Uncertainty quantification of vaccination policies:

a model for stock management with random fluctuations.

YHG, SDIV, AMS

June 11, 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 vaccine doses—convey significant 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

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 a ODE systeme to describe a disease and evalute its response accordingly.

Vaccine Shipment Program

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Motivation

Methodology

Model Formulation on continuous time

Non standar discrete approximation

Numeric Results

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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With vaccination

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"Classic" Vaccination

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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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$\lambda_V \approx 0.003\,29$

If $S(0)N$ corresponds to HMS (812 229 inhabitants) $\approx 2668\,\text{jabs}/\text{day}$.

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How to optimize vaccination?

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Common Objectives

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-

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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

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- 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

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

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

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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).

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- How and when? **(Administration)**

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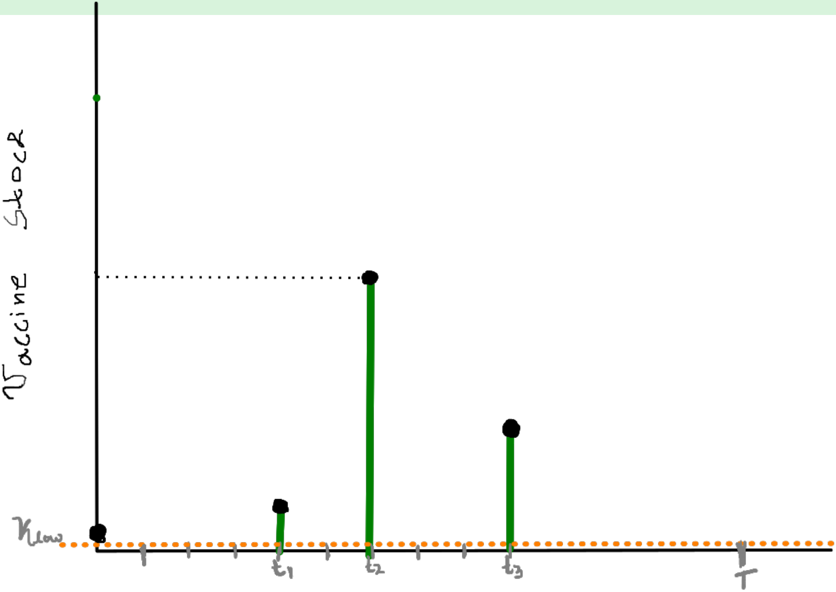

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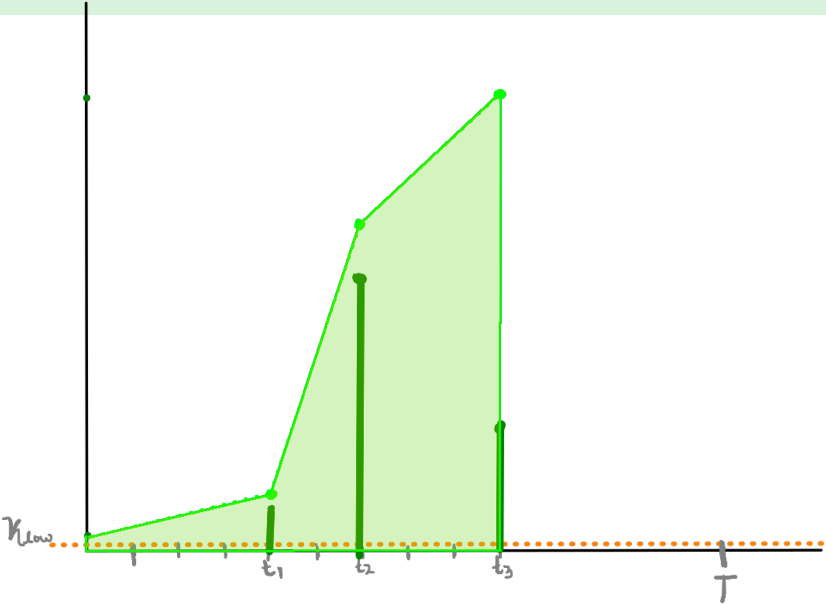

