Uncertainty quantification of vaccination policies:

a model for stock management with random fluctuations.

YHG, SDIV, AMS

June 9, 2022

UNACH, CONACYT-Universidad de Sonora, Universidad de Sonora

Introduction

Motivation

Problem

CALENDARIO DE ENTREGAS (miles de personas inmunizadas):

		2021											
Laboratorio	DIC-20	ENE	FEB	MAR	ABR	MAY	JUN	JUL	AGO	SEP	OCT	NOV	DIC
1. Pfizer	125	969	969	969	969	1,875	1,875	1,875	1,875	1,425	1,425	1,425	1,425
2. CanSino	2,500	2,500	2,500	2,500	2,667	2,667	2,667	5,667	5,667	5,667			
3. COVAX(*)				2,579	2,579	2,579	2,579	2,579	2,579	2,579	2,579	2,579	2,579
4. AstraZeneca				5,000	7,870	7,870	6,270	6,450	5,240				
TOTAL	2,625	3,469	3,469	11,048	14,085	14,991	13,391	16,571	15,361	9,671	4,004	4,004	4,004

Los contratos establecidos hasta hoy permitirían la inmunización de hasta 116.69 millones de personas al término de 2021.

(*) / Pendiente de confirmación del fabricante elegido.

Argument

We argue that sufficiently large random fluctuations in deliveries—due to lags or the number of vaccines doses—convey significantly effects on the mitigation of symptomatic cases.

Aims

We pursue quantifying the uncertainty due to time lags or amount delivery, and evaluates its implications.

Introduction

Methodology

Methodology

Given a shipment of vaccines calendar, describe the stock management with backup protocol and quantify random fluctuations due to schedule or quantity. Then plug this dynamic with an ODE system that describes the disease and evaluates its response accordingly.

Vaccine Shipment Program

As part of the COVID-19 vaccination campaign, on December 02, 2020, the Mexican government annunciated a delivery plan of vaccines by Pfizer-BioNTech and other firms.

Vaccine Shipment Program

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Outline

Toy example and classic vaccination OC

To fix ideas:

$$
\begin{aligned}
S'(t) &= -\beta IS \\
I'(t) &= \beta IS - \gamma I \\
R'(t) &= \gamma I
\end{aligned}
$$

$$S(0) = S_0, I(0) = I_0, R(0) = 0$$

$$S(t) + I(t) + R(t) = 1$$

“Classic” Vaccination

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Toy example and classic vaccination OC

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"Classic" Vaccination

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With vaccination

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\begin{aligned}
S'(t) &= -\beta IS - \lambda_V(t) \\
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“Classic” Vaccination

- Gumel,

$$\lambda_V := \underbrace{\xi}_{cte.} \cdot S(t)$$

Alexander, M. E., Bowman, C., Moghadas, S. M., Summers, R., Gumel, A. B., and Sahai, B. M. (2004). **A vaccination model for transmission dynamics of influenza.** *SIAM Journal on Applied Dynamical Systems*, 3(4):503–524.

Iboi, E. A., Ngonghala, C. N., and Gumel, A. B. (2020).

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Optimal Controlled:

Hethcote, H. W. and Waltman, P. (1973). **Optimal vaccination schedules in a deterministic epidemic model.** *Mathematical Biosciences*, 18(3-4):365–381.

Wickwire, K. (1977). **Mathematical models for the control of pests and infectious diseases: A survey.** *Theoretical Population Biology*, 11(2):182–238.

Hypothesis

Cost: The **effort** expended in "**preventing-mitigating** an epidemic" by vaccination is **proportional** to the vaccination rate λ_V.

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Jabs Counter: If $S(0) \approx 1$, $X(\cdot)$: counts vaccine doses, then

$$X(t) = 1 - \exp(-\lambda_V t),$$

estimates the fraction of vaccinated individuals. Thus, for time horizon T and vaccination coverage

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Given X_{cov}, T

$$\lambda_V = -\frac{1}{T}\ln(1 - X_{cov})$$

estimates the constant vaccination rate s.t., after time T, we reach X_{cov}.

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X_{COV} : 70%, T: one year

$\lambda_V \approx 0.00329$

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If $S(0)N$ corresponds to HMS (812 229 inhabitants) ≈ 2668 jabs/day.

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How to optimize vaccination?

