_0[\rho_{\text{opt}}] \leq 1$ .
- 3  $\mathbb{E}[\rho_{\text{opt}}] < \mu + \alpha$ .
- 4 Assume that  $\rho_{\text{Nash}} \notin \chi_{\text{p}}$ . Then,  $\mathbb{E}[\rho_{\text{Nash}}] < \mathbb{E}[\rho_{\text{opt}}]$ .

# Facts and comparisons

---

- 1  $\mathbb{E}[\rho_{\text{opt}}[\beta]] < \mathbb{E}[\rho_{\text{opt}}[\langle\beta\rangle]]$ .
- 2  $\mathcal{R}_0[\rho_{\text{opt}}] \leq 1$ .
- 3  $\mathbb{E}[\rho_{\text{opt}}] < \mu + \alpha$ .
- 4 Assume that  $\rho_{\text{Nash}} \notin \chi_{\text{p}}$ . Then,  $\mathbb{E}[\rho_{\text{Nash}}] < \mathbb{E}[\rho_{\text{opt}}]$ .
- 5 In the conditions of the explicit formulas:  
$$\mathbb{E}[\rho_{\text{opt}}] - \mathbb{E}[\rho_{\text{Nash}}] = r(\gamma + \mu + \alpha)\langle\beta^{-1}\rangle > 0.$$

# Examples

## The constant case

---

If  $\beta < \gamma + \mu$ ,  $p_{\text{opt}} = 0$ .

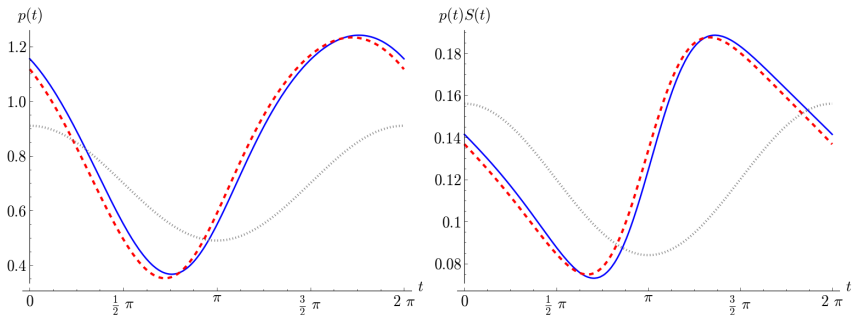
If  $\beta > \gamma + \mu$ ,

$$p_{\text{opt}} = \mu \left( \frac{\beta_0}{\gamma + \mu} - 1 \right)$$

$$p_{\text{Nash}} = \mu \left( \frac{\beta_0}{\gamma + \mu} - 1 \right) - (1 - \mu)r = p_* - (1 - \mu)r < p_{\text{opt}} .$$