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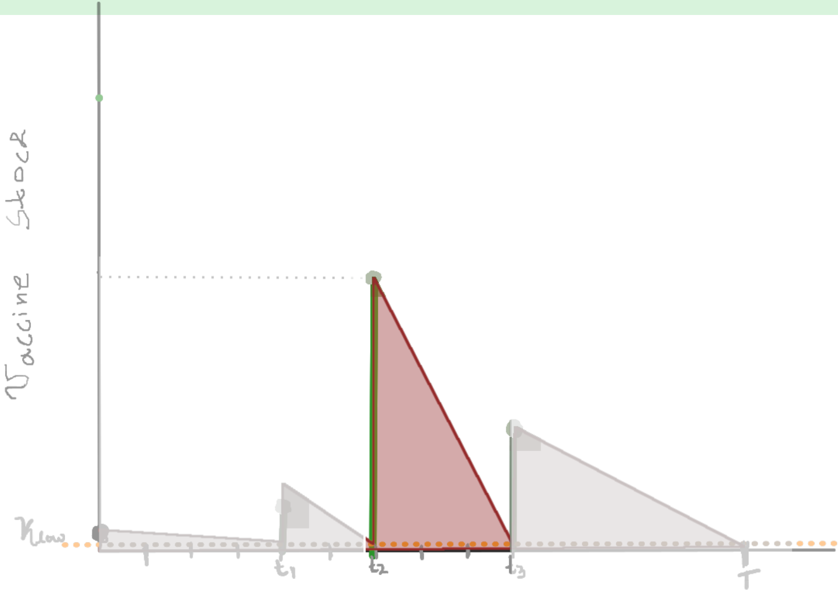

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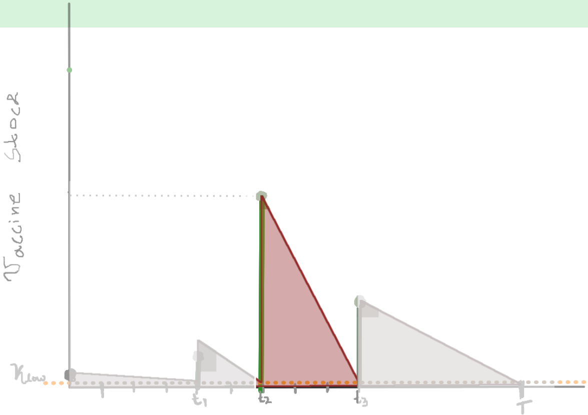

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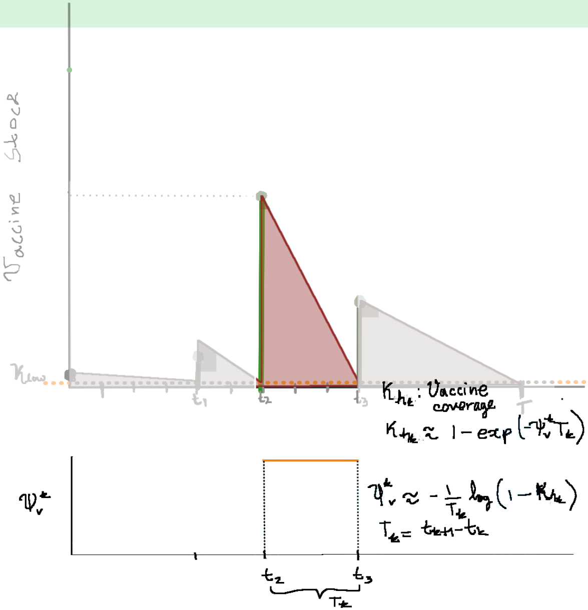
Vaccine Stock
K_{low}
t_1
t_2
t_3
T
K_{t_k}: Vaccine coverage
$K_{t_k} \approx 1 - \exp(-\psi_v^k T_k)$
ψ_v^k
$\psi_v^k \approx -\frac{1}{T_k} \log(1 - K_{t_k})$
$T_k = t_{k+1} - t_k$
t_2
t_3
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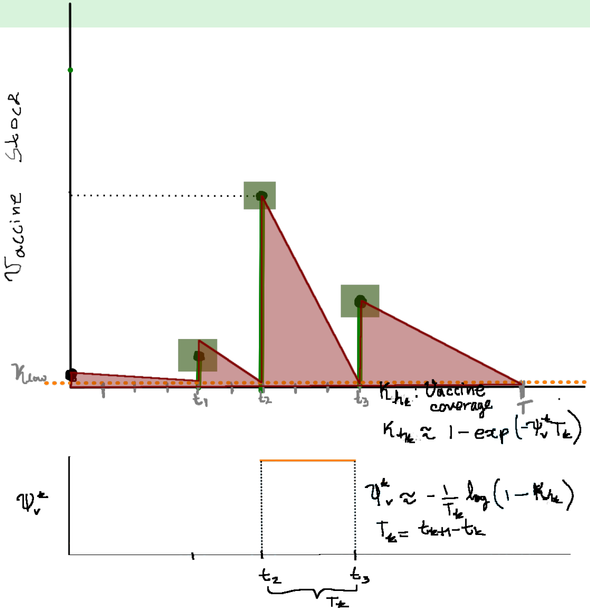
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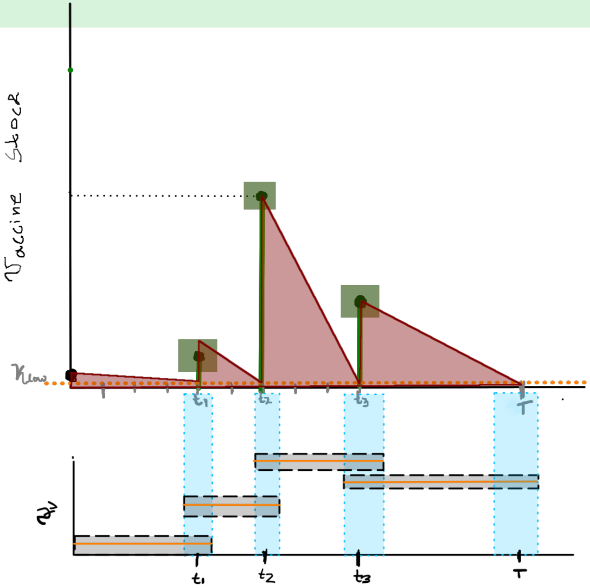