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Common Objectives

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Common Objectives

- Who to vaccine first? (Allocation)
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- Who to vaccine first? (Allocation)
- How and when? (Administration)

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Vaccine optimiztion for COVID-19

Common Objectives

- Who to vaccine first? (Allocation)

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Cost

Vaccine optimiztion for COVID-19

Common Objectives

- Who to vaccine first? (Allocation)
- How and when? (Administration)

Cost

$$J(u) := \varphi(x(T)) + \int_0^T f(t, x(t), u(t))$$

Vaccine optimiztion for COVID-19

Common Objectives

- Who to vaccine first? (Allocation)
- How and when? (Administration)

Optimal Control Problem

$$\min_{\mathbf{u}\in\mathscr{U}} J(u) = \varphi(x(T)) + \int_0^T f(t, x(t), u(t))$$

$$\dot{x}(t) = b(t, u(t), x(t)), \quad \text{a.e. } t \in [0, T].$$

Vaccine optimiztion for COVID-19

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Bubar, K. M., Reinholt, K., Kissler, S. M., Lipsitch, M., Cobey, S., Grad, Y. H., and Larremore, D. B. (2021).
Model-informed covid-19 vaccine prioritization strategies by age and serostatus.
Science, 371(6532):916–921.

Matrajt, L., Eaton, J., Leung, T., and Brown, E. R. (2020).
Vaccine optimization for covid-19: Who to vaccinate first?
Science Advances, 7(6).

Vaccine optimiztion for COVID-19

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Common Objectives

- Who to vaccine first? (Allocation)
- How and when? **(Administration)**

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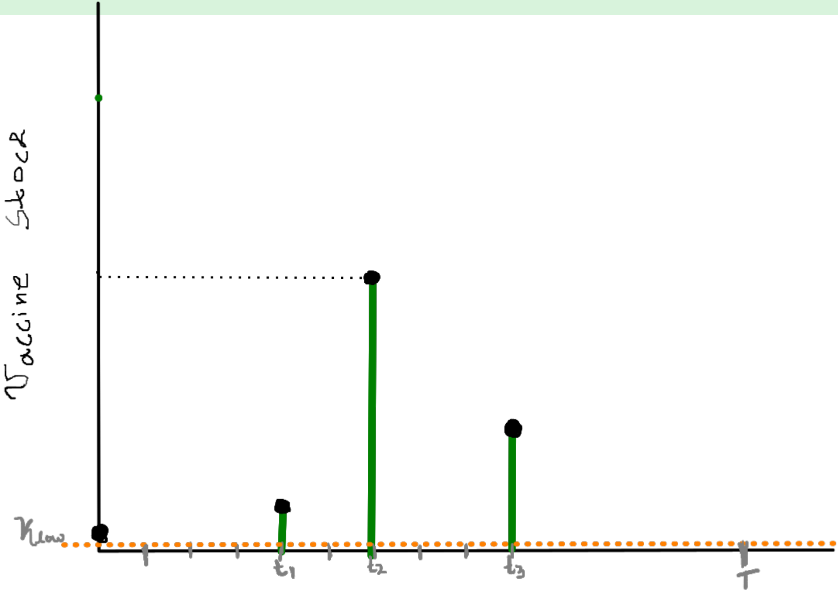

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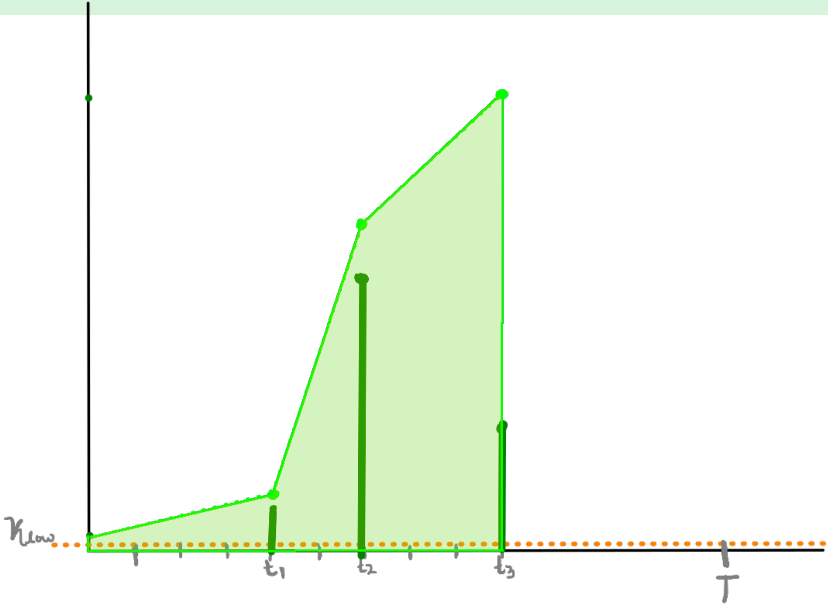