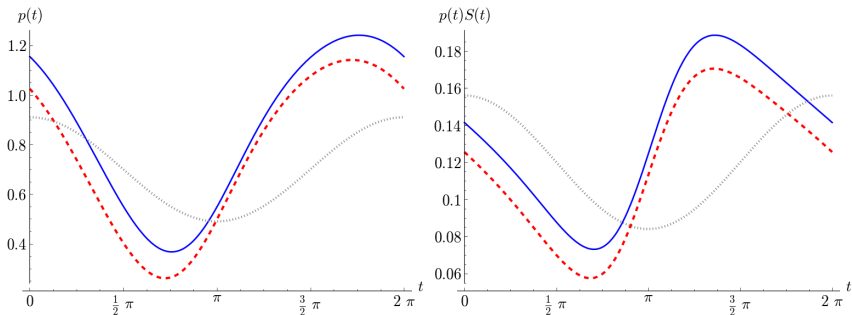


# Simulations



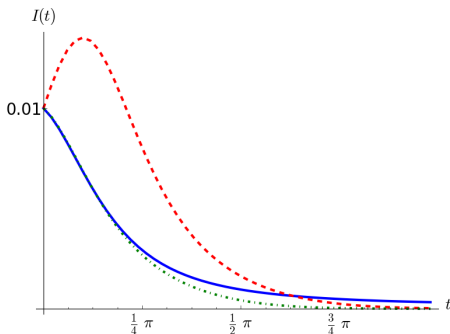
**Figure :** We use  $\mu = (80T)^{-1}$ ,  $\gamma = 52/T$ ,  $\alpha = 1/T$ , with  $T = 2\pi$ ,  $r = 0.01$  and  $\beta(t) = 52(1 + 0.3 \cos(t))$ , implying  $\frac{\gamma}{\beta_0 \alpha} = 1$ . Left:  $p_{\text{Nash}}$  (red)  $>$   $p_{\text{opt}}$  (blue) in the beginning of the epidemic season and smaller otherwise. The peak  $p_{\text{opt}}$  is  $\pi/4$  before the peak of the transmission rate; the peak of  $p_{\text{Nash}}$  is slightly before. Right: Time dependent vaccination effort, in the two cases. For simplicity, we plot in both cases  $\beta(t)$  in dark dashed line (out of scale). The choice of parameters implies that, in the absence of vaccination, there is only one stable attractor.

# Simulations



**Figure :** We use  $\mu = (80T)^{-1}$ ,  $\gamma = 52/T$ ,  $\alpha = 1/T$ , with  $T = 2\pi$ ,  $r = 0.1$  and  $\beta(t) = 52(1 + 0.3 \cos(t))$ , implying  $\frac{\gamma}{\beta_0 \alpha} = 1$ . Left:  $p_{\text{Nash}}$  (red)  $>$   $p_{\text{opt}}$  (blue) in the beginning of the epidemic season and smaller otherwise. The peak  $p_{\text{opt}}$  is  $\pi/4$  before the peak of the transmission rate; the peak of  $p_{\text{Nash}}$  is slightly before. Right: Time dependent vaccination effort, in the two cases. For simplicity, we plot in both cases  $\beta(t)$  in dark dashed line (out of scale). The choice of parameters implies that, in the absence of vaccination, there is only one stable attractor.

# Simulations



**Figure :** All parameters as before and assume initial conditions given by  $I(0) = 0.01$ . We consider three different vaccination profiles  $p_{\text{opt}}[\beta]$  (blue, continuous),  $p_{\text{opt}}[\langle \beta \rangle]$  (red, dashed) and  $p_{\text{opt}}[\text{sup } \beta]$  (green, dash-dot). Note that the optimal strategy against the average transmission rate is unable to prevent initial outbreaks (however,  $I(t) \rightarrow 0$  when  $t \rightarrow \infty$ ). Vaccination efforts  $\mathbb{E}[p_{\text{opt}}[\text{sup } \beta]] = 0.141 > \mathbb{E}[p_{\text{opt}}[\langle \beta \rangle]] = 0.135 > \mathbb{E}[p_{\text{opt}}[\beta]] = 0.133$ , respectively.

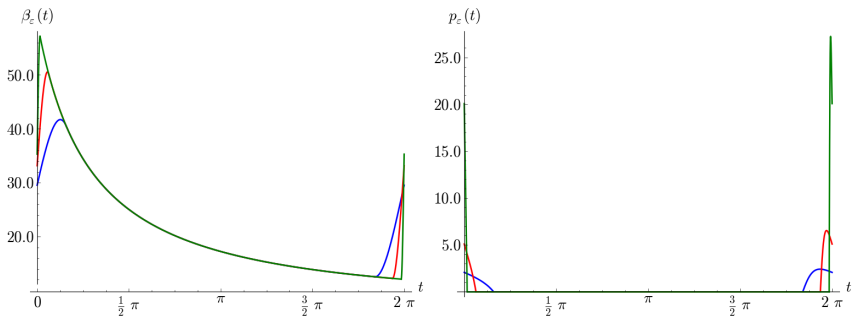


Figure :  $\beta(t) = \frac{\gamma + \mu}{1 - K \exp(-(\mu + \alpha)t)}$ ,  $t \in [0, 2\pi)$ ,  $K \in (0, 1)$ . We consider a sequence  $\beta_\varepsilon$  of differentiable functions, such that  $\beta_\varepsilon(t) = \beta(t)$  for  $t \in (\varepsilon, 2\pi - \varepsilon)$  and the points  $2\pi - \varepsilon$  and  $2\pi + \varepsilon \equiv \varepsilon$  are connected by a third order polynomial. Right: a sequence of  $p_\varepsilon := p_{\text{opt}}[\beta_\varepsilon]$ ; note that  $(p_\varepsilon)_{\varepsilon > 0}$  resembles a delta-sequence.