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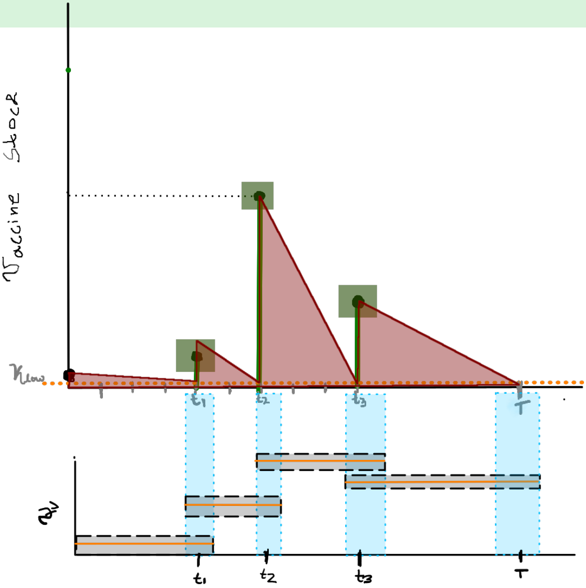

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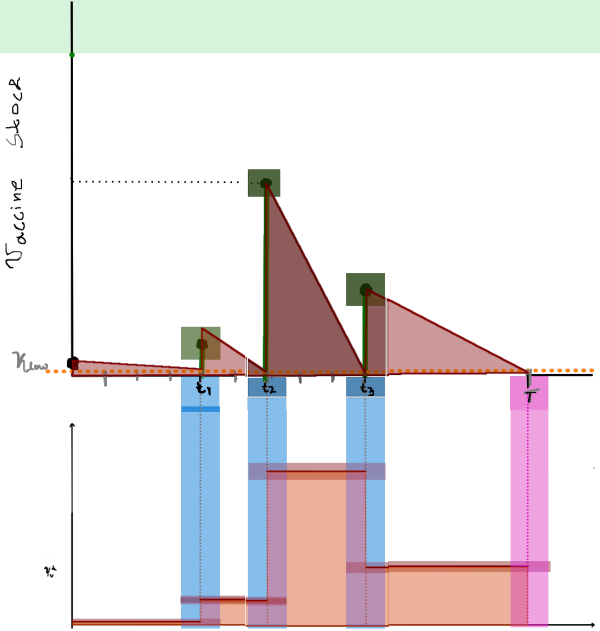

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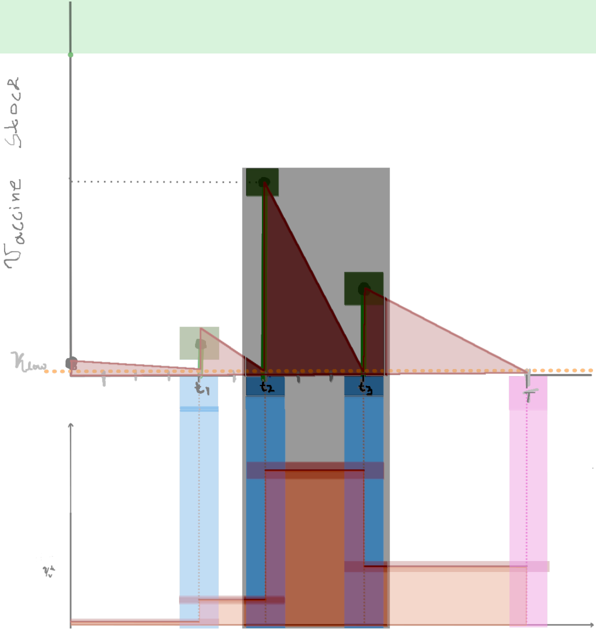
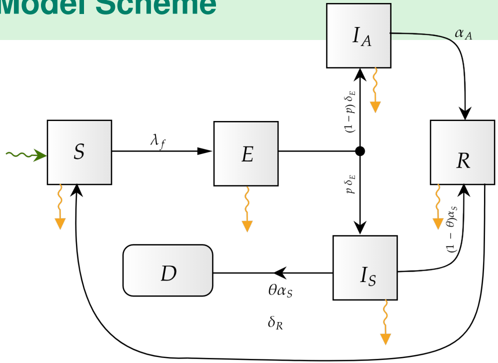


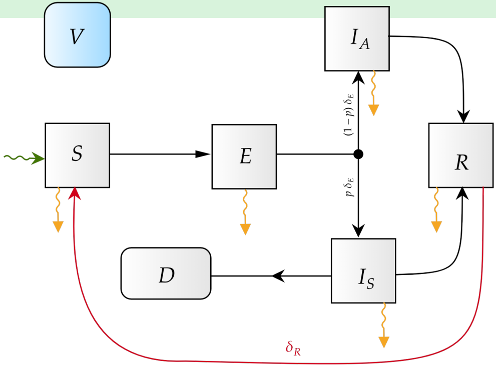
Model Scheme



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

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

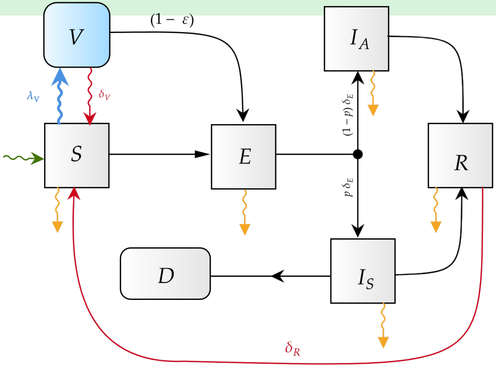
Model Scheme



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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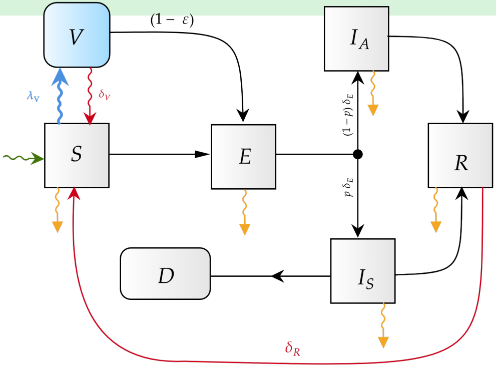

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ε	vaccine efficacy
p	Generation of symptoms probability

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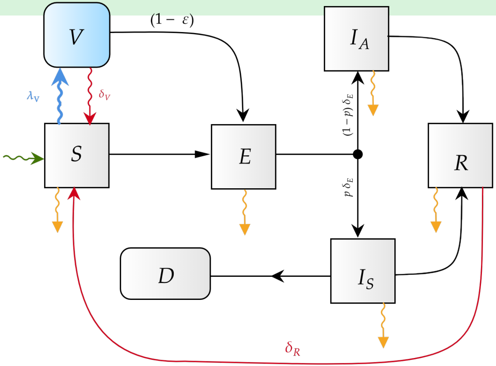

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- Vaccine profile (Efficacy, immunity)
- Coverage
- Time Horizon

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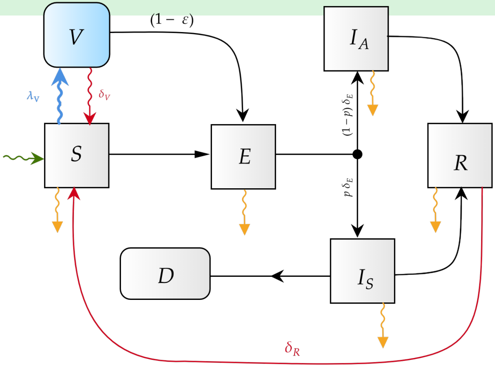

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Immunity:

- natural (reinfection)
- vaccine-induced

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

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

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

Also, we use an adaptive functional discretization

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

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

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

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

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
- $DW(c,s,a)$: disability weight for cause c
- $L(c,s,a,t)$: average duration of the case

Int

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$$\min_{a_V \in \mathscr{U}[0,T]} J(a_t) :=$$

$$a_t := p_k \Psi^k,$$

$$s.t. \{\text{Stock constrains}\}$$

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$$\min_{a_V \in \mathscr{U}[0,T]} J(a_t) := \underbrace{a_D(D(T) - D(0))}_{:=YLL} + \underbrace{a_S(Y_{I_S}(T) - Y_{I_S}(0))}_{:=YLD}$$

$$a_t := p_k \Psi^k,$$

$$s.t.\{\text{Stock constrains}\}$$

Motivation

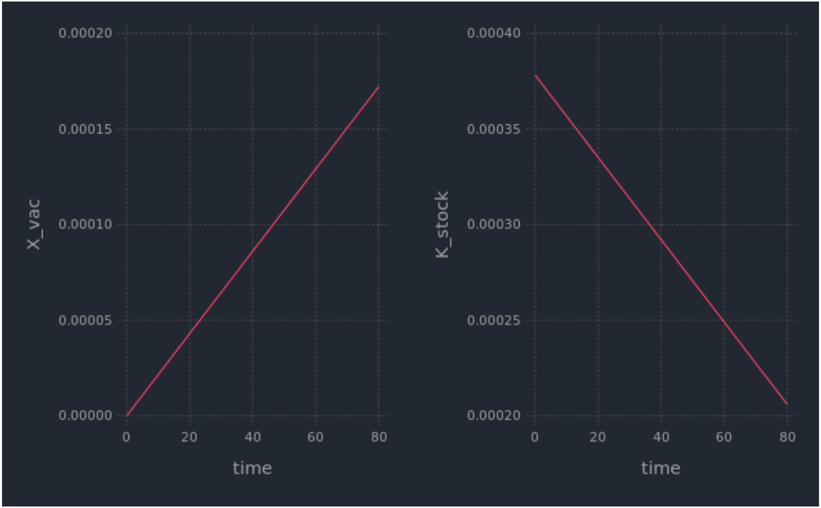
Methodology

Model Formulation on continuous time

Non standar discrete approximation

Numeric Results

Results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0.00010
0.00005
0.00000
0
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40
60
80
time
K_stock
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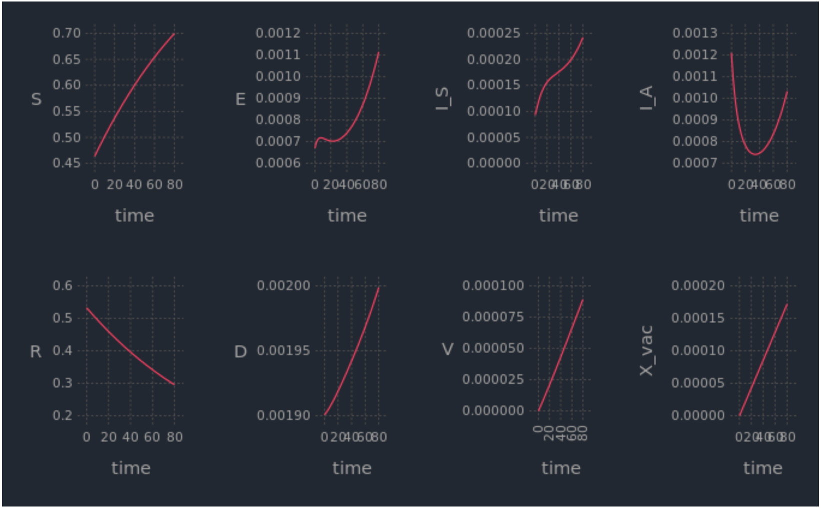
0.00035
0.00030
0.00025
0.00020
0
20
40
60
80
time

Results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0.60
0.55
0.50
0.45
0 20 40 60 80
time
E
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0.0011
0.0010
0.0009
0.0008
0.0007
0.0006
time
I_S
0.00025
0.00020
0.00015
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0.0013
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0.0008
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time
R
0.6
0.5
0.4
0.3
0.2
0 20 40 60 80
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D
0.00200
0.00195
0.00190
time
V
0.000100
0.000075
0.000050
0.000025
0.000000
time
X_vac
0.00020
0.00015
0.00010
0.00005
0.00000
time

Outline

Motivation

Methodology