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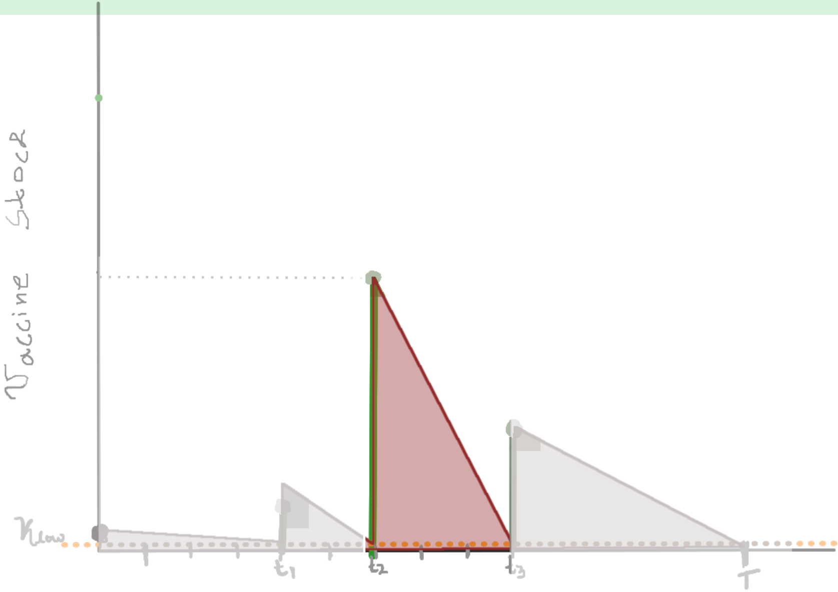

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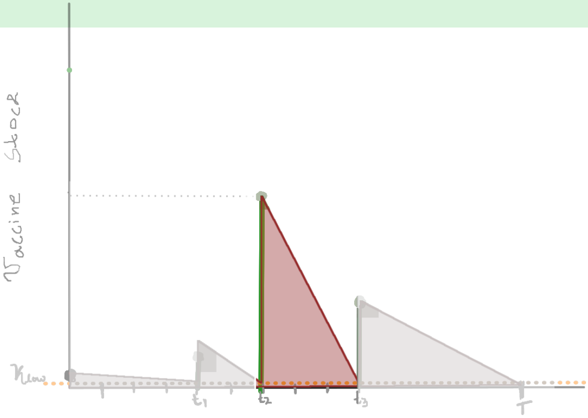

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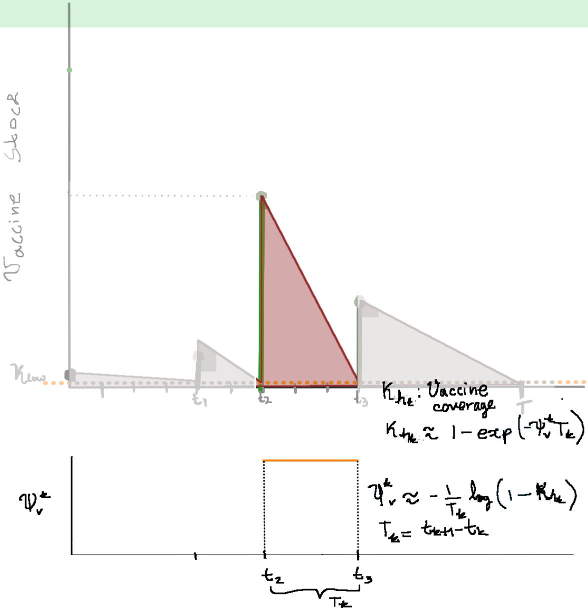
Vaccine Stock
K_{low}
t_1
t_2
t_3
T
K_{t_k}: Vaccine coverage
$K_{t_k} \approx 1 - \exp(-\psi_v^k T_k)$
ψ_v^k
$\psi_v^k \approx -\frac{1}{T_k} \log(1 - K_{t_k})$
$T_k = t_{k+1} - t_k$
t_2
t_3
T_k

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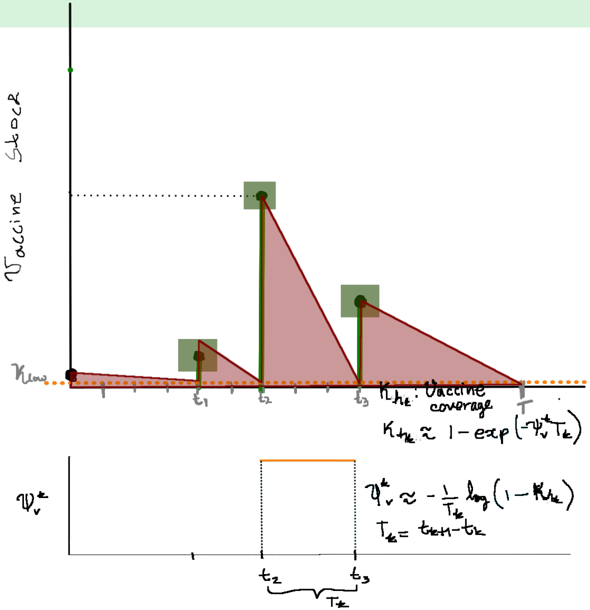
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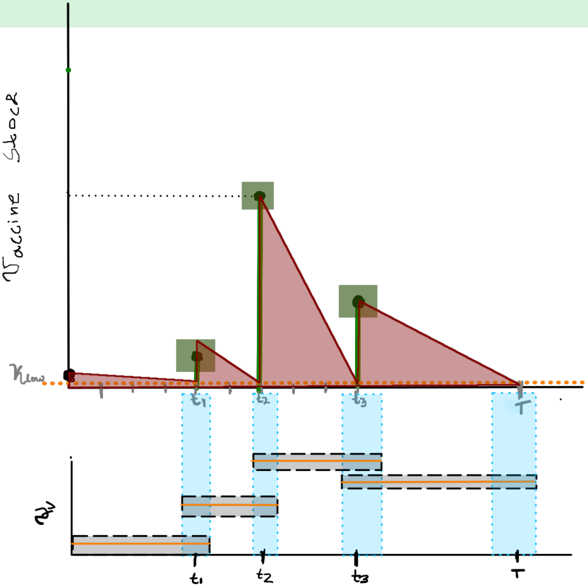

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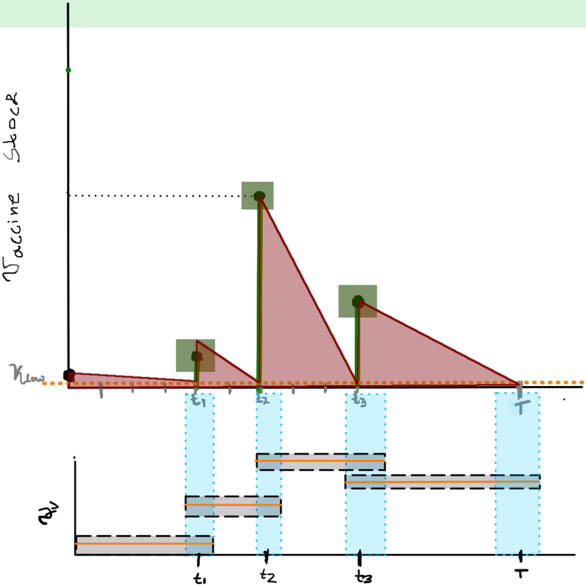

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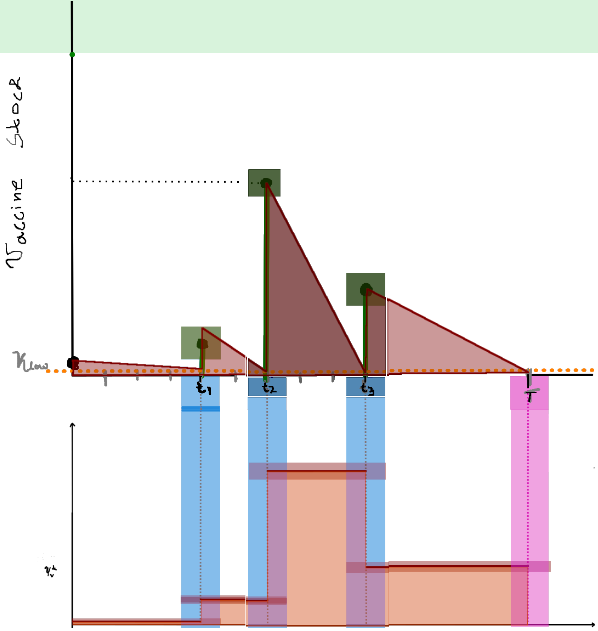

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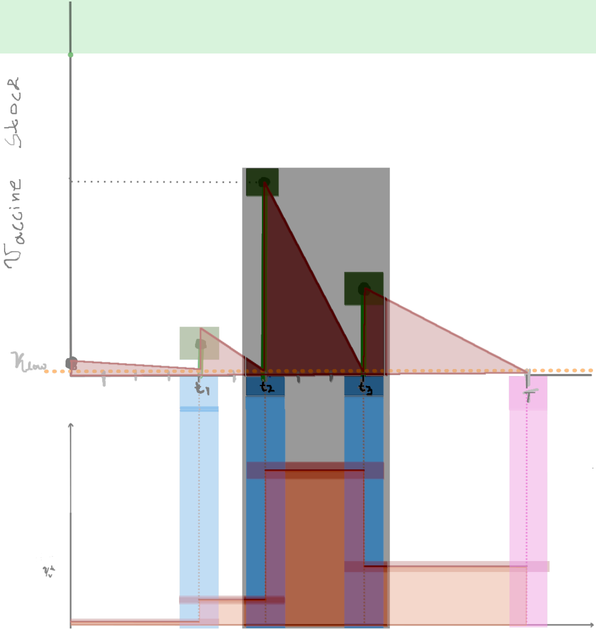
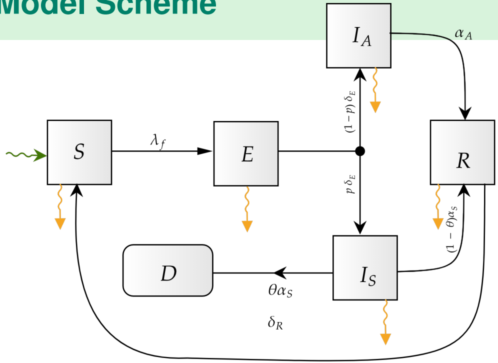


Model Scheme



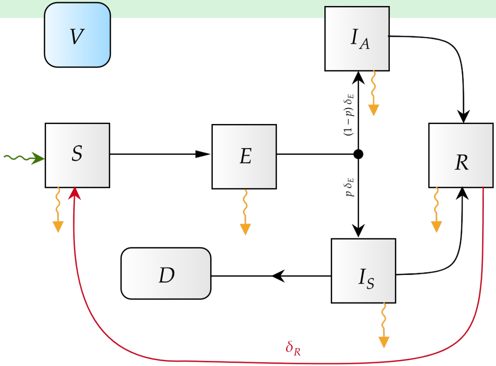
$$\lambda_f := \frac{\beta_A I_A + \beta_S I_S}{N^*}$$

$$N^* := N - D$$

natality

natural death

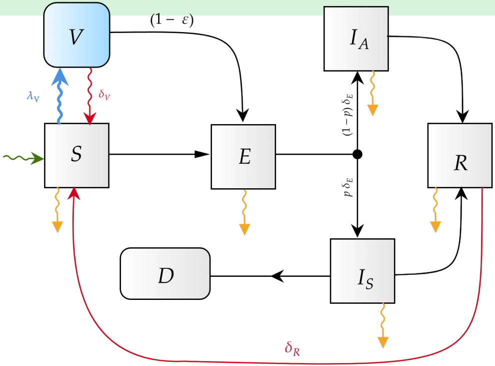
Model Scheme



Vaccine Hypotheses

- Imperfect preventive
- One dose
- Symptomatic exception
- Action over susceptible

Model Scheme



λ_V : vaccination rate

immunity periods

$\frac{1}{\delta_V}$: vaccine-induced

$\frac{1}{\delta_R}$: natural

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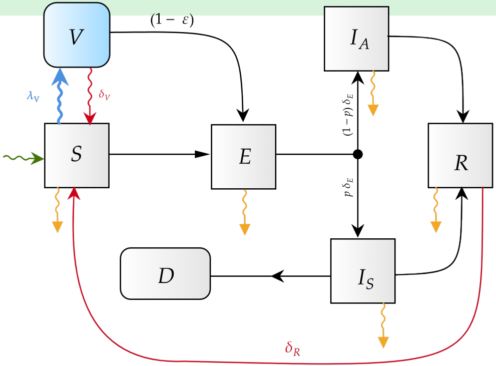

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ε	vaccine efficacy
p	Generation of symptoms probability

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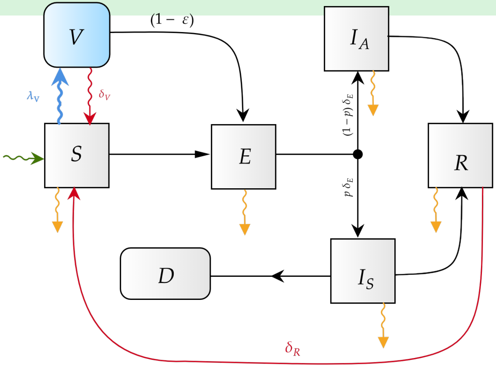

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- Vaccine profile (Efficacy, immunity)
- Coverage
- Time Horizon

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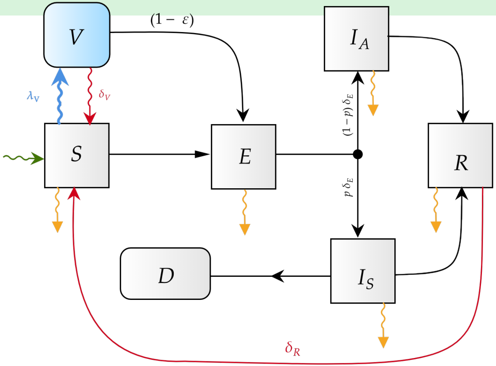

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Immunity:

- natural (reinfection)
- vaccine-induced

$$
\begin{aligned}
\frac{dS}{dt} &= \mu \widehat{N} - (\lambda_f + \mu + \psi_V) S + \omega_V V + \delta_R R \\
\frac{dE}{dt} &= \lambda_f S + (1-\varepsilon) V - (\mu + \delta_E) E \\
\frac{dI_S}{dt} &= p \delta_E E - (\mu + \alpha_S) I_S \\
\frac{dI_A}{dt} &= (1-p) \delta_E E - (\mu + \alpha_A) I_A \\
\frac{dR}{dt} &= (1-\theta) \alpha_S I_S + \alpha_A I_A - (\mu + \delta_R) R \\
\frac{dD}{dt} &= \theta \alpha_S I_S \\
\frac{dV}{dt} &= \psi_V S - \left[(1-\varepsilon)\lambda_f + \mu + \omega_V\right] V \\
X'_{vac} &= \psi_V (S + E + I_A + R) \\
\widehat{N} &= S + E + I_A + I_S + R, \quad \widehat{N} + D = 1 \\
\lambda_f &:= \frac{\beta_S I_S + \beta_A I_A}{\widehat{N}}
\end{aligned}
$$

Nonstandard Finite Differences: Dynamic consistency

We study the evolution of SEIR - mitigation model between deliveries.Consider for each time sub-interval k a grid time N_k partition of sub-interval $[t_*^{(k)}, t^{*(k)}]$,

$$h_k := \frac{t^{*(k)} - t_*^{(k)}}{N_k}.$$

If $t_n^{(k)}$ denotes the time of the n step SEIR model for the k sub-interval, then

$$t_n^{(k)} = nh_k \in [t_*^{(k)}, t^{*(k)}], \qquad k = 1, \ldots, K.$$

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Jódar, L., Villanueva, R. J., Arenas, A. J., and González, G. C. (2008).
Nonstandard numerical methods for a mathematical model for influenza disease.
Mathematics and Computers in Simulation, 79(3):622–633.

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Also, we use an adaptive functional discretization

$$\varphi(h) := h + \mathscr{O}(h^2)$$
$$\varphi(h) = \frac{1 - \exp(-h)}{h}$$

$$\frac{S^{n+1}-S^{n}}{\varphi(h)} = \mu\widehat{N}^{n} - (\lambda_f + \varphi_V^{(k)})S^{n+1} - \mu S^{n} + \omega_V V^{n} + \delta_R R^{n}$$

$$S^{n+1} = \varphi(h)[\mu\widehat{N}^{n} - (\lambda_f + \varphi_V^{(k)})S^{n+1} - \mu S^{n} + \omega_V V^{n} + \delta_R R^{n}] + S^{n}$$

$$S^{n+1} = \frac{(1-\varphi(h)\mu)S^{n} + \varphi(h)\mu\widehat{N}^{n} + \varphi(h)[\omega_V V^{n} + \delta_R R^{n}]}{(1+\varphi(h))(\lambda_f + \Psi_V^{(k)})}$$

Discrete Model

$$S^{n+1} = \frac{(1-\varphi(h)\mu)S^n + \varphi(h)\mu\widehat{N}^n + \varphi(h)[\omega_V V^n + \delta_R R^n]}{(1+\varphi(h))(\lambda_f + \Psi_V^{(k)})}$$

$$E^{n+1} = \frac{(1-\mu\varphi(h))E^n + \varphi(h)\lambda_f[S^{n+1} + (1-\varepsilon)V^n]}{(1+\varphi(h)\delta_E)}$$

$$I_S^{n+1} = \frac{(1-\varphi(h)\mu)I_S^n + \varphi(h)p\delta_E E^{n+1}}{1+\varphi(h)\alpha_S}$$

$$\vdots$$

$$V^{n+1} = V^n(1-\varphi(h)[(1-\varepsilon)\lambda_f + \mu + \omega_V]) + \varphi(h)(\psi_V^{(k)})S^{n+1}$$

$$X_{vac}^{n+1} = \varphi(h)\psi_V^{(k)}(S^n + E^n + I_A^n + R^n) + X_{vac}^n$$

$$K^{n+1} = \max\{0, K^n - (X_{vac}^{n+1} - X_k^0 - L)\}$$

$$DALY(c,s,a,t) = YLL(c,s,a,t) + YLD(c,s,a,t)$$

For given cause c, age a, sex s and year t

YLL : Years of life lost due to premature death.

$$YLL(c,s,a,t) = N(c,s,a,t) \times L(s,a)$$

- $N(c,s,a,t)$: is the number of deaths due to the cause c
- $L(s,a)$: is a standard loss function specifying years of life lost

YLD : Years of life list due to disability

$$YLD(c,s,a,t) = I(c,s,a,t) \times DW(c,s,a) \times L(c,s,a,t)$$

- $I(c,s,a,t)$: number of incident cases for cause c
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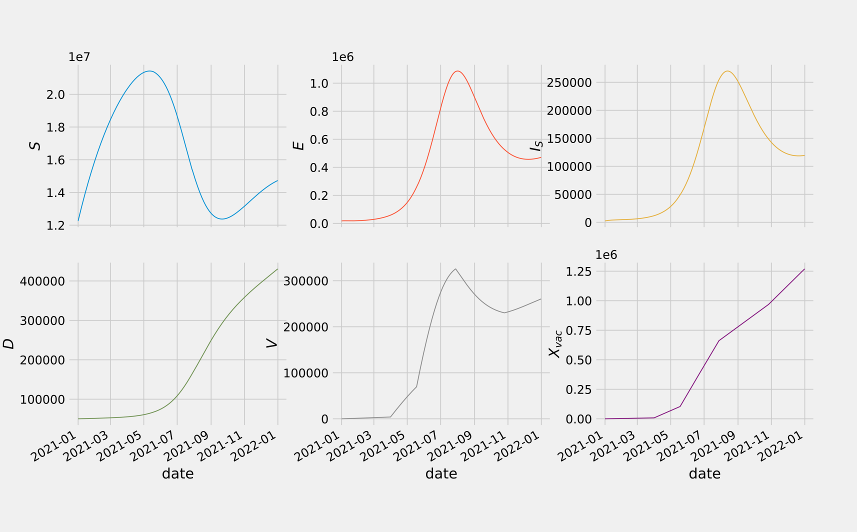
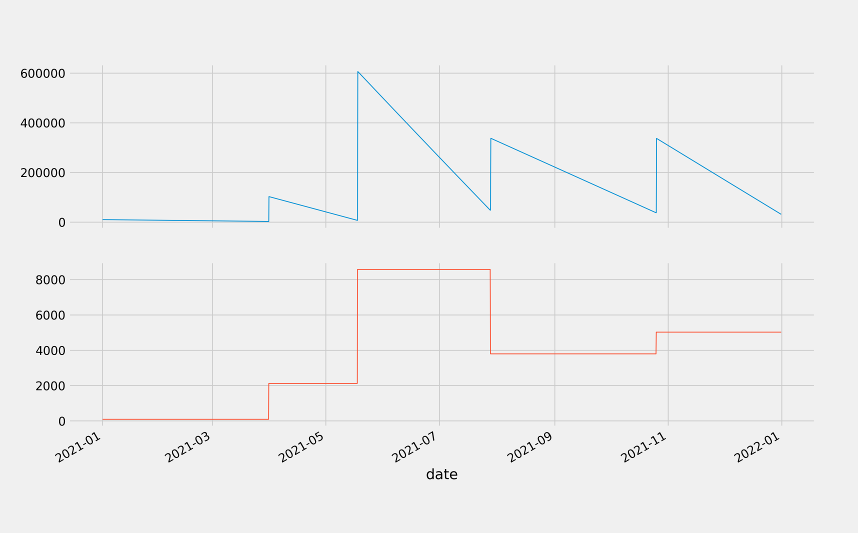
$$

$$
\begin{aligned}
a_V &:= \{a_{t_0}, a_{t_1}, \cdots, a_{t_K}\} \\
a_{t_k} &:= p_k \Psi_V^k, \\
s.t. &\quad \{\text{Stock constrains}\}
\end{aligned}
$$

Results: deterministic controlled dynamics



Results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8000
6000
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2000
0
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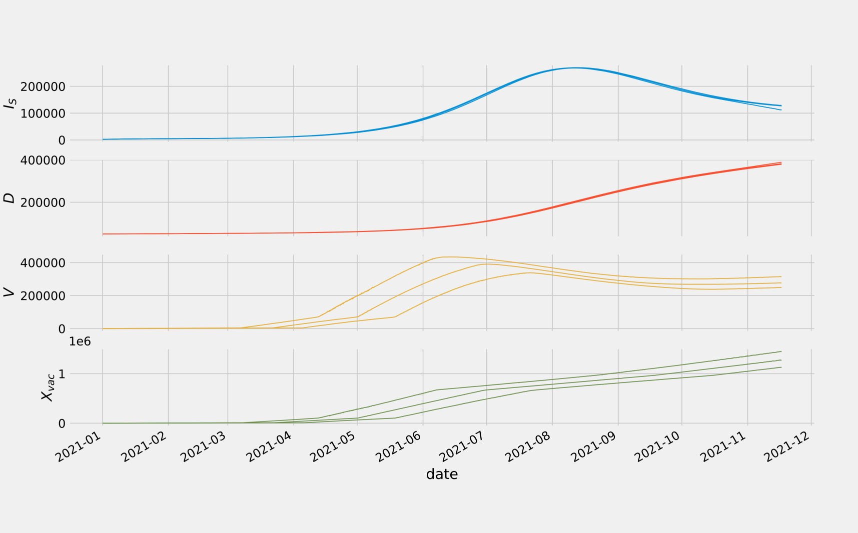
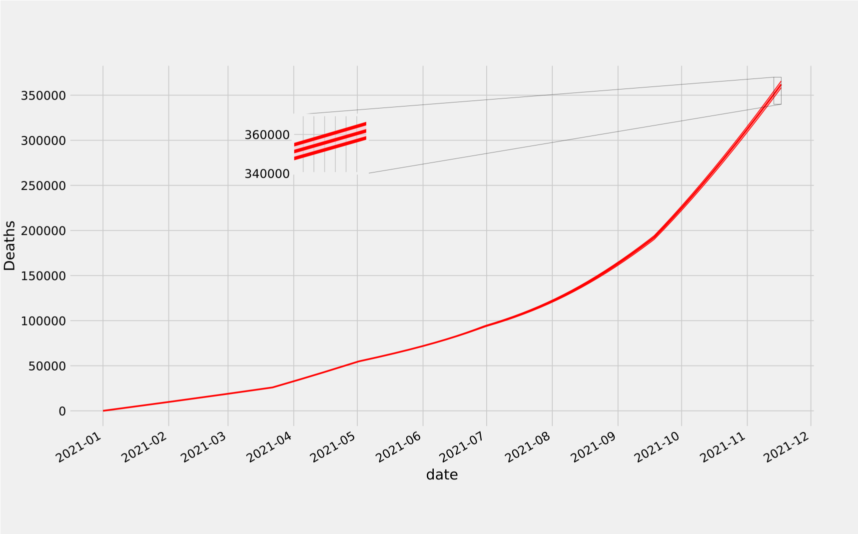
2021-03
2021-05
2021-07
2021-09
2021-11
2022-01
date

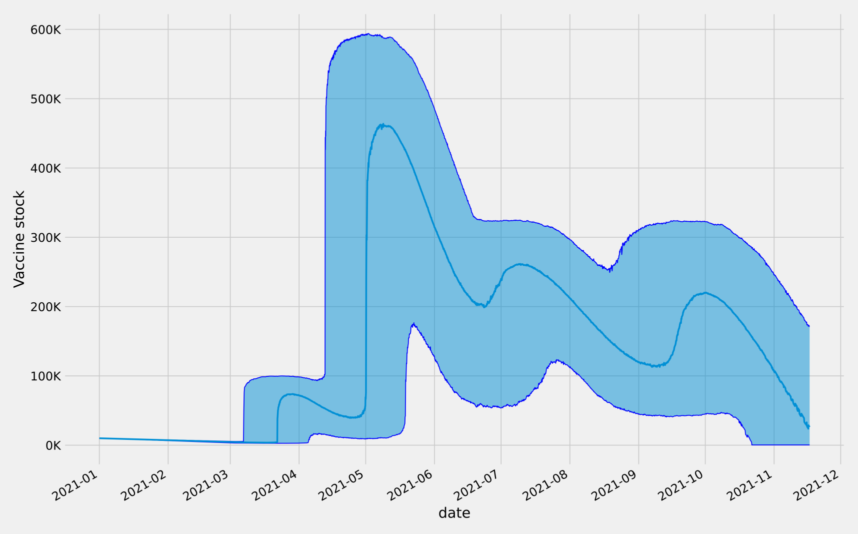
Results: stochatic dynamics



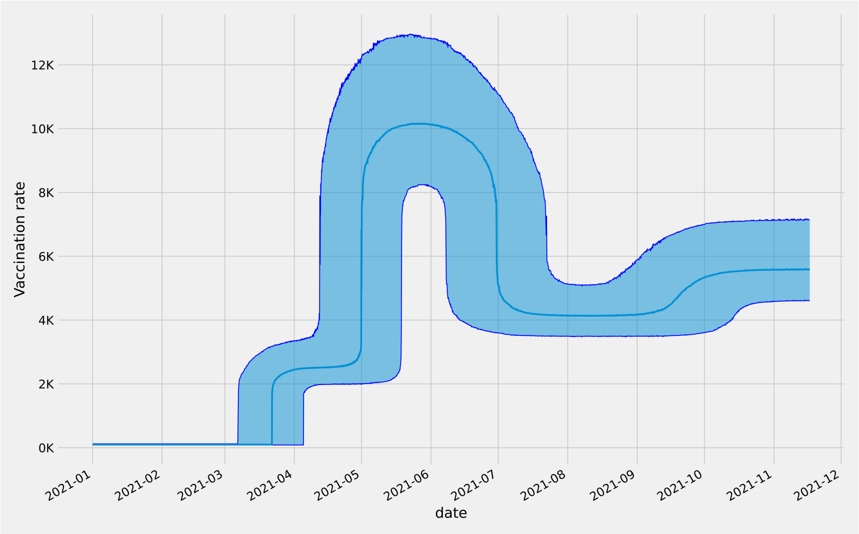
Results: stochatic dynamics



Results: Stcok CI



Results: Actions (vaccination rate) CI



Motivation

Methodology

Model Formulation on continuous time

Non standar discrete approximation

Numeric Results

TODO list

TODO List

- To describe fluctuations due to the uncertainty of vaccine immunity by a mean reversible process.

$$d\Psi_V(t) = r_k(\Psi_V^K - \Psi_V(t))dt + \sigma\sqrt{\Psi_V(t)}dW$$

- Propose a cost functional (DALYs, Risk, R_t)
- Optimize in a convenient space of actions.
- Partially observable models
- Stochastic GAMES

GRACIAS!!

Git Hub