# Conclusions

## ... and future work

---

- 1 We considered two extreme definitions of vaccination strategies.

Further informations:

<http://arxiv.org/abs/1507.02940>

<http://ferrari.dmat.fct.unl.pt/personal/chalub/>  
[chalub@fct.unl.pt](mailto:chalub@fct.unl.pt)

# Conclusions

## ... and future work

---

- 1 We considered two extreme definitions of vaccination strategies.
- 2 Realistic vaccination scenario must fall in between.

Further informations:

<http://arxiv.org/abs/1507.02940>

<http://ferrari.dmat.fct.unl.pt/personal/chalub/>  
[chalub@fct.unl.pt](mailto:chalub@fct.unl.pt)

# Conclusions

## ... and future work

---

- 1 We considered two extreme definitions of vaccination strategies.
- 2 Realistic vaccination scenario must fall in between.
- 3 Peak vaccination are recommended for discontinuous increases in the transmission rate.

Further informations:

<http://arxiv.org/abs/1507.02940>

<http://ferrari.dmat.fct.unl.pt/personal/chalub/>  
[chalub@fct.unl.pt](mailto:chalub@fct.unl.pt)

# Conclusions

## ... and future work

---

- 1 We considered two extreme definitions of vaccination strategies.
- 2 Realistic vaccination scenario must fall in between.
- 3 Peak vaccination are recommended for discontinuous increases in the transmission rate.
- 4 Future work:

Further informations:

<http://arxiv.org/abs/1507.02940>

<http://ferrari.dmat.fct.unl.pt/personal/chalub/>  
[chalub@fct.unl.pt](mailto:chalub@fct.unl.pt)



# Conclusions

## ... and future work

---

- 1 We considered two extreme definitions of vaccination strategies.
- 2 Realistic vaccination scenario must fall in between.
- 3 Peak vaccination are recommended for discontinuous increases in the transmission rate.
- 4 Future work:
  - 1 Child diseases

Further informations:

<http://arxiv.org/abs/1507.02940>

[http://ferrari.dmat.fct.unl.pt/personal/chalub/  
chalub@fct.unl.pt](http://ferrari.dmat.fct.unl.pt/personal/chalub/chalub@fct.unl.pt)

# Conclusions

## ... and future work

---

- 1 We considered two extreme definitions of vaccination strategies.
- 2 Realistic vaccination scenario must fall in between.
- 3 Peak vaccination are recommended for discontinuous increases in the transmission rate.
- 4 Future work:
  - 1 Child diseases
  - 2 Numerical schemes

Further informations:

<http://arxiv.org/abs/1507.02940>

[http://ferrari.dmat.fct.unl.pt/personal/chalub/  
chalub@fct.unl.pt](http://ferrari.dmat.fct.unl.pt/personal/chalub/chalub@fct.unl.pt)

# Conclusions

## ... and future work

---

- 1 We considered two extreme definitions of vaccination strategies.
- 2 Realistic vaccination scenario must fall in between.
- 3 Peak vaccination are recommended for discontinuous increases in the transmission rate.
- 4 Future work:
  - 1 Child diseases
  - 2 Numerical schemes
  - 3 Ring vaccinations.

Further informations:

<http://arxiv.org/abs/1507.02940>

[http://ferrari.dmat.fct.unl.pt/personal/chalub/  
chalub@fct.unl.pt](http://ferrari.dmat.fct.unl.pt/personal/chalub/chalub@fct.unl.pt)

# Conclusions

## ... and future work

---

- 1 We considered two extreme definitions of vaccination strategies.
- 2 Realistic vaccination scenario must fall in between.
- 3 Peak vaccination are recommended for discontinuous increases in the transmission rate.
- 4 Future work:
  - 1 Child diseases
  - 2 Numerical schemes
  - 3 Ring vaccinations.

Further informations:

<http://arxiv.org/abs/1507.02940>

<http://ferrari.dmat.fct.unl.pt/personal/chalub/>  
[chalub@fct.unl.pt](mailto:chalub@fct.unl.pt)

# Thank